EFFECTS OF BODY ADIPOSITY INDICES, DIGIT RATIO AND LEVEL OF PHYSICAL ACTIVITY ON METABOLIC SYNDROME AND SERUM BIOMARKERS AMONG THE HAUSAS OF KANO STATE, NIGERIA

BY

Asuku Yusuf ABDULLAHI
(MBBS BUK, 2009, M.Sc. BUK, 2015)

DEPARTMENT OF HUMAN ANATOMY, FACULTY OF BASIC MEDICAL SCIENCES, AHMADU BELLO UNIVERSITY, ZARIA, NIGERIA

JUNE, 2018

EFFECTS OF BODY ADIPOSITY INDICES, DIGIT RATIO AND LEVEL OF PHYSICAL ACTIVITY ON METABOLIC SYNDROME AND SERUM BIOMARKERS AMONG THE HAUSAS OF KANO STATE, NIGERIA

BY

Asuku Yusuf ABDULLAHI
(MBBS BUK, 2009, M.Sc. BUK, 2015)
P15MDHA9006

A THESIS SUBMITTED TO THE SCHOOL OF POSTGRADUATE STUDIES AHMADU BELLO UNIVERSITY, ZARIA

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF DOCTOR OF PHILOSOPHY DEGREE IN HUMAN ANATOMY

DEPARTMENT OF HUMAN ANATOMY, FACULTY OF BASIC MEDICAL SCIENCES, AHMADU BELLO UNIVERSITY, ZARIA, NIGERIA

JUNE, 2018

DECLARATION

I, Asuku Yusuf ABDULLAHI hereby declare that the work in this thesis titled "***Effects of Body Adiposity Indices, Digit Ratio and Level of Physical Activity on Metabolic Syndrome and Serum Biomarkers among Hausas of Kano State, Nigeria***" was performed by me in the department of Human Anatomy, Faculty of Basic Medical Sciences, ABU, Zaria, under the supervision of Dr. B. Danborno, Prof. S. A. Akuyam and Dr. J.A. Timbuak. The information derived from the literature has been duly acknowledged in the text and a list of references provided. No part of this work has been presented for another degree at any institution.

Asuku Yusuf ABDULLAHI _____ _____

Signature Date

CERTIFICATION

This thesis entitled "***Effects of Body Adiposity Indices, Digit Ratio and Level of Physical Activity on Metabolic Syndrome and Serum Biomarkers among Hausas of Kano State, Nigeria***" by Asuku Yusuf ABDULLAHI meet the regulation governing the award of Doctor of Philosophy (Ph.D) degree in Department of Human Anatomy, Faculty of Basic Medical Sciences, Ahmadu Bello University, Zaria, under the supervision of Dr. B. Danborno, Prof. S. A. Akuyam and Dr. J.A. Timbuak. It is therefore approved for its contribution to knowledge and literary presentation.

Dr. B. Danborno(B.Sc., M.Sc., Ph.D) _____ _____
Chairman, Supervisory Committee Signature Date
Department of Human Anatomy,
Faculty of Basic Medical Sciences,
Ahmadu Bello University, Zaria

Prof. S. A. Akuyam
(B.Sc., M.Sc., PhD., FMLSCN., PGDE**)**_____ _____
Member, Supervisory Committee Signature Date
Department of Chemical Pathology,
Faculty of Basic Medical Sciences,
Ahmadu Bello University, Zaria

Dr. J.A. Timbuak (B.Sc., M.Sc., Ph.D) _____ _____
Member, Supervisory Committee Signature Date
Department of Human Anatomy,
Faculty of Basic Medical Sciences,
Ahmadu Bello University, Zaria

Dr. Z. M. Bauchi(B.Sc., M.Sc., Ph.D) _____ _____
Head, Department of Human Anatomy, Signature Date
Faculty of Basic Medical Sciences,
Ahmadu Bello University, Zaria

Prof S. Z. Abubakar (B. Eng., M.Sc., Ph.D) _____ _____
Dean, School of Postgraduate Studies, Signature Date
Ahmadu Bello University, Zaria

DEDICATION

I dedicate this work to my late sisters Hauwa Abdullahi and Barrister Maryam Abdullahi.

ACKNOWLEDGEMENT

All praises and glorifications are due to Allah, the originator, sustainer and cherisher of all that exist in the heavens and the earth and by whose decree all good works are accomplished.

I shall remain thankful and indebted to my supervisors Dr. B. Danborno, Prof. S. A Akuyam and Dr. J.A. Timbuak for their mentorship, guidance, valid, objective and constructive criticism in the course of this work. Simply put, their role was that of a Teacher and a Father. The conceptualization of the idea of the research, its conduction and completion would not have been possible without your guidance and mentorship. Having you as supervisors and academic mentors is truly a rare priviledge.

I would also use this opportunity to thank the Human Anatomy Departmental PG Coordinator in person of Dr. S.A. Musa who in spite of his tight schedules creates time to offer useful advices on how to overcome difficult challenges, I am indeed grateful sir. Worthy of mention is Dr. L.H. Adamu of the Department of Anatomy, Bayero University, Kano whose imput in this work can not be over emphasized. Your brotherly support, the assistance offered in data collection and data analysis will forever be appreciated. I would also like to acknowledge and thank all my teachers in the Department of Anatomy, ABU Zaria. Your academic inputs in this training were remarkable and worthy of emulation. Dr. I. A. Ilya isa teacher and elder brother who always inspired me with the spirit of courage and optimism. S. B. Abdul Rafiu, M. H. Yahuza, Z. A. Aisha, and S. Zubaida are well appreciated for agreeing to work with me as research assistants. My gratitude is also due to all members of academic staff of Anatomy Department, ABU for approving the title of this dissertation. I am also grateful to Dr. M.H. Modibbo of BUK and Dr. A. Abdullahi of Kano

State Ministry of Health for the assistance they rendered while seeking ethical clearance from the ethical committee of Kano. I wish to express my appreciation also to my teachers from the Dept. of Physiology, ABU for their contribution in the course of the training. Prof. Mabruk, Dr. (Mrs.) A.M Danborno, Dr. I. A Imam, Your contributions are sincerely appreciated. My appreciation also goes to other friends and members of academic staff of the Department of Anatomy, BUK namely Mal. Sa'ad Datti and Mal Abdullahi Gudaji who assisted me with some research instruments. The help offered to me by the Head of Department of Family Medicine, Murtala Muhammad Specialist Hospital, Kano, Dr. M.L. Shehu and Dr. Abdulwahab Suleiman, Dr. Jamila Mustapha, Dr. Musa Suleiman Abdullahi who are all medical officers in Murtala Muhammad Specialist hospital, Dr Idris Muhammad, the Head of the General Outpatient clinic, Mallama Amina Yusuf, Mallam Kabir Salisu both of whom are supporting staff of the clinic cannot be over emphasized. Special thanks are due to Alh. Yushau Maruf and Alh. Sunusi AbdulRahman of Zakirai in Gabassawa Local Government, Dr. Ibrahim Haladu and Dr. Nuhu Itopa of Dawakin Tofa and Mall. Samaila Danliti of Wudil for their assistance in subjects mobilization. Also, I wish to express my unique appreciations to my beloved wife for her care, support and understanding during this period of "No time syndrome". You are indeed an ideal companion. I wish to express my unquantifiable appreciations to my dear parents who nurtured and supported me from the cradle and by whose prayers I am able to sail through the huddles of life.

Finally, I wish to acknowledge with gratitude the financial support offered to me by the management of BUK in the form of Tetfund scholarship without which this work would have been difficult to accomplish.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF PLATES

LIST OF APPENDICES

LIST OF ABREVIATIONS

ABU: Ahmadu Bello University

AdipoR1: adiponectin receptor 1

AdipoR2: adiponectin receptor 2

AIP: atherogenic index of plasma

AMPK: 5CAMP-activated protein kinase

ANS; autonomic nervous system

AR : androgen receptor

ATP: adenosine triphosphate

BAI: body adiposity index

BDNF: brain-derived neurotrophic factor

BMI: body mass index

BP: blood pressure

CAG: cysteine-adenine-guanine

CB1: cannabinoid receptor type 1

cDNA: complimentary DNA

CI: confidence interval

CNS: central nervous system

CNV: copy number variation

AMY1: alpha amylase 1

CRP: c-reactive protein

CT: computed tomography

CTNNBL1: beta-catennin-like protein 1

CVD: cardiovascular disease

DBP: diastolic blood pressure

DNA: deoxyribonucleic acid

FBG: fasting blood glucose,

FFAs: free fatty acids

FTO: fat mass and obesity gene

GH: growth hormone

GLUT4: glucose transporter type 4

HC: hip circumference

HDL –C: high density lipoprotein cholesterol

IBM: international business machine

IDF: International Diabetes Federation

IGFBP-3: insulin-likegrowth factor binding protein-3

IGF-I: insulin like growth factor 1

INSIG2: insulin induce gene 2

IR: insulin resistance

IRX3: iroquois homeobox protein 3

L2D:4D: left second to fourth digit ratio

LDL-C: low density lipoprotein cholesterol

LEP: leptin

LEPR: leptin receptor

LI: left first digit

LII: left second digit

LIII: left third digit

LIN28B: lin-28 homologue B gene

LIV: left fourth digit

LPL: lipoprotein lipid

LV: left fifth digit

Mc4r: melanocortin 4 receptor

MCR: melanocortin receptors

MD: mean difference

MetS: Metabolic syndrome

MMSH: Murtala Muhammad Specialist Hospital

MRI: magnetic resonance imaging

mRNA: messenger RNA

NBH : neurobehavioral hypothesis

NC: neck circumference

NPC: national population

NTRK2: neurotrophine 2 receptor

PA: physical activity

PCOS: polycystic ovarian syndrome

PCSK1: prohormone convertase 1

POMC: proopiomelanocortin

POMC: proopiomelanocortin

PPARγ: peroxisome proliferator-activated receptor gamma

PPAR-α: peroxisome proliferatoractivated receptor alpha

PT: prenatal testosterone

R2D:4D: right second to fourth digit ratio

RI: right first digit

RII: right second digit

RIII: right third digit

RIV: right fourth digit

RNA:ribonucleic acid

ROC: receiver operating characteristic

RV: right fifth digit

SBP: systolic blood pressure

SD: standard deviation

SDM: screen detected diabetes

SE: standard error

SEE: Standard error of estimate

SG: Serum glucose

SHBG: sex hormone-binding globulin

*SIM1:*Single-minded Homolog 1

SLC6A14: Solute Carrier Family 6 member 14

SNPs: Single nucleotide polymorphisms

SPSS: statistical package of social sciences

SUA: serum uric acid

T2DM: type 2 diabetes mellitus

TC: total cholesterol

TG: triglyceride

TNF-α: Tumor necrosis factor

UA: uric acid

US: United State

USA: United State of America

VAI: visceral adiposity index

VAT: visceral adipose tissue

VF: visceral fat

VLDL: very low density lipoprotein

WHR: waist-to-hip ratio

WHtR: waist-to-height ratio

WC: waist circumference

WHO: world health orgnisation

YI: Youden's index

ABSTRACT

Various anthropometric markers of adiposity such as body mass index (BMI), waist circumference (WC), neck circumference (NC), hip circumference (HC), waist-hip ratio (WHR), waist-height ratio (WHtR) and body adiposity index (BAI) have shown varying degree of correlation with the components of metabolic syndrome (MetS) among different sexes, races and ethnic groups. There are conflicting data from previous reports on the relationship between digit ratio(2D:4D) and adiposity markers. Data on relationship between 2D:4D and MetS are scarce. The aim of the study was to investigate the effects of body adiposity indices, 2D:4D and level of physical activity (PA) on metabolic syndrome components and biomarkers among Hausas of Kano, Nigeria. The study comprised of a total of 465 participants pooled from rural and urban communities comprising of 266 males and 199 females selected by systematic random sampling out of which blood samples of 161 subjects were used for serum analysis (male n = 120, female n = 41). Body mass index (BMI), waist circumference (WC), neck circumference (NC), hip circumference (HC), waist-hip ratio (WHR), waist-height ratio (WHtR), body adiposity index (BAI), digit length and 2D:4D were measured and calculated using standard protocols. Visceral adiposity was measured using sex specific visceral adiposity index (VAI). After at least 8 hours of fasting, venous blood samples were drawn for estimation of glucose, high density lipo-protein cholesterol (HDL–C), low density lipo-protein cholesterol (LDL–C), total cholesterol (TC), triglyceride (TG), uric acid (UA) and adiponectin using standard laboratory protocols. Physical activity levels were assesed using self reported PA questionnaire. Chi-square test, independent sample t-test, Pearson's correlation, multiple

and binary logistic regression, receiver operating characteristic curve were used as statistical tools. $P < 0.05$ was set as the level of significance. The results show that 2D:4D and all the indices of adiposity with exception of BAI, WC and BMI are sexually dimorphic. 2D:4D, HC, WHtR and VAI were higher in females than in males whereas, WHR, NC were higher in males. TC, HDL-Cand fasting blood glucose (FBG) were significantly higher in females ($P< 0.05$). TG, LDL, SUA, adiponectin and blood pressure (BP) showed no significant sex difference. 2D:4D, all the indices of body adiposity and BP were significantly higher in urban participants ($P < 0.05$). While adiponectin and HDL were significantly higher ($P < 0.05$) in rural subjects, all other serum parameters were higher in urban participants ($P < 0.05$). Effect of urbanization was higher on central indices ($P < 0.05$) and in females ($P < 0.05$). 2D:4D, VAI and other adiposity indices correlated positively with serum uric acid (SUA) and serum components of MetS but negatively with HDL and adiponectin. VAI was superior to all the anthropometric indices. WHR was the best anthropometric predictor of MetS [example for LDL-C = 361.12 (WHR) + (-215.15) in males and LDL-C = 472.19 (WHR) + (-308.21) in females]. BAI, NC and HC were weak predictors. Compared to L2D:4D, R2D:4D was a stronger MetS correlate (with adiponectin, L2D:4D and R2D:4D correlation coefficients were -0.572 and - 0.634 respectively, $P < 0.001$). Adiposity measures and MetS components decreased significantly ($P < 0.05$) with increased PA level. The effects of moderate and optimal PA levels on most adiposity and metabolic indices showed no significant difference ($P > 0.05$). 2D:4D correlated inversely with PA levels. MetS components were predicted from anthropometric measures of adiposity, digit length and digit ratio with WHR having the highest percentage contribution (for LDL, 67% in males and 82% in females). Cut off values of adiposity

measures for MetS components were mostly higher in males than in females and slightly different from those reported for other races. It is conluded that 2D:4D is a positive correlate of body adiposity and MetS, a possible marker of physical activity behaviour and that WHR is the best anthropometric predictor of MetS while VAI is superior to simple anthrpometric measure for MetS prediction in Hausas of Kano. Also, urbanization adversely affects body adiposity and MetS, while PA lowers adiposity and MetS measures.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background of the Study

Various anthropometric markers of adiposity (body mass index, waist circumference, neck circumference, hip circumference, waist-hip ratio, waist-height ratio, body adiposity index) have shown varying degrees of correlation with the components of metabolic syndrome among different sexes, races and ethnic groups (Akuyam *et al.,* 2009; Anyanwu *et al.,* 2011; Zhang *et al.*, 2013a,b), suggesting that there are gray areas to be unraveled about the determinants and factors that affect this relationship. The cut off values of anthropometric measurements that predict metabolic syndrome have been redefined based on races and/or ethnicity. For example, the Asians and Europeans have stipulated the cut off values for the indices of truncal adiposity (WC, HC and WHR) and BMI based on the peculiarity of the relationships between the components of metabolic syndrome and critical measures of adiposity markers in their population (Tulloch-Reid *et al*., 2003). Enviromental factors specific to certain populations such as urbanization have been shown to affect obesity and its relationship with some components of the metabolic syndrome (Ekezie *et al.*, 2011).

Blacks are known to have lower body fat for the same anthropometric adiposity measure than Caucasians and since the interrelationships between the adiposity markers and metabolic syndrome is tightly tied to their ability to quantify body fat, this has implications on the relationship between adiposity markers and the components of the metabolic syndrome (Deurenberg *et al.,* 1998). The close association between either absolute total fat or adipose tissue distribution and metabolic syndrome has been well documented (Wajchenberg, 2000). Nevertheless, controversy remains over which anthropometric

parameter best defines obesity and conveys the highest risk of cardiometabolic disturbance and the uniform applicability of these markers across populations of different races and ethnicity. In recent years, waist-to-height ratio (WHtR) has been regarded as the best screening tool for detecting cardiometabolic risk factors, especially in Asians (Lin *et* al., 2002; Hsieh *et al*., 2003; Shao *et al*., 2010). Some studies in other populations have proposed the use of waist circumference (WC) or waist-to-hip ratio (WHR) (Ho *et al*., 2003; Esmaillzadeh *et al*., 2004), whereas others advocate their combined use (Al-Odat *et al.,* 2012; Feng *et al.,* 2012). Although BMI, WHtR, WC and WHR are simple and convenient measures for epidemiological studies, their validity in measuring adiposity has been questioned because they do not directly measure the amount of visceral adipose tissue and cannot differentiate between fat and lean mass (Wannamethee *et al.,* 2005). The notion that BMI and other simple anthropometric measurements may not fully define metabolic risk has led to increased attention on other distinct aspects of adiposiy (Kramer *et al*., 2013). Visceral adiposity has been suggested as a complementary risk factor, given its pathogenic consequences in animal models and the significant epidemiologic data suggesting its role in metabolic dysfunction (Bays, 2011). In animal models of obesity, dysfunctional visceral adipocytes represent a locus of inflammation and insulin resistance (Samaras *et al.,* 2010; Kabir *et al.,* 2011). Indeed, in humans, an improvement in insulin sensitivity is associated with changes in visceral fat (Borel *et al.,* 2012) and inflammation within visceral adipose tissue is associated with systemic insulin resistance, inflammation and endothelial dysfunction (Farb *et al.,* 2011).

Visceral fat has been associated with cardiovascular events (Britton *et al.,* 2013), left ventricular remodeling (Neeland *et al.,* 2013) and dysglycaemia (Kanai *et al.,* 1996; Fox *et*

al., 2007; Liu *et al.,* 2010) in multiple large, community-based cohort study. Although it has been suggested that a direct estimation of visceral adiposity would have higher value in predicting obesity-related health risks (Borruel *et al.,* 2014), previous studies in multiethnic population have produced inconsistent findings. Some studies have found that direct visceral adiposity indictors exhibited better predictive performance than simple anthropometric parameters (Muller *et al.,* 2012) and others have found them to be equivalent (Mueller *et al.,* 1991; Marno *et al.,* 2008; Mbanya *et al.,* 2015). However, some studies have observed the discriminatory capability of the simpler measures to be more robust for some metabolic parameters (Ike *et al.,* 2000;Smith and Haslam,2007).

Visceral adiposity, the amount of visceral fat deposit in the body, is documented to have a strong relationship with serum lipid profile, glycaemic level and blood pressure and thus, a major step in the pathogenesis of metabolic syndrome (hyperlipidaemia, hyperglycaemia and hypertension) (Ike *et al.,* 2000). Visceral adipose tissue is a pro-inflammatory endocrine tissue and may account for an increased cardiometabolic risk across BMI as seen in certain populations (Bays, 2011).

A recent report in obese individuals of European ancestry demonstrated that a single measurement of visceral fat (VF) was associated with risk of dysglycaemia, dislipidaemia and hypertension independent of weight or other anthropometric indices, suggesting that visceral adiposity could be a hallmark of metabolically obese phenotype regardless of other adiposity status and may serve as a marker and target of therapy in cardiometabolic diseases (Bays, 2011). Also comparative evaluation of body composition of Nigerians by bioimpedance analysis showed that individuals with type 2 diabetses mellitus (DM) have

significantly higher total body and visceral fat than age and sex-matched counterparts (Owolabi *et al.,* 2016).

There is controversy regarding the specific mechanisms by which fat in the visceral compartment confers greater risk than subcutaneous fat (Kissebah and Peiris, 1989; Kraegen *et al.,*1991). Some investigators have suggested that one or more moieties secreted by the visceral adipocyte might mediate insulin resistance and thus, metabolic syndrome. Among the mediators are free fatty acids (FFAs) and adipose tissue–released cytokines (adipokines) such as interleukin-1, interleukin-6, tumor necrosis factor - resistin or a reduction in adiponectin (Kissebah and Peiris, 1989). Also that the anatomical position of the visceral adipose depot (that is., portal drainage into the liver) plays an important role in the pathogenesis of the MetS (Kraegen *et al.,* 1991). In recent years, visceral fat has emerged as an important measure of cardiometabolic risk. Although magnetic resonance imaging (MRI) and computed tomography (CT) scan can estimate the degree of visceral fat, these methods are not feasible in the routine clinical setting (Borruel *et al.,* 2014).

The gold standard assessment method for the estimation of visceral fat content has been MRI and CT scan. However, these methods are not pragmatic owing to the cost and time involved in their utilization (Borruel *et al.,* 2014). Visceral adiposity which is mainly aggregation of unwanted fats in the abdominal region is known to rise steadily as age advances in both genders.

Visceral adiposity index (VAI) is a recently derived index to measure visceral fat based on the knowledge of waist circumference (WC), plasma HDL, triglycerides and BMI. The

visceral adiposity index has been adjusted for gender and is based on the formula proposed by Amato and Giordano (2014).

The recent development of this sex-specific mathematical model –VAI provides a simple means by which the quantity of visceral fat can be estimated and since it is even shown that VAI was highly correlated with body visceral adiposity measured by sophisticated methods such as MRI and CT scan, the indication for its use is strengthened. Consequently, the index is presumed to be a more reliable predictor of MetS than simple anthropometric measures (Zhang *et al.*, 2013b). While this theory is upheld by the findings of some researchers (Al-Daghri *et al.*, 2013; Li *et al.*, 2013), others maintain that simple anthropometric measures demonstrates better relationship with certain components of the MetS in some populations (Bozorgmanesh *et al.*, 2011; Ciresi *et al.*, 2012). These conflicting opinions may suggest that in addition to the insulin resistance theory associated with visceral adiposity, there are probably other complex pathophysiological mechanisms linking body adiposity with MetS and the ethnic and racial discrepancy in this relationships further suggest ethnic predilections in the aetiopathogenesis.

Adiponectin (also known as: ACRP30, apM1, adipoQ and GBP28) is a hormone produced exclusively by the adipocyte. Initial identification of this protein was made in 1995 through the isolation of a cDNA using a subtractive hybridization screen designed to identify genes up-regulated during adipocyte differentiation (Scherer *et al*., 1995). Adiponectin is dramatically up-regulated during adipogenesis and remains one of the most adipocyte specific gene products identified to date. Adiponectin consists of an amino-terminal signal sequence, a variable region and a collagenous domain (Pajvani *et al.*, 2003). Adiponectin functions as an insulin sensitizer by decreasing hepatic glucose output and thereby

contributing to the regulation of whole-body glucose homeostasis. It prevents insulin resistance, a major step in the pathogenesis of metabolic syndrome, thus, making its serum level to correlate negatively with the components of the syndrome (Stefan *et al*, 2003). Although there are slight ethnic variations in the serum levels of adiponectin, it is generally agreed to correlate negatively with MetS regardless of age and ethnicity (Hu *et al*.,1996; Hotta *et al*., 2000; Weyer *et al*., 2001; Hotta *et al.,* 2001 and Stefan *et al*., 2002).

The sex difference in thepattern of body fat distribution is explainable by fat distribution effect of the sex hormones, in that while oestrogen encourages fat deposition in the thigh and buttocks, testosterone enhances fat deposition in the abdomen (Lemieux *et al.*, 1993). The study of finger lengths and especially the ratio of second to fourth digit (2D:4D) has received great attention (Manning *et al.*, 1998; Putz *et al.*, 2004; Hone and McCullough, 2012; Manning *et al.,* 2014).

Transmitted through genetic inheritance and later unchanging, the ratio of 2^{nd} and 4^{th} fingers (2D:4D) is related to prenatal exposure to testosterone (Umut *et al.,* 2015). Studies on the genetics of obesity performed on twins, suggests that the BMI, an indicator of generalized obesity may be transmitted through genetic inheritance (Sengier, 2005). Another anthropometric measure transmitted by genetic inheritance is finger length ratio as research has found that from the moment these are determined in the mother's womb during the 13^{th}-14^{th} week of intra-uterine life (Van Anders and Hampson, 2005), this does not change either in the adolescent period or in adulthood (Çelik *et al.,* 2010). There are studies reporting that 2D:4D on the hand is related to the level of sex hormones in the body (Manning *et al.,* 1998; Manning *et al.*, 2001) . Accordingly, there is a relationship between index finger length and the level of the estrogen in the female gender and a relationship

between ring finger length and the level of the hormone testosterone in the male gender (Manning *et al.,* 2001). Sequel to above, it can be deduced that 2D:4D of the hand is hormonally and genetically determined.

Since there are also evidences to suggest that body fat distribution pattern is determined by sex hormones and are also genetically predisposed (Lemieux *et al.,* 1993) it is possible that 2D:4D may be related to the adiposity markers, its metabolic consequences and serum biomarkers since 2D:4D ratio has been reported to correlate positively with traits putatively linked to testosterone (Benderlioglu and Nelson, 2004; Van Anders and Hampson, 2005; Muller *et al.,* 2011; Kangassalo *et al.,* 2011). Indeed it has been demonstrated that 2D:4D positively correlates with BMI (Danborno *et al.,* 2008; Umut *et al.,* 2015) negatively with muscle mass (Umut *et al.,* 2015), positively with waist-to-hip ratio (Oyeyemi *et al.,* 2014). Also its significant relationship with chest, waist and hip circumferences has also been documented (Danborno *et al.,* 2008).

Low levels of physical activity are associated with a high prevalence of MetS (Guinhouya *et al.,* 2011). The inverse relationship between physical activity levels and the prevalence of metabolic risk factors independent of age, gender, BMI and adiposity is well documented (Andersen, 2006; Butte *et al.,* 2007).

Physical activity is known to be protective against adiposity and its metabolic consequence. The indicators of generalized adiposity (BMI) and truncal adiposity (WC, HC, WHR, WHtR, BAI, NC) have been shown to correlate negatively with level of physical activity and so are the components of MetS (Guinhouya *et al.,* 2011). The various components of the metabolic syndrome are modulated to different extent and by different mechanisms by

physical activity levels (Dietz, 1997). Exercise increases insulin sensitivity both acutely and chronically (Henriksen, 2002). Acute exercise is characterized by changes in insulin signaling in response to muscle contraction (Henriksen, 2002). There is an increased translocation of glucose transporter type 4 (GLUT4) to the cell surface and GLUT4 are found in adipose tissues and striated muscle and are responsible for insulin-related glucose uptake and storage (Ren *et al.,* 1994). Physical activity (PA) increases GLUT4 content, glycogen synthase activity, mitochondrial enzyme activity and density in skeletal muscle (Holloszy, 2005; Eisenmann *et al.,* 2007; Venables and Jeukendrup, 2008). However, some evidences exist to suggest that there is gender discrepancy in PA induced insulin sensitivity, in that females respond better than males for age matched counterparts following the same dose and duration of aerobic PA (Lee, 2012). The acute effect of aerobic exercise can last up to 48 hours, which provides a rationale for recommendations to exercise regularly (Venables and Jeukendrup, 2008).

The blood pressure lowering effect of aerobic physical activity has been reported by many researchers (Meyer *et al.,* 2006; Tjønna, 2009; Ben Ounis, 2010) but there seem to be some inconsistency on the findings concerning the extent to which exercise lowers blood pressure and which component of the blood pressure is more affected. While some studies revealed significant reduction in both systolic and diastolic blood pressure (Meyer *et al.,* 2006; Tjønna, 2009), others revealed signicant reduction only in the systolic blood pressure (Naylor, 2008).

Abnormal serum lipid profile is associated with a poor quality diet rich in fat. A balanced diet, low in saturated fat, aiming to reduce triglyceride concentrations and TC as well as increase HDL-C concentration is usually the first line of treatment. However, the varying

effects of exercise on blood lipids have been investigated. Serum cholesterol, TG, LDL-C and HDL-C are reported to respond differently to aerobic exercise by different studies (Kelly, 2004; Meyer *et al.,* 2006; Lee *et al.,* 2010)

Overall, a negative and dose- related relationship exists between physical activity and most MetS parameters despite using a wide range of participants, sample sizes and exercise programmes that differed in intensity, duration, modality and setting. This relationship appears to be either independent of other factors or alternatively, simultaneously mediated by the physical fitness and adiposity of the participants (Guinhouya *et al.*, 2011).

1.2 Statement of Research Problem

MetS is one of the leading causes of morbidity and mortality both in developed and developing countries. Despite the ongoing global efforts at determining ethnic specific anthropometric predictors and cut-off values for the syndrome, such data are lacking in Nigeria and among the Hausa ethnic group. Prediction of MetS by anthropometric studies had focused mainly on using BMI and more recently the indices of truncal obesity (WC, NC, WHR, WHtR, HC) with varying and sometimes contrasting predictive powers for the different components of the syndrome The usefulness of sex-specific visceral adiposity index and its possible superiority over the simple anthropometric parameters has not been well documented in Nigeria, with particular paucity of such data among the Hausa ethnic group. Furthermore, correlating the various anthropometric markers of adiposity with specific components of the MetS and its serum biomarkers have received less attention in the literature. Additionally, 2D:4D like body fat distribution, is an anthropometric variable that is hormonally and genetically determined. Conflicting data from previous researches on the relationship between 2D:4D and adiposity markers suggests that although genetic

constitution and sex hormones are crucial to both, there are probably other factors that affect this relationship which needs to be further explored. Moreover, most of the studies made little attempt to determine and quantify sexual dimorphism in this relationship. Also correlating this important variable with the components of MetS and its serum biomarkers has received little attention. Although the inverse relationship between physical activity levels with MetS parameters and adiposity indices is well documented, studies comparing the impact of the various levels of physical activity on the different measures of adiposity and individual components of MetS is scarce in Nigeria and especially among the Hausa ethnic group.

1.3 Justification of the Study

The availability of population specific anthropometic predictors of the various components of MetS in some parts of the world and the paucity of such data in Nigeria and particularly among the Hausas may provide a justification for this work. Also the establishment of a relationship between the visceral adiposity index and anthropometric markers of adiposity with serum triglyceride, low density lipoprotein cholesterol, high density lipoprotein cholesterol, glucose and systemic blood pressure and comparing the sensitivity and specificity of each for these components of MetS are justified.

Following the recent declaration of the World Health Organisation that obesity is assuming an epidemic and pandemic dimension and the emphasis on its tight association with MetS which is a leading cause of morbidity and mortality worldwide, it is important to identify germane population specific adiposity markers for the components of MetS. Establishing a direct relationship between digit ratio and the various metabolic consequences of adiposity (dislipidaemia, disglycaemia and hypertension) is particularly an interesting idea as it opens

another window of opportunity for predicting MetS from a simple anthropometric measurement. Since the different measures of body adiposity (truncal, generalized and visceral) do not pose equal metabolic risk, it is therefore justified to quantify the impact of various levels of physical activity on the adiposity indices and their metabolic consequences.

The variability and discriminatory strength of the anthropometric markers of adiposity in predicting or identifying the MetS phenotype is of immense clinical significance. The study may provide effective and cheap initial screening criteria for individuals susceptible to MetS especially in a large scale epidemiological survey where invasive procedures are relatively more expensive and often not feasible. The idea is to ensure early diagnosis and commence early treatment in view of halting disease progression and preventing complications. The various components of MetS are associated with specific but interrelated complications. Consequently, establishment of a relationship between anthropometric indices and each component will be interesting and certainly an improvement of the current status of knowledge. Moreover, comparing the visceral adiposity index with the simple anthropometric indices will be useful in identifying the merits and demerits of each in the Hausa population.

Additionally, finding the Hausa ethnic specific cut-off values of the various anthropometric measures of adiposity for the different MetS components and using serum adiponectin and uric acid as biomarkers to validate the relationship of the adiposity indices with MetS parameters will certainly add value to the biochemical and clinical evaluation of the MetS. Furthermore, finding the relationship between digit ratio with body adiposity indices, MetS and its serum biomarkers may provide yet another simple anthropometric variable for

initial screening of individuals susceptible to MetS especially among the Hausa population where exposure of certain body parts such as waist, hip and neck for anthropometric studies may not be convenient for female subjects due to cultural factors, especially during a large scale epidemiological survey where ensuring privacy for every subject may not be practically feasible.

In addition, quantifying the relationship between mild, moderate and rigorous physical activity with different adiposity measures and various MetS parameters may serve as the basis for recommendation of therapeutic exercise regimen for the different obesity phenotypes and for individuals with obesity related metabolic disorders.

1.4 Aim and Objectives of the Study

1.4.1 Aim of the Study

To determine the effects of body adiposity indices, digit ratio and level of physical activity on MetS and serum biomarkers among the Hausas of Kano State.

1.4.2 Objectives of the study

The objectives of the study were to:

i. determine sexual dimorphism in the visceral and anthropometric adiposity markers, digit ratio and MetS parameters,
ii. investigate the comparative effect of urbanization on digit ratio, different body adiposity measures, component of metabolic syndrome, serum uric acid and adiponectin,

iii. find the relationship between anthropometric and visceral adiposity indices with metabolic syndrome components, serum adiponectin and uric acid,

iv. compare the effect of physical activity and urbanization on different measures of body adiposity, digit ratio and components of MetS,

v. find the correlation of digit ratio with visceral and anthropometric adiposity indices,

vi. find the relationship between digit ratio with MetS parameters, uric acid, adiponectin,

vii. formulate a linear regression equation for predicting the components of the MetS from anthropometric indices and digit ratio,

viii. determine the cut-off values of the anthropometric measures of adiposity for each component of the MetS.

1.5 Research Questions

i. The different body adiposity measures are not equally associated with the components of MetS.

ii. Visceral adiposity index is superior to simple anthropometric measurement in its relationship with components of MetS.

iii. Digit ratio ratio has a strong relationship with body adiposity and MetS.

iv. Physical activity has different impact on the body adiposity measures and MetS components.

v. Urbanization has varying adverse effects on body adiposity and MetS indices.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Molecular and Genetic Basis of Body Adiposity

2.1.1 Overall body adiposity

Genetic factors are believed to play a central role in etiopathogenesis of body adiposity. Genetic studies have revealed that mutations of several genes accounts for a higher predisposition to excessive accumulation of adipose tissue (Farooqi and O'Rahilly, 2006). These findings are strengthened by evolutionary trend explained by the "thrifty genotype" hypothesis which states that "the likelihood of man to accumulate more adipose tissue was preferred in evolutionary terms by genetic mutation as it allowed the ancestors of man to survive through the periods of famine" This hypothesis is further confirmed by the results of numerous population researches. For example, the inhabitants of small islands in the Pacific Ocean, the Pima Indians and the societies of the Kingdoms of Tonga and Samoa had inhabitants with very high obesity index due to extremely effective adaptive mechanisms for quick storing of energy excesses in the form of triglycerides deposited in the adipose tissue (Konarzewski , 2006).Genetic mechanisms behind human adipose tissue accumulation has also been demonstrated by experimental studies conducted on model laboratory animals particularly the gene knockout mouse model (Lutz and Woods, 2012).

Genetic mutation in the leptin-melanocortinpathway has been implicated in excessive adipose tissue accumulation along with the associated voracity effect in model animals (Speakman *et al,* 2007). In the case of the *Mc4r* knockout mouse, an intensified process of depositing adipose tissue and increase in theamount of food intake, leading to obesity in such animals was identified (Lutz and Woods, 2012). In contrast to the effects observed in

the *Mc4r* knockout mouse, the mice with *Mc3r* knockout were characterized by a unique phenotype defined by higher percentage of adipose tissue with a constant weight, decreased physical activityand hyperleptinaemia (Lutz and Woods, 2012). On this account, many scientists working on genetics of obesity now have their efforts directed towards analogous polymorphisms and mutations in man, with emphasis on genes and their protein products participating in various metabolic pathways, mainly related to maintaining the correct level of the physiological energy management.

Monogenic obesity with mutations occurring in various genes have been identified. For example, mutation in the gene of leptin (*LEP*), leptin receptor (*LEPR*), proopiomelanocortin (*POMC*) and melanocortin 4 receptor (*Mc4r*) (O'Rahilly *et al.*, 2003; Farooqi, 2008). Monogenic obesity is a rare but important group of genetic diseases because it provides an opportunity to understand the mechanisms responsible for appetite control and regulation. It follows theMendelian's pattern of inheritance. As a result of experiments conducted on mice with hereditary significant obesity (homozygotes ob/ob, db/db and fat with alleles encoding leptin, leptin receptor and carboxypeptidase respectively), it was possible to find analogous mutations in man (Pillot *et al.*, 2011).

Excessive adipose tissue accumulation may result from imbalance between caloric intake and utilization. Appetite is regulated by the centres located in various regions of the central nervous system (CNS). The arcuate nucleus of hypothalamus, responsible for coordinating the mechanism is controlled by a number of factors, including the melanocortin receptors (MCR). Mutation and malfunctioning of such receptors may result in excessive food intake which in turn leads to obesity. Considering the crucial role that neural melanocortin receptors play in various aspects of maintaining the energy homeostasis in the organism,

neuroendocrine anomalies, caused by melanocortin receptors mutations have an obesogenic effect (Tao, 2009; Tao, 2010). Other important genes whose mutations have been implicated in adiposity are those of leptin (*LEP*), leptin receptor (*LEPR*), melanocortin 4 receptor (*Mc4r*), proopiomelanocortin (*POMC*), prohormone convertase 1 (*PCSK1*), neurotrophine 2 receptor (*NTRK2*) and brain-derived neurotrophic factor (*BDNF*) (Choquet and Meyre, 2011). Also, mutations in *LEP*, *LEPR* and *Mc4r* which are important in the central regulation of appetite are contributory. Consequently, leptin malfunctioning which may be caused by lack of the gene expression or dysfunction of its receptor may lead to hyperphagia and obesity in the early stage of life. Other mutations are related to proteins of the melanocortin pathway, contributing in the neurogenesis and correct functioning of the hypothalamic regulation (Meczekalski *et al.,* 2008).

Recently, the polygenic basis of body adiposity is becoming more clear. This means that obesity may be consequential to a number of different genetic mutations, which when analyzed individually may not show any significant effect on overall body adiposity (Choquet and Meyre, 2010). Additionally, certain chromosomal regions associated with polygenic obesity have been identified and the number of genes are increasing. Such genes include *FTO, INSIG2, PPARγ,* and *SLC6A14*. Furthermore, genetically predetermined hereditary factors play important role in forming psychophysical behaviours which may influence susceptibility of individuals to obesity and the complex genetic mechanism often need to interact with environmental factors for adequate gene expression (Clee, 2009; Braud *et al.*, 2010).

2.1.1.1 Genetic variants of obesogenes

The genetic determinants of endemic obesity remain unclear. However, over fifty loci have been shown to be associated with generalized obesity measured by BMI in a reported meta analysis (O'Rahilly, 2009; Choquet and Meyre, 2011; El-Sayed *et al.,* 2013). But the combined effects of all variants account for only a small fraction of the phenotypic variation, leaving a vast majority of the heritability unclear.

FTO: Single nucleotide polymorphisms (SNPs) in the *FTO* region have the largest effect of any variants, but that effect is said to be too small to make a significant contribution to detectable segregation signal. However, a possibility is that other variants in the same region could contribute. Obesity associated sequences within *FTO* are functionally connected through noncoding RNA with an increased expression of the homeobox gene *IRX3,* deletion of which results in reduced fat mass in mice (Smemo *et al.,* 2014). Studies in humans have found associations between obesity-associated *FTO* variants and levels of the satiety hormone leptin (Benedict *et al.,* 2014), the hunger hormone ghrelin (Karra *et al.,* 2013;Benedict *et al.,* 2014) and brain responsiveness to food cues (Karra *et al.,* 2013). It therefore implies that while common *FTO* SNPs do not contribute significantly to common obesity susceptibility, they do illustrate the potential of other rarer variants affecting the same process.

SIM1: SIM1is homologous to the transcription factor in mice, which is involved in the hypothalamic appetite regulation and its insufficiency leads to hyperphagia and obesity in mice and humans. SNPs around *SIM1* regions are associated with BMI changes in a candidate gene study in Pima Indians (Traurig *et al.,* 2009). The risk alleles were common

in Pima Indians but less so in Europeans with no association with BMI in the European sample.

CTNNBL1: multiple SNPs mainly in intronic regions of *CTNNBL1* are associated with BMI and fat mass in a sample of unrelated US Caucasians and were supported in a French Caucasian case–control study of categorical obesity (Liu *et al.,* 2008) but not in a central European sample (Voge *et al.,* 2009) or a Danish sample (Andreasen *et al.,* 2009). Failure of replication is an expected feature of a heterogenetic model in which different populations or smaller groups could be expected to have different genetic origins of obesity susceptibility. Directly measured fat mass as a control on the BMI analyses has been used but did not control for effects of body size on fat mass, and so both phenotypes contain information about non-fat body compartments (Liu *et al.,* 2008). In line with this, the replication studyconducted by some scientists (Andreasen *et al.,* 2009) found no association with BMI, but significant associations with weight and height. *CTNNBL1* variants may be associated with increased risk of obesity and the measured effect on BMI may probably be substantial.

AMY1: AMY1 which encodes salivary amylase has been associated with variations in BMI, with lower copy number associated with higher BMI in two independent samples (Falchi *et al.,* 2014). The CNV in *AMY1* was investigated in relation to BMI after an initial screen of effects on gene expression in adipose tissue (Falchi *et al.,* 2014) but the salivary amylase product is also expressed in saliva under the influence of copy number and in various other tissues (Perry *et al.,* 2007). The mechanisms linking *AMY1* expression and BMI have not been established, but *AMY1* is known to have a role in sensory perception of starch in foods as well as being regulated by autonomic nervous system (ANS) activity,

providing potential links to and from hypothalamic appetite-regulating centers (Santos *et al.,* 2012).

POMC: POMC is a complex pro-peptide, the products of which are secreted by neurons that are critically involved in appetite regulation. Congenital deficiency of POMC is the cause of a rare form of monogenic obesity, and haplo-insufficiency of POMC is linked to increased BMI in affected families (Farooqi *et al.,* 2006). The effects of POMC deficiency are important elements in the development of the neurobehavioral hypothesis (O'Rahilly and Farooqi, 2008).

LEP and LEPR: leptin functions as a feedback signal from adipose tissue fat via the leptin receptor with significant suppressive effects on appetite through the hypothalamic leptin–melanocortin signaling pathway. Both homozygous leptin and leptin receptor deficiencies cause rare monogenic severe obesity in humans driven by hyperphagia, and both are crucial elements in the development of the neurobehavioural hypothesis (NBH). Heterozygous loss-of-function variants in both genes are associated with substantial effects on body fatness. In both cases, the phenotype affected are directly measured by body fat percent adjusted for age, sex, height and weight, and the effects are substantial (Farooqi *et al.,* 2001; Farooqi *et al.,* 2007).

16p11.2: independent associations with obesity of large deletions at two locations in 16p11.2have been detected following a strategy of resequencing at loci known to be associated with rare forms of extreme obesity (Walters *et al.,* 2010; Walters *et al.,* 2013). The responsible loci are unclear, but the deleted region contains *SH2B1*, which has

established links to hyperphagia and obesity in humans and animals acting through leptin signaling pathways (Doche *et al.,* 2012).

2.2 Visceral Adiposity

2.2.1 Pathophysiology

Excessive intra-abdominal adipose tissue accumulation known as visceral obesity is a component of an adiposity phenotype which includes dysfunctional subcutaneous adipose tissue expansion and ectopic triglyceride storage tightly linked to clustering metabolic risk factors. The metabolic derangement is in the form of hypertriglyceridaemia, increased free fatty acid availability, release of proinflammatory cytokines from adipose tissue, hepatic insulin resistance and inflammation, increased liver very low density lipoprotein (VLDL) synthesis and secretion, reduced clearance of triglyceride-rich lipoproteins, presence of small, dense LDL particles and reduced HDL cholesterol levels are inclusive of the many metabolic derangements closely related to visceral adiposity (Tchernof and Després, 2013).

Physiological characteristics of abdominal adipose tissues such as size and number of adipocyte, lipolytic responsiveness, lipid storage capacity and inflammatory cytokine production are significantly correlated with and even possible determinants of the increased cardiometabolic risk of visceral obesity. Lifestyle modifications exemplified by weight loss and PA generally induce preferential mobilization of visceral fat. In practice, measuring WC in addition to the body mass index could be helpful for the identification and management of a subgroup of overweight or obese patients at high cardiometabolic risk (Tchernof and Després, 2013).

Visceral adiposity has been proven to be a component of an adiposity phenotype that includes adipose tissue storage dysfunction and ectopic triglyceride accumulation in many sites including the liver (Tchernof and Després, 2013). The role of visceral adiposity in the pathogenesis of MetS has also been detailed in the literature (Jensen, 2008; Matsuzawa, 2008; Mathieu *et al.,* 2009; Browning *et al.,* 2010).

The biological and functional characteristics of visceral adipocytesprovides a clue on the cellular determinants of human body fat distribution patterns and the pathophysiological association of visceral obesity and cardiometabolic risk. Only intraperitoneal adipose tissues are drained by the portal vein, a feature which has been at the center of some hypotheses linking visceral adipose tissue accumulation and metabolic disease (Bergman *et al.,* 2001; Bélanger *et al.,* 2002). Lobules of adipose tissue in the subcutaneous layer are arranged in a regular fashion, whereas those of the deep intra abdominal compartment are large, irregular and less organized (Markman and Barton, 1987). The Vascularization, blood flow and innervation may also differ (Kreier *et al.,* 2002; Ibrahim, 2010).

Adipose tissue blood flow in the postprandial state may also represent an important determinant of regional differences in lipid accumulation (Romanski, 2000). Higher blood flow is observed in lower body adipose tissue following meal in females, but not in males (Romanski, 2000). Also synthesis of triglyceride from glucose is reduced in omental adipose tissue compared with abdominal subcutaneous adipose tissue in females (Maslowska, 1993) but is similar in both fat depots in males (Maslowska, 1993). These observations suggest that there are probably divergent mechanisms that may explain regulation of lipid accumulation in each body fat compartment (Votruba and Jensen, 2007). Also in line with this hypothesis, femoral fat has a diminished fatty acid flux compared to

abdominal subcutaneous fat (McQuaid *et al.,* 2010; Labbe *et al.,* 2011) and proportion relies more heavily on plasma non-esterified fatty acids and VLDL triglyceride-derived fatty acids compared with abdominal adipose tissue which relies more heavily on chylomicrons (Labbe *et al.,* 2011).

The amount of adipose tissue in a body compartment is an index of the balance between triglyceride synthesis and rates of lipolysis and analyses of adipocytes according to cell size revealed that larger fat cells have higher rates of lipolysis at rest and following stimulation (Farnier *et al.,* 2003). Basal lipolysis rates in subcutaneous adipose tissue is reported to be higher when compared with abdominal adipose cells (Privette *et al.,* 2012).

Although subcutaneous adipose tissue is reported to be the major source of circulating non-esterified fatty acids, accounting for more than 85%, in lean individuals, 5–10% of non-esterified fatty acid released in the portal vein originates from visceral adipose tissue lipolysis. But in a state of increased visceral fat mass, visceral adipose tissue may contribute up to 50% of non-esterified fatty acid released into the portal vein (Nielsen *et al.,* 2004). The result of studies in experimental animals points to a potential role of excess lipolysis in the development of abdominal obesity related metabolic derangement. In general, studies on adipose tissue metabolism suggest that the size of adipocyte is a significant determinant of regional differences in lipid metabolism (Masuzaki *et al.,* 2001; Arner *et al.,* 2010; Hoffstedt *et al.,* 2010; Ledoux *et al.,* 2010).

Men demonstrate higher efficiency in visceral lipid accumulation compared with women (Fried and Kral, 1997). Also, the inability to efficiently store postprandial lipids probably contributes to excess non-esterified fatty acids and subsequent development of metabolic

alterations (Frayn 2002; Gray and Vidal-Puig, 2007; Varlamov *et al.*, 2010; McQuaid *et al.*, 2011).The quantity of fatty acids released from visceral adipose tissues increases proportionately with visceral adipose reserve probably via visceral adipocyte hypertrophy andenhanced lipolytic responsiveness to positive stimuli and inhibition by insulin (Tchernof, 2006).

2.2.2 Pathophysiological Link between Visceral Adiposity and Metabolic Profile

Robust evidence shows that visceral obesity is associated with insulin resistance, a major step in the pathogenesis of MetS (Després and Lemieux, 2006). However, whether the relationship is causal or contributory remains unclear. A number of hypothesis have been proposed to explain the possible mechanism linking visceral adiposity to metabolic complications (Després and Lemieux, 2006; Després *et al.*, 2008).

The first hypothesis focused on the peculiar metabolic profile of visceral adipocytes, being hyperlipolytic and resistant to the antilipolytic effect of insulin, resulting in overexposure of non-esterified fatty acids to the liver and to impairment in liver metabolism leading to overproduction of apolipoprotein B, increased hepatic glucose production and reduced hepatic degradation of insulin, precipitating systemic hyperinsulinaemia. The second hypothesis emphasizes the inflammatory potential of visceral adipose tissue, in that when hypertrophied, it is infiltrated by inflammatory macrophages, triggering a systemic pro-inflammatory response, further exacerbating insulin resistance (Yki-Jarvinen and Westerbacka, 2005). It has also been proposed that excess visceral adipose tissue may be a consequence of the relative inability of the subcutaneous adipose tissue to act as an

expanding metabolic buffer, protecting other organs against ectopic fat deposition, not only in the liver, the heart and the skeletal muscle but also in other potentially important organs such as the kidney and the pancreas (Taskinen *et al.,* 2011).

Serum triglyceride is a major correlate of visceral adiposity. Hypertriglyceridaemia is caused by both increased liver VLDL triglyceride production and impaired clearance from the circulation (Taskinen *et al.,* 2011). The availability offatty acid within the hepatocyte and insulin are major modulators of VLDL aggregation and secretion. Due to the hyperlipolytic state of the expanded visceral adipose tissue, the liver of viscerally obese patients is succeptible to an increased flux of fatty acids which contribute to an increased synthesis of triglycerides, which are incorporated into VLDL particles and secreted into the circulation mainly as VLDL particles. Therefore, a fatty liver is a major contributor to the hypertriglyceridaemic state of visceral obesity (Taskinen, 2003; Taskinen, 2005; Yki-Jarvinen and Westerbacka, 2005). Impaired insulin action in the liver is another feature contributing to hypertriglyceridaemia. In individuals who have excess visceral adipose tissue, hyperinsulinaemia promotes lipogenesis via the activation of sterol regulatory binding protein 1c, a transcription factor controlling the expression of enzymes involved in hepatic fatty acid synthesis (Shimomura *et al.,* 200; Yahagi *et al.,* 2002; Ferre and Foufelle, 2007). Insulin normally reduces hepatic secretion of VLDL but has a blunted ability to inhibit VLDL secretion in visceral obesity, leading to elevated VLDL secretion and hypertriglyceridaemia (Taskinen, 2003; Taskinen, 2005; Yki-Jarvinen and Westerbacka, 2005). A key factor regulating lipid oxidation in the liver is an adipose tissue-derived cytokine adiponectin and plasma concentrations of this cytokine are reduced in visceral obesity and type 2 DM (Côté *et al.,* 2005).

Abnormal levels of cytokine reaches the liver via portal circulation and along with locally produced cytokines alter hepatic lipid metabolism, worsening fat accumulation and VLDL triglyceride output into the bloodstream (Mlinar *et al.,* 2007). Insulin resistance in addition to VLDL secretion by the liver may also be associated with overproduction of triglyceride-rich lipoproteins (such as chylomicrons and VLDL) by the intestine using endogenous fatty acids. This phenomenon may explain fasting hypertriglyceridaemia

(Duez *et al.,* 2006). Overall, there are evidences that the close relationship of visceral adipose tissue content to the plasma metabolic risk profile, is tied to overproduction of triglyceride-rich lipoproteins and glucose, leading to the dysglyecaemic and dyslipidaemic states found in viscerally obese subjects (Yki-Jarvinen and Westerbacka, 2005; Adiels *et al.,* 2008; Korenblat *et al.,* 2008).

2.2.3 Factors affecting visceral fat accumulation

Age: Previous researches have documented age related changes in adipose tissue distribution as indicated by an increase in the WHR and WC (Lemieux *et al.,* 1999; Després *et al.,* 2000; Lara-Castro *et al.,* 2002). These studies show age related increase in WC and WHR attributable to increase adipose tissue deposition in the abdominal and gluteofemoral regions in both sexes. Also age was found to be a strong correlate of selective abdominal adipose tissue accumulation as estimated by an increased waist circumference. In young individuals, excess energy is preferentially stored in subcutaneous fat depots, although visceral adipose stores may also increase selectively in some genetically susceptible individuals (Lanska *et al.,* 1985).

DeNino *et al.* (2001) estimated that in non-obese females, visceral adipose tissue volume measured by CT scan increases with age at a rate of 2.36 cm^2 per year.The significance of increasing visceral adipose tissue deposition with age is particularly of concern in men and postmenopausal women who averagely have up to twice the amount of visceral adipose tissue than premenopausal women (Kotani *et al.,* 1994). These findings suggest that continuous monitoring of changes in the indices of centripetal adiposity such as waist circumference and waist-hip-ratio over time could be useful to clinicians in detecting changes in visceral adiposity and provides further evidence that clinicians should look beyond the BMI to properly assess adiposity and metabolic risk.The prevalence of adverse metabolic profile has been shown to increase with age (Kotani *et al.,* 1994). For example, the age-related increase in visceral adiposity has been shown to be an important correlate of alterations in lipoprotein-lipid metabolism and in plasma glucose homeostasis (Kotani *et al.,* 1994). Lemieux *et al.* (1999) have reported that age is associated with increased LDL-C particle in the circulation. Such increase of LDL-C particles observed in some individuals appears to be mainly related to an increase in triglyceride levels in both sexes (McNamara *et al.,* 1987; Lemieux *et al.,* 1999).

Sex: Males and females differ significantly in terms of body fat composition and distribution and such anatomical differences attributable to regional adipose tissue partitioning are unique to humans (Pond, 1992). Men are more likelyto accumulate adipose tissue in the upper body,whereas women usually accumulate adipose tissuein the lower body (hips and thighs) (Kuke *et al.,* 2005). Also Kuke *et al.*(2005) suggested that sex hormones might be involved in regulating the typical gender differences in regional body fat distribution. Studies have shown that women have less visceral adipose tissue even

though they have higher BMI, total body fat and abdominal subcutaneous adipose tissue values (Kuke *et al.,* 2005). Premenopausal women therefore accumulate a substantial amount of total body fat before a substantial amount of visceral adipose tissue is observed.

CT and MRI have been used to test the usefulness of the waist circumference as an index of abdominal adipose tissue deposition in both men and women. For a given waist circumference, women generally have greater body fat mass and abdominal subcutaneous adipose tissue than men (Kuke *et al.,* 2005).

Sex hormones: The sexual dimorphism in the pattern of body fat distribution and accumulation in humans suggests the key role of sex hormones (Tchernof *et al.,* 2006). This impression is further confirmed by reported cases of transsexuals who have been treated with sex hormones. Female-to-male transsexuals treated with intramuscular testosterone injections show a progressive shift in body fat distribution from the gynoid to android pattern over a few months to 3 years. Conversely, oestrogen treatment of male-to-female transsexuals significantly increases fat deposition in all subcutaneous fat depots but has little effect on the visceral fat, suggesting that prevailing hormonal milieu is a critical determinant of regional body fat distribution in both males and females (Elbers *et al.,* 2003).

Some studies reported that men with low circulating levels of total testosterone have higher rates of visceral obesity (Gapstur *et al.,* 2002; Phillips *et al.,* 2003; Shi *et al.,* 2007). Others reported that the role of free testosterone levels as related to body fat distribution patterns remains uncertain because of issues related to the methodology of measurement (Vermeulen *et al.,* 1999; Rosner *et al.,* 2007). There are also studies that demonstrated that

plasma concentrations of sex hormone-binding globulin (SHBG), a determinant of testosterone bioavailability, are negatively associated with abdominal obesity in both men and women (Couillard *et al.,* 2010; Gapstur *et al.,* 2002; Phillips *et al.,* 2003; Tsai *et al.,* 2004). Furthermore, men withl ow plasma SHBG or testosterone levels are reported to be characterized by altered metabolic parameters (Laaksonen *et al.,* 2003; Phillips *et al.,* 2003). However, these observations regarding the role of testosterone in adiposity are not a unanimous contention.The controversies are based on other reports showing that exogenous androgens, supraphysiological testosterone treatment of female-to-male transsexuals leads to increased visceral adipose tissue accumulation and concomitant alterations in the metabolic profile (Elbers *et al.,* 2003; Sigurjonsdottir *et al.,* 2006). Similarly, it is reported that anabolic androgen use by athletes leads to pronounced and lasting alterations in the metabolic profile. Because of this observation and the discovery that abdominal obesity is a common finding in females with the polycystic ovarian syndrome (PCOS), it is widely believed that hyperandrogenic state leads to abdominal obesity and hyperinsulinaemia (Dunaif, 1997).

Oestrogens are produced principally by the ovaries in premenopausal women (Beaulieu Kelly, 1990). However, in both sexes, oestrogens are also produced through aromatization of androgens in peripheral tissues, particicularly adipose tissues (Bélanger *et al.,* 2002; Mattsson and Olsson, 2007).The possibility of the central role of oestrogen in body fat distribution is widely speculated. Parallel sexual dimorphisms in oestrogen levels with body fat patterning as well as evidences obtained from transsexual studies have provided a fertile ground for such speculations (Guthrie *et al.,* 2004; Lovejoy *et al.,* 2008; Keller *et al.,* 2010). Moreover, decline in oestrogen level postmenopausally has been shown to be

associated with increased adiposity and visceral fat accumulation (Lovejoy *et al.,* 2008; Keller *et al.,* 2010).

The experimental rodent models in which oestrogens was shown to have a tonic inhibitory effect on food intake in all phases of the ovarian cycle and that ovariectomy leads to hyperphagia and weight gain are also highly supportive (Brown and Clegg, 2010). Studies have demonstrated that estradiol signaling in the brain interacts with neuronal pathways involved in regulating energy balance (Shi and Clegg, 2009; Brown and Clegg, 2010). Additionally,there are evidences of a direct oestrogen action on peripheral metabolism in the muscle and adipose tissue (D'Eon, 2005). Exogenous oestradiol administration decreases lipoprotein lipid (LPL) activity in lower body adipose tissue of premenopausal women but a contrary effect is observed in postmenopausal women (Price *et al.,* 1998).

Evidences for the lipolytic effects of oestrogen on adipose tissue are inconsistent (Jensen *et al.,* 1994; Tchernof and Labrie, 2004). It is documented that high oestradiol decrease LPL and increase hormone sensitive lipase expression in subcutaneous adipocytes, while the opposite is seen at low estrogen doses, indicating that oestrogens may have a biphasic action on adipose tissue lipogenic and lipolytic capacity (Palin *et al.,* 2003). Studies have also shown that oestrogens stimulate preadipocyte proliferation and that this effect is depot-specific and more pronounced in preadipocytes from females compared to males (Dieudonne *et al.,* 2000; Anderson *et al.,* 2001). The action of oestrogens on adipose tissue is indicated by the presence of receptor isoforms (Dieudonne *et al.,* 2004) and deletion of the oestrogen receptor in experimental male and female mice was associated with increased adiposity (Heine *et al.,* 2000).Cases of polymorphisms in the oestrogen receptor and genes have been associated with higher body fat mass and visceral fat accumulation compared to

women with the more frequent genotype (Okura *et al.,* 2003; Nilsson *et al.,* 2007; Goulart *et al.,* 2009).

Genetics: Family studies have shown that heritability rates of total body fat are up to 50% (Henkin *et al.,* 2003; Katzmarzyk *et al.,* 2010). About 135 candidate genes have been identified as being linked with obesity-related phenotypes and 253 trait loci (Pérusse *et al.,* 2005). A study on obesity related genetic variants performed on about 250,000 people and 2.8 million single nucleotide polymorphisms were genotyped (Speliotes *et al.,* 2010). Factors other than DNA sequence variants alone are likely to explain the high heritability rates of body adiposity. These factors may include gene-gene interactions, gene-environment interactions, as well as epigenetics. Segregation analyses even pointed toward a major gene effect accounting for 51% of the differences in visceral adipose tissue accumulation (Bouchard *et al.,* 1996). In line with this, there are documented twin studies in which weight gain was induced by overnutrition and the variance in visceral adipose tissue increase between pairs of twins was about six times higher than within twin pairs (Bouchard *et al.,* 1990), pointing to major genetic effect on visceral fat resserve. Family studies have shown clustering of visceral adiposity (Pérusse *et al.,* 1996; Rice *et al.,* 1996). Similarly, several studies have identified genetic variants that may be related to preferential accumulation of visceral adipose tissue accumulation in different populations (Berthier *et al.,* 2004; Bouchard *et al.,* 2004; Peeters *et al.,* 2007; Peeters *et al.,* 2008; Mussig *et al.,* 2009; Pausova *et al.,* 2010). Genetic variants which are associated with an increased susceptibility to the metabolic complications of visceral obesity have been identified but the relative impact of isolated variants, similar to generalized adiposity is quite low and this

clearly underscores the complexity and genetic basis of visceral adiposity (St-Pierre *et al.*, 2002; Couillard *et al.*, 2003; St-Pierre *et al.*, 2003).

Ethnicity: There is marked variation in compartmental adipose tissue distribution among various populations world-wide. This is following the observation that, for a given amount of weight gain, some populations may be susceptible to accumulate adipose tissue in the subcutaneous adipose depots, whereas some others may be more likely to accumulate adipose tissue in the visceral cavity. Thus, the recommendation that ethnicity should be factored in the definition criteria of obesity,especially in the definition of cut-off values of anthropometric measures (Lear *et al.*, 2007a; Lear *et al.*, 2010; Katzmarzyk *et al.*, 2011).

A United States study of over 9000 people consisting of several ethnic groups revealed significant ethnic differences in anthropometric measures, with African-American and Hispanic populations having higher adiposity measures compared with Caucasian populations (McTigue *et al.*, 2002). A meta-analysis revealed significant differences in adiposity measures among Ethiopians, Chinese, Indonesians,Thais, Caucasians, African Americans and Polynesians for the same age, sex and body fatness (Deurenberg *et al.*, 1998). Among the Asians, a disproportionately higher body fat content was observed at lower values compared with Caucasians (Deurenberg *et al.*, 2002). The significant ethnic differences in the mean adiposity measures may possibly be explained by inherent differences in body composition (Lear *et al.*, 2009). It is becoming a popular notion in recent time that the World Health Organization anthropometric cut-off values can no longer be applied universally without taking into account ethnicity and population peculiarities. On this note, many ethnic groups or populations such as South Asians, Chinese and Aboriginals among others have revised threshold values of adiposity measures

that predict high blood glucose, dyslipidaemia, and hypertension (Razak *et al.,* 2007). Interestingly, these cut-off values were found to be lower in these populations than in individuals of European ancestry (Razak *et al.,* 2007).

Variations have also been observed in terms of susceptibilityto visceral adiposity. For the same measure of adiposity, Caucasians have been reported to have higher visceral adipose tissue than African Americans (Després *et al.,* 2000; Katzmarzyk *et al.,* 2010; Camhi *et al.,* 2011). Also, Asians and Indian-Asians are said to be more vulnerable to visceral fat accumulation despite lower total adiposity values compared with individuals of other ethnicity (Kadowaki *et al.*, 2006a; Lear *et al.,* 2007b; Misra and Khurana, 2009).

Differences in the genetic and epigenetic programming of the potential of various fat compartments to store lipids have been put forward as the likely hypothesis that explains the ethnicity related differences in body fat distribution (Sniderman *et al.,* 2007; Misra and Khurana, 2009). Some authorities have even speculated that the higher propensity of some populations to accumulate visceral adipose tissue partially accounts for their higher prevalence of adverse metabolic profile and that additional research is needed to establish aclear definition of high-risk visceral adiposity in various populations worldwide (Després *et al.,* 2000; Gallagher *et al.,* 2000; Lear *et al*., 2007; Lear *et al.,* 2009).

The Endocannabinoid System: The discovery on the regulation of body weight and food appetite by an endogenous agonists of the endocannabinoid receptor type 1 (CB1) has brought about improvement in the understanding of the pathophysiologyof obesity (Piazza *et al.,* 2007; Di Marzo, 2008). The anandamide or N-arachidonoylethanolamine (a fatty acid neurotransmitter derived from non-oxidative metabolism of eicosatetraenoic with

poly-unsaturated fatty acid) and 2-arachidonoylglycerol together with the receptors and the enzymes that synthesize them from the endocannabinoid system (Di Marzo, 2008). Antagonists of CB1 receptor decrease appetite thereby causing significant weight loss and improvement in the metabolic alterations associated with obesity (Bifulco *et al.,* 2009; Scheen, 2009). Altered balance in the regulation of the endocannabinoid system is preferentially associated with visceral adiposity rather than with overall adiposity (Bluher *et al.,* 2007; Côté *et al.,* 2007). Adipose tissue expresses CB1 receptors and endocannabinoids are seen in subcutaneous and visceral adipose tissue (Matias *et al.,* 2006). They have both proadipogenic and prolipogenicactivity (Di Marzo, 2008). It is currently hypothesized that the endocannabinoid system plays a role in adipogenesis and lipogenesis by activating adipose tissue in a depot-specific manner, thereby contributing to visceral obesity and the associated metabolic alterations (Di Marzo, 2008; Di Marzo *et al.,* 2009).

Growth Hormone: There are documented evidences in the literature suggesting that altered growth hormone (GH) have an association with visceral obesity and high cardiometabolic risk (Miller *et al.,* 2005; Veldhuis *et al.,* 2005; Van der Klaauw *et al.,* 2007; Makimura *et al.,* 2008; Misra *et al.,* 2008) and that the association with visceral obesity is independent of total adiposity (Pijl *et al.,* 2001; Weltman *et al.,* 2003; Miller *et al.,* 2005; Makimura *et al.,* 2008). Moreover, fat distribution along with aging and the sex steroid level interact in a very complex manner to modulate secretion ofGH (Weltman *et al.,* 2003; Veldhuis *et al.,* 2005; Veldhuis *et al.,* 2009). Weight loss has also been shown to lower IGF-I and increase insulin-like growth factor binding protein-3 (IGFBP-3) concentrations, thereby altering the association between visceral adipose tissue

accumulation and these serum markers (De Pergola *et al.*, 1998). But whether the altered GH secretion noticed among viscerally obese patients is a cause or a consequence is not fully understood (De Pergola *et al.*, 1998).

High levels of circulating glucocorticoid, as seen in Cushing's syndrome, produces a phenotype of abdominal obesity, dyslipidaemia, insulin resistance and hypertension (Peeke and Chrousos, 1995). People with idiopathic abdominal obesity share many of the structural and metabolic alterations observed in Cushing's syndrome (Pasquali and Vicennati, 2000; Duclos *et al*, 2001). Primate studies suggest that social stress in primate colonies may be linked to increased visceral obesity (Shively *et al.*,2009a,b) and similar studies and in humans point toward similar effect (Kyrou and Tsigos, 2007; Kyrou and Tsigos, 2008; De Vriendt *et al.*, 2009; Donoho *et al.*, 2011). These studies give an idea that long term exposure to stressful conditions or poor coping in stressful situations is associated with hypercortisolaemia and chronic sympathetic nervous system activation, which inturn favour accumulation of visceral fat (Kyrou and Tsigos, 2009). Increased synthesis of cortisol is now recognized as an important aetiologic factor in non-Cushing abdominal obesity (Masuzaki *et al.*, 2001; Seckl *et al.*, 2001; Masuzaki *et al.*, 2003).

Nutritional Factors: studies on experimental rats have shown that saturated fat consumption may predispose to preferential accumulation of visceral fat compared with other fatty acids (Shillabeer and Lau, 1994). A study on dog shows that saturated fat feeding leads to significant increase in both the visceral and subcutaneous fat deposit (Kim *et al.*, 2007). On the other hand, similar study on monkeys had a specific effect on visceral fat accumulation which was associated with insulin resistance (Kavanagh *et al.*, 2007). Such studies on animal fat distribution are believed to be difficult to extrapolate to humans,

because of the high level sexual dimorphism of such phenomenon in humans. Moreover, demonstrating that a given nutrient influences the accumulation of visceral fat does not necessarily imply a specific impact of this nutrient on body fat distribution. With these considerations borne in mind, there is a study indicating that adding monounsaturated fat to the diet prevented increase visceral fat when compared with other dietary fats (Paniagua *et al.,* 2007). In keeping with this, a large scale epidemiological studies have shown that adherence to the monounsaturated fat diet was associated with lower waist circumference values independent of BMI in both sexes (Romaguera *et al.,* 2009). Also, *in vitro* studies showed that oleic acid and palmitic acid have different effects on lipid accumulation in cells isolated from various fat depots (Sabin *et al.,* 2007).

Some cross-sectional studies have demonstrated associations between dietary fatty acid composition and visceral fat accumulation (Garaulet *et al.,* 2006; Hernandez-Morante *et al.,* 2007; Kishino *et al.,* 2008). There are evidences showing that high intake of fructose and concomitant high soft drink consumption which have become a public health issue in recent years (Vartanian *et al.,* 2007) are associated with obesity, metabolic alterations and the development of type 2 DM (Vartanian *et al.,* 2007; Forshee *et al.,* 2008; Olsen *et al.,* 2009; Malik *et al.,* 2010).The impact of high fructose consumption in experimental animal models aswell as humans are well documented (Stanhope, 2008; Tappy and Le, 2010). Overall, available evidences demonstrate that fructose consumption increases serum fasting triglyceride and glucose levels, promotes deposition of triglycerides in non-adipose tissues, depletes glucose and insulin responses to an oral sucrose challenge and causes hepatic insulin resistance (Teff *et al.,* 2009; Stanhope and Havel, 2010; Tappy and Le, 2010). Fructose has a stimulatory effect on hepatic lipogenesis which possibly explains its impact

on triglyceride responses (Stanhope *et al.*, 2009). Indeed, there are comparative studies in which subjects were given either glucose or fructose sweetened beverages and an increase in visceral fat was observed in the fructose treatment arm. The mechanisms explaining this effect is unclear but is assumed to involve depot-specific modulation of lipogenic enzymes (Stanhope *et al.*, 2009).

Sedentary Lifestyle: Whether physical inactivity increases susceptibility to selective visceral fat deposition is not clearly established. However, according to Ross and Janiszewski (2008) regular physical activity is associated with marked reduction in waist circumference even without statistically significant change in body weight. Significant reduction in waist circumference in the absence of weight loss was accompanied by improvements in cardiometabolic risk variables in most studies. Studies that measured the amount of visceral adipose tissue by imaging techniques also found that regular physical activity could induce a substantial reduction in visceral adiposity even in the absence of weight loss (Ross and Janiszewski, 2008). From a biological point of view, the peculiar adrenergic responsiveness of visceral adipose tissue could explain the selective and greater mobilization of lipids from this depot compared with subcutaneous fat which is driven by the sympathetic drive associated with vigorous exercise (Van Harmelen *et al.*, 1997; Ross and Janiszewski, 2006).

2.3 Digit Length and Digit Ratio

2.3.1 Association of digit ratio with body traits

2D:4D digit ratio is regarded as a physiological marker for the prenatal concentrations of the sex hormones testosterone and oestrogen, which organizes the architecture of the body and the brain and the distribution of hormone receptors (Manning*et al*., 2003). Digit ratio has been associated with many biological traits including the *in utero* levels of testosterone (Lutchmaya *et al*. 2004), aggression (Bailey and Hurd 2005; Millet and Dewitte 2007), spatial ability (van Anders and Hampson 2005; Bull and Benson 2006) and academic performance (Romano *et al*., 2006). Some disease conditions like autism, depression and developmental psychopathology, congenital adrenal hyperplasia, polycystic ovarian syndrome have also correlated with digit ratio (Manning *et al*., 2001; Brown *et al*., 2002; Okten *et al*., 2002; Catrall *et al*., 2005; Fink *et al*., 2007). 2D:4D ratio has also been shown to correlate well with neonatal birth weight, an important determinant of many health conditions in later life (Ronalds *et al*., 2002; McIntyre *et al*., 2006; Danborno *et al.*, 2010).

There are a number of associated traits which have been found to be significantly correlated with low digit ratio, and these include: better male visual spatial ability, as assessed by mental rotation and judgment of line tasks (Manning and Taylor, 2001), left hand preference in peg moving in children (Manning, 2000b), a higher occurrence of autism (Wheelwright and Sanders, 2001), greater representation in membership of a symphony orchestra compared to controls, with higher ranking musicians found to have lower ratios than low-ranking ones (Slumming and Manning, 2000), a higher occurrence of congenital adrenal hyperplasia (Brown *et al.*, 2002), increased reproductive success and frequency in males (Manning *et al*., 2000a), superior mathematical ability (Kimura, 1996), increased

incidence of male/female homosexuality (McFadden and Champlin, 2000; Robinson and Manning, 2000) and low digit ratio is negatively correlated with verbal fluency (Varley, 1995).

It has been suggested that high levels of *in-utero* testosterone may affect behaviour leading to greater assertiveness. Digit ratio may therefore be a marker for behaviour" (Manning, 2002a). Also sports performance has been associated with 2D:4D (Manning and Taylor, 2002). Other associated traits include behavioural and physiological characteristics (McIntyre *et al.,* 2006), breast cancer (Muller *et al*., 2012). Earlier reports showed that 2D:4D might be affected by ethnicity (Manning *et al*., 2004; 2007) and latitude of the study area (Loehlin *et al*., 2006). These Studies have shown that the ethnic variation in the ratio is far greater than the difference between the sexes. According to Manning *et al*. (2004), in addition to the significant sexual dimorphism in digit ratio, the mean ratios varied between the English, Scottish, Uygur, Han and Jamaican children. Another study on paediatric age group showed higher ratios among the Caucasians when compared to the Blacks and the Hans ethnicity of China (Jacob *et al.,* 2015). The normal range of digit ratio ratios among males and females have been reported to be 0.947±0.029 and 0.965±0.026, respectively (Loehlin *et al.,* 2012).

2.3.2 Development of digit length and digit ratio

The specific reason for the sex hormone influence upon 2D:4D digit ratio is that: "testosterone appears to stimulate the prenatal growth of the fourth digit, while oestrogen promotes the growth of the second digit" (Manning, 2002b). Recent studies showed that digit ratio is determined not by prenatal testosterone (PT) alone but also by the balance of

PT to prenatal oestrogen signaling in a restricted time window of foetal digit development (Manning, 2011; Zheng and Cohn, 2011). Moreover, a recent study by Medland *et al.* (2010) showed that a variant situated in the intron 2 of *LIN28B* gene (rs314277) was associated with digit ratio. Variation in digit ratio has been suggested to have evolutionary relevance because of its associations with fitness components. The Homeobox genes *HoxA* and *HoxD* control the differentiation of the urinogenital system and may therefore indirectly influence the prenatal production of testosterone and oestrogen and the development of the digits (Kondo *et al.*, 1997; Mortlock *et al.*, 1997).

Molecular studies on the development of digit length and ratio have revealed that prenatal testosterone is related to *HoxA* and *HoxD* gene expression. *HoxA* genes are conserved in mammals and they influence the differentiation of digits and toes. *HoxA* genes have also been implicated in sex determination, morphogenesis of urinogenital system, fertility and haematopoiesis (Zhang *et al.*, 2013a). This partly explains the embryological origin of the sexual dimorphism pertaining to digit ratios. Also, studies have shown the influence of variations in the X- linked androgen receptor gene on the digit ratios. Digit ratio is also affected by increased DNA replication of cysteine-adenine-guanine (CAG) in the androgen receptor gene(Romano *et al.*, 2006). If the alleles in the androgen receptor (AR) genes have more CAG, then it makes the AR gene insensitive to the testosterone while it is compensated by producing more testosterone in the embryo. Development of digit ratio therefore appears to be a function of androgen sensitivity, rather than the androgen concentration (Romano *et al.*, 2006).

2.3.3 Sexual dimorphism in digit ratio

Digit ratio have been reported by many researchers to be sexually dimorphic (Manning *et al*., 1998; Manning *et al*., 2002; Putz *et al*., 2004; McIntyre *et al*., 2006; Trivers *et al*., 2006; Danborno *et al.,* 2010; Oyeyemi *et al*., 2014; Xu and Zheng, 2015; Oyeyemi *et al*., 2016). This sexual difference has also been observed in other animals and primates (Brown *et al*., 2002; Burley and Foster 2004). Studies in South Indian population have also identified the sexual dimorphism in digit ratios (Xi *et al.,* 2014). It is generally believed that the lower the individual's digit ratio, the higher testosterone but the lower the oestrogen levels experienced during intrauterine life. In humans, the basis for this hypothesis emanates from studies showing that digit ratio is sexually dimorphic with lower ratios among males than females from the end of the first trimester of foetal development and remain relatively stable throughout life (Manning *et al.,* 1998; Malas *et al.,* 2006; Trivers *et al.,* 2006; Galis *et al.,* 2010; Manning, 2010; Zhao *et al.,* 2012).

Also, congenital adrenal hyperplasia, an inborn condition which causes excessive production of androgen prenatally, has been shown to be related to low digit ratio in both sexes (Ciumas *et al.,* 2009). Further, women with polycystic ovarian syndrome that is believed to be associated with increased prenatal testosterone (PT) levels have lower digit ratio (Carall *et al.,* 2005). In addition, females who belong to opposite sex twin pair have also been reported to show a masculinized pattern of digit ratio (Voracek and Dressler, 2007).

2.4 Metabolic Syndrome

The metabolic syndrome is a cluster of interrelated common clinical disorders, including hypertension, hyperglycaemia, glucose intolerance and dyslipidaemia, in addition to obesity (Moller and Kaufman, 2005). MetS is defined based on the presence of three or more of the following criteria: abdominal obesity with waist circumference > 94 cm for men or > 80 cm for women (Grundy *et al.,* 2005), triglycerides > 150 mg/dl (1.71 mmol/l), high density lipoprotein cholesterol (HDL-cholesterol) < 40 mg/dl (1.04 mmol/l) for men or < 50 mg/dl (1.3 mmol/l) for women (Bergman *et al.*, 2006), blood pressure >130/85 mmHg (Tremblay *et al.*, 2004) and fasting glucose >100 mg/dl (5.6 mmol/l) (Grundy *et al.*, 2005). Although genetic factors may be involved, it has been generally accepted that accumulation of excess body fat, particularly abdominal obesity or intra-abdominal visceral obesity caused by over nutrition and physical inactivity, promotes the development of the metabolic syndrome (Kissebah *et al.,* 1982; Fujioka *et al.,* 1987; Grundy *et al.,*1999; Kahn *et al.,* 2000).

2.4.1 Serum biomarkers of metabolic syndrome

There are a number of serum biomarkers whose levels have proven to independently predict MetS and have been used to test the relationships between the syndrome and many of its predictors (Lara-castro *et al.,* 2007; Ghantous *et al.,* 2015). Most widely studied are the serum adiponectin and serum uric acid. While hyperuricaemia is associated with adverse metabolic states (Billiet *et al.,* 2014), hyperadiponectinaemia has been proven to be protective (Kadowaki *et al.,* 2006; Lara-castro *et al.,* 2007; Ghantous *et al.,* 2015). Correlation of these independent biomarkers of MetS with the various adiposity indices

may be a guide to discriminatory powers of these indices for components of metabolic syndrome in a population (Ghantous *et al.,* 2015).

Alarmingly, high prevalence rates of the MetS in developed and developing countries and the associated high mortality and morbidity are forcing scientists to review promising therapeutic agents and population specific anthropometric criteria for defining its phenotype. One of these agents is adiponectin, which is a novel peptide abundantly expressed in adipose tissue (Matsuzawa, 2005). What makes this adipocytokine so attractive is its recently discovered anti-atherogenic (Okamoto *et al.,* 2000; Ouchi *et al.*, 2001), anti-diabetic (Yamauchi *et al.,* 2002; Stefan *et al.,* 2003) and anti-inflammatory (Engeli *et al.,* 2003) properties. In contrast to other adipocytokines, adiponectin levels are inversely related to visceral fat area, and low levels have been associated with obesity, type 2 diabetes mellitus (DM), and cardiovascular disease (Hu *et al.,* 1996; Arita *et al.,* 1999; Hotta *et al.,*2000; Weyer *et al.,* 2001). Low plasma levels of adiponectin characterise both obesity and insulin resistance (Engeli *et al.,* 2003). Even though negative correlations have been found between adiponectin and obesity (Arita *et al.,* 1999; Weyer *et al.,* 2001), it has been suggested that plasma adiponectin concentrations are closely related to insulin sensitivity, fasting insulinaemia and to adiposity and glycaemia and that factors other than adiposity may play a role in determining adiponectinaemia (Hotta *et al.,* 2000; Ryan *et al.*, 2003). Adiponectin exerts its function through activation of two kinds of receptors, adiponectin receptor 1 (AdipoR1) and adiponectin receptor 2 (AdipoR2). AdipoR1 receptors are found in different tissues and are connected to activation of 5CAMP-activated protein kinase (AMPK) pathways, while adipoR2 receptors are mostly expressed in the liver and mainly linked to the activation of peroxisome proliferator activated receptor alpha

(PPAR-α) reducing inflammation and oxidative stress (Yamauchi *et al.,* 2007). Adenoviral selective expression of AdipoR1 receptors in *db/db* mice leads to activation of AMPK and decreased expression of gluconeogenic enzymes such as glucose-6-phosphatase and phosphoenolpyruvate carboxykinase 1. Increased expression of enzymes regulating glucose uptake (such as glucokinase and PPAR-α) results from enhanced hepatic expression of AdipoR2 receptors (Yamauchi *et al.,* 2007). Expression of both receptors augments fatty acid oxidation and improves diabetes. Conversely, disruption of these receptors reduces the activity of related pathways and leads to significant glucose intolerance and aggravation of diabetes that is accompanied by increased hepatic triglyceride, inflammation and oxidative stress (Yamauchi *et al.,* 2007).

As an end-product of the purine metabolism in humans, the serum uric acid (SUA) concentration is determined by an interaction of genetic and environmental factors.The SUA levels are higher in humans and the great and lesser apes due to parallel mutations of the uricase gene that occurred during the mid Miocene era (Wu *et al.,* 1992).The consequence of the mutation is that humans not only have higher UA levels than most other mammals but they cannot regulate UA levels as effectively as others either (Johnson and Rideout, 2004). The uricase mutation may have conferred a survival advantage by helping to maintain blood pressure (BP), stimulate salt-sensitivity, and induce insulin resistance (IR) and mild obesity, thereby helping to promote survival during a period of famine or stress (Johnson *et al.,* 2008).

Western lifestyle, however, including western diet and physical inactivity have swept the world during the past few decades. Since the current western diet is high in meat and fructose, both of which generate UA, humans today have higher UA levels (range 238–

595µmol/l) compared with primates that lack uricase (whose UA levels are typically in the 178–238 µmol/l range) (Johnson *et al.,* 2005). Hyperuricaemia is defined as SUA concentration above the upper limit of the population reference range that is in excess of urate solubility, which is about 420µmol/l in men and 360 µmol/l in women (Fang and Alderman, 2000). This difference is explainable by the uricosuric effect of oestrogen which further explains why the serum level seem similar in both sexes after menopause (Nicholls *et al.,* 1973).

2.5 Anthropometric and Visceral Adiposity Indices

2.5.1 Generalized adiposity versus abdominal adiposity

The adverse metabolic consequence of excessive body fat collection is well recognized (Mathieu *et al.,* 2009; Whitlock *et al.,* 2009; Eckel *et al.,* 2010; Simmons *et al.,* 2010). In the past, attention on risk assessment was mainly consolidated on measurement of total body fat content as indicated by indices of generalized adiposity such as BMI. The discovery of inherent deficiencies with the BMI otherwise known as the Quetelet index (Gallagher *et al.,* 2000) in body fat estimation and that certain individuals who harbour excess fat in the trunk have higher incidence of adverse metabolic parameters even at normal BMI led to increase attention on the concept of centripetal adiposity (Gallagher *et al.,* 2000).These limitations in BMI are well recognized and include differences in performance in males and females, inappropriateness in children and athletes, differences between ethnic groups (Camhi *et al.,* 2011; Freedman *et al.,* 2012).Currently, there is an ongoing controversy on the adiposity measure with the highest discriminatory power for MetS because of conflicting reports from different ethnicity and populations. It is believed

that the different adiposity measures do not carry equal metabolic risk in all populations. There is increasing number of publications pointing at the probable superiority of central measures of adiposity compared to others. This is because of its assumed tight association with intra–abdominal visceral fat which is a critical determinant of insulin resistance and MetS.

Investigation discovered twice as many macrophages in visceral compared to subcutaneous adipose tissue. These cell-accumulations were significantly associated with a higher incidence for hepatic fibro-inflammatory lesions in obese subjects (Eckel *et al.*, 2010). Measurements of interleukin-6 demonstrated significantly higher concentrations in plasma obtained from the portal vein compared to peripheral venous plasma samples in obese subjects. This indicates VAT as an important source of interleukin-6. Beyond that, interleukin-6 concentrations were significantly correlated to C-reactive protein-concentrations. Therefore, VAT accumulation seems to be accompanied by systemic inflammation (Fontana *et al.*, 2007). Higher mRNA concentrations for angiotensinogen were reported for visceral compared to abdominal subcutaneous tissue (Dusserre *et al.*, 2000). Angiotensinogen precedes angiotensin II, which is involved in the pathophysiologic mechanism of hypertension as well as in adipocyte differentiation. This makes VAT a likely conjuncture for hypertension (Dusserre *et al.*, 2000).

However, all the central measures of adiposity do not show a uniform pattern of association with MetS across ethnicities. It believed that abdominal fat collection is compartmentalized into subcutaneous abdominal fats, intra–abdominal visceral and peritoneal fats, and that the predictive power of a particular central index is mainly linked to its ability to predict intra-abdominal visceral fats. For this reason, sophisticated methods

to quantify visceral fat directly such as CT scan and MRI are currently employed. More recently, Amato and Giordano (2014) proposed a sex specific model for visceral fat estimation with variable sensitivity and specificity across different populations.

2.6 Effect of Physical Activity and Urbanization on Measures of Body Adiposity and Metabolic Syndrome

Epidemiological studies suggest that a significant part of the cardiovascular disease (CVD) epidemic is attributable to changes in lifestyle risk factors, exemplified by reduction in physical activity (PA) and increased consumption of high-energy processed foods (Lopez *et al.,* 2001). Rapid urbanization in many sub-Saharan African countries may contribute to the epidemiological transition in the region. Previous studies demonstrate a positive rural-urban gradient in terms of the prevalence of risk factors. This has made physical inactivity a perceived component of urban dwelling, making the adiposity and metabolic profile of both urban dwellers and physically inactive people to be somewhat identical (Sobngwi *et al.,* 2004; Fezeu *et al.,* 2008). Previous studies have shown the inverse relationship between PA and adverse metabolic parameters, thus indicating its protective effect against MetS (Franks *et al.,* 2004; Ekelund *et al.,* 2007; Healy *et al.,* 2008).

Exercise training can have a profound effect on reducing body and visceral adiposity and therefore reduces MetS risk (Pattyn *et al.,* 2013; Vissers *et al.,* 2013). Exercise training or increased PA, especially that which is associated with reduced fat mass, corrects the dysfunction in adipokine and cytokine expression so that expression of adiponectin is increased in adipose tissue and production of inflammatory cytokines is reduced (Bradley *et al.,* 2008; Kim *et al.,* 2013). Many believe that the beneficial effect of exercise is partly

mediated through changes in the adipokines profile, that is, by increasing anti-inflammatory cytokines and decreasing pro-inflammatory ones (Bruunsgaard *et al*., 2005; Petersen *et al.,* 2005).This effect has been described at the levels of gene expression, protein ligands and receptor bindings (Moldoveanu *et al.,* 2001). For instance, exercise increases insulin sensitivity through reduction of resting levels of tumor necrosis factor aipha (TNF-α) and C-reactive protein (CRP) and augmentation of adiponectin levels (Kasapis *et al.,* 2005). But quantification of the impact of the different levels of PA on each adiposity index and each component of MetS has not been widely studied.

Franks *et al*. (2004) however, showed that the impact of physical activity on adiposity and MetS may have a threshold. The study of Felix *et al.*(2011) conducted on sub-Saharan African populace which used physical activity energy expenditure to stratify subject according to their level of activity into four categories and to determine the impact of urbanization and PA on metabolic health also showed an inverse trend. An attempt to compare the effect of the various strata of activity showed different impacts (Felix *et al.,* 2011). On the BMI, only the 4^{th} stratum of PA was able to yield the desired result in both males and females. On the WC, while the second stratum of PA was able to yield the desired result in males, only the third stratum was significant in females. The DBP and FBG were only significantly influenced by the third and second activity levels in males and females respectively. The first and third strata of physical activity levels were significant on HDL in males and females respectively. It is also noteworthy that in the same study there was no beneficial impact of physical activity observed on HDL between the third and fourth levels of PA. In fact, according to the study, a slight drop in HDL-C was recorded between stratum three and four.

Previous studies have demonstrated that higher levels of self-reported physical activity is related to lower WC, BMI and prevalence of the adverse metabolic profile. These findings were shown in both cross-sectional observational studies (Edwardson *et al.,* 2012; Stamatakis *et al.,* 2012) and longitudinal studies (Hu *et al.,* 2003; Saunders *et al.,* 2012). Cross-sectional studies have reported stronger association for self-reported than objectively measured PA (Atienza *et al.,* 2011; Celis-Morales *et al.,* 2012; Stamatakis *et al.,* 2012). The differences may be due to measurement error in the objectively measured activity method or recall bias in self reports method which is particularly common among older adults (Van Cauwenberg *et al.,* 2014; Gennuso *et al.,* 2015). However, earlier studies have shown that self-administered questionnaires can produce reliable data when estimating habitual PA (Lichtman *et al.,* 1992; Wolf *et al.,* 1994).

Some studies suggest that intensity rather than volume of PA is important to reduce cardiometabolic risk (Schnohr *et al.,* 2007; Hamer *et al.,* 2008; Zheng *et al.,* 2009; Hassinen *et al.,* 2010; Ilanne-Parikka *et al.,* 2010). In a study to find out whether sedentary behaviour is associated with particular patterns of regional fat deposition in a high-risk population, objectively measured sedentary behaviour was positively associated with visceral fat, but not subcutaneous or whole body fat (Gorely *et al.,* 2015).

Studies have shown that acute exposure to mild or moderate physical activity may not affect serum adiponectin levels especially in non obese healthy adults (Ferguson *et al.,* 2004; Punyadeera *et al.,* 2005; Bobbert *et al.,* 2007), while longer duration of physical activity are accompanied by increased expression of adiponectin mRNA levels in skeletal muscle (Kraemer and Castracane, 2007). Jamurtas *et al.* (2006) evaluated the effects of a suboptimal aerobic exercise on adiponectin in 9 healthy overweight males and found no

significant correlation between the adiponectin and activity level. Conversely, a more recent study of plasma adiponectin levels in inactive, abdominally obese men showed that even a short-term aerobic exercise training of one week significantly increased plasma values (Saunders *et al.*, 2012).

The literature indicates that long term aerobic PA significantly lowers serum uric acid (SUA) level. In previous studies, the effects of one week aerobic training programme on changes in SUA levels was investigated in a group of initially extremely active subjects and a sedentary control group. It was found that exercise lowered SUA significantly among the active subjects (Bosco *et al.*, 1970; Williams, 1997). Also, another study on the relationship of PA levels to SUA levels using over 2400 subjects demonstrated that the higher the PA level, the lower the SUA values (Cooper *et al.*, 1976; Cooper, 1982). Several observers have however reported a rise in SUA in the immediate period following acute strenuous PA.

Urbanization is widely believed to be an important contributor to rising global obesity prevalence and its attendant MetS. A substantial contributor to the difference in adiposity and metabolic characteristics of urban and rural dwellers is believed to be the difference in activity levels alongside other important life style measures such as diet (Abubakari *et al.*, 2008; Ramachandran *et al*., 2008; Mbanya *et al*., 2014). Urban participants might be less active and consume unhealthy food containing more saturated fat and high calorie diet, while rural participants eat the traditional high carbohydrate, low protein and low fat diet (Amuna and Zotor, 2008). Urbanization appears to be associated with extreme changes in dietary habits, psychological stress and physical inactivity (Taro *et al.*, 2001; Nyenwe *et al.*, 2003; Amuna and Zotor, 2008). Sabir *et al*.(2013) conducted a study to compare the

adiposity profile of a rural and urban settlement in Nigeria and showed that the mean values of WC, BMI, WHR, DBP and SBP were higher for the urban than for the rural inhabitants. Sabir *et al.*(2013) also found that, the. TC was significantly higher in urban than rural participants. They noted that mean serum LDL-C and TG concentrations were higher in the urban than rural participants but the difference was not statistically significant. Mean serum HDL-C was also insignificantly higher in the rural than in urban participants. Aside the rural-urban difference in adiposity and metabolic profile, age has also been shown to positively correlate with serum lipids (Iloh *et al.,* 2012).

Ageing can lead to increased sedentary living, increased dietary requirement, reduced cholesterol metabolism and thus increased accumulation of body lipids. Similarly the result of the study of Steinhagen-Thiessen *et al.*(2008) found that the proportion of subjects with dyslipidaemia was low in theyounger age group up to age 20 years and peaked in the age group of 61–70 years in both sexes before a gradual decline thereafter. In addition to its association with age, dyslipidaemia may be a consequence of obesity (Siminnialayi *et al.*, 2008).

Adediran *et al.* (2012) conducted an observational study on a rural and urban settlement of Abuja, Nigeria to compare the distribution of MetS parameters among the people in both communities and found that WC, WHR, BMI, DBP and SBP were significantly lower in rural than in urban settlements. Also TC, LDL and TG were all higher in urban settlement, while HDL was higher in rural than urban settlements. While the impact of urbanization on BMI, WC, DBP, SBP, HDL and TG were all significant and comparable, the impact on LDL, TC and FBG was much less. Obirikorang *et al.*(2015) conducted a comparative study to look at the adiposity and metabolic trend in rural and urban communities in Ghana, the

results suggested that, among the serum and blood pressure components of MetS, significant differences were onlyobserved in DBP, TC, LDL and FBG. However, in the anthropometric measures of adiposity, significantly higher values were recorded for all indices amongst participants in the urban area.

Markers of adiposity were also reported to be higher amongst females than males in both areas. Similarly, a study on Africa community has shown that measures of cardio-metabolic risk are higher amongst women than in men (Amoah, 2003) and that across all ages, higher number of females had BMI within the upper quartile (Amoah, 2003). Ekezie *et al.*(2011) conducted a study to compare obesity trends, anthropometric profile and blood pressure of rural and urban igbo ethnic group in Nigeria and found the mean measures of adiposity markers, DBP and SBP to be higher in the urban participants when compared with their rural counterparts. In the same study, the anthropometric index with the strongest correlation with blood pressure for Igbos in the urban setting was WC followed by BMI, while WC followed by WHtR was noted for the Igbos in the rural setting. WHtR followed by WC showed the strongest indication of blood pressure in men, for both rural and urban settings. While for women in the rural communities, WC followed by WHtR showed the highest correlation.

There is considerable geographical variation in population serum uric acid (SUA) concentrations. These discrepancies may be due to ethnic factors or may be the consequence of environmental influences. Beighton *et al.*(1974) compared the SUA of Negroes from urban and rural South African communities and reported a significantly higher values among the urban dwellers. Within the same populace, SUA steadily increased with age in a linear fashion and was significantly higher in males. There is a speculation

that the urban-rural difference in SUA is a reflection of the differences in weight and body adiposity measures, making adiposity the principal mediator. Studies have shown that reduction in weight and values of adiposity measures in obese individuals is accompanied by commensurate fall in SUA levels (Nicholls and Scott, 1972; Choi *et al.,* 2005). Also, it is documented that, the Chinese of Taiwan have lower SUA levels than their relatives who have emigrated to Malaya and Western Canada (Ford and de Mos, 1964).

2.7 Relationship of Digit Ratio with Body Adiposity Measures, Metabolic Syndrome and Biomarkers

The idea of finding a relationship between digit length and digit ratio with MetS components is an evolving one. Few attempts have been made by researchers in the field of biological anthropology to correlate digit ratio with some anthropometric indices of adiposity, as an indirect link with MetS. Accordingly, digit ratio was correlated with neck circumference among Europeans (Fink *et al.*,2003; Fink *et al.,* 2006) and with WC and HC among Ugandans (Abba *et al.,* 2012), with NC, WC, HC, CC, BMI, WHtR among Nigerians (Danborno *et al.,* 2008; Oyeyemi *et al.*,2016). The correlation of digit ratio with birth weight as demonstrated by Danborno *et al.* (2010) also strengthens the likelihood of an association between digit ratio and MetS since low birth weight has been shown to be an important predictor of hypertension, DM and obesity in adulthood (Baker 1998; Huxley *et al*., 2000; Anazawa *et al*., 2003). Globally, only very few attempts were made to establish any relationship with the actual measures of MetS (BP, serum glucose and lipid profile). In north india, Ranvider and Manju (2016) conducted a cross-sectional observational study on

200 subjects to assess the relationship between digit length and digit ratio with hypertension that revealed a positive and significant correlation. Also, Pınar *et al.*(2015) recruited 137 female subjects in Turkey for a study to assess the relationship of digit ratio with WC, BP, SG, HDL and TG and found no significant association with all these measured parameters. In the same study, digit ratio unlike in a vast majority of other studies did not correlate with WC, NC, BMI and WHR. Such studies on Africans including Nigerians are very scarce in the literature. This is the first study attempting to find if there is any relationship between digit ratio and serum biomarkers of MetS (uric acid and adiponectin) which like digit ratio demonstrate sexual dimorphism in their normal mean serum values in that, while adiponectin is reported to be higher in female, uric acid is higher in males (Fang and Alderman, 2000). Similarly, the relationship of digit ratio with a relatively newer measure of body adiposity called body adiposity index (BAI), which is derived from HC measurement independent of height and with VAI is somewhat a new idea. Some studies have shown that the BAI is a reliable adiposity measure with good sensitivity in some populations (Bergman *et al.,* 2011). Body size and proportion have implication on cardiometabolic profile and Ronalds *et al.* (2002) have shown that digit ratio ratio is associated with body size and proportion. Digit ratio has also been associated with myocardial infarction, one of the terminal complications of adverse cardiometabolic profile (Manning and Bundred, 2001; Manning, 2002; Kyriakidis *et al.,* 2010; Wu *et al.,* 2013).

It has been suggested that prenatal androgen exposure, the major determinant of digit ratio might enhance the development of the cardiovascular system (English *et al.,* 2000; Pokrywka *et al.,* 2005). Many studies have shown a relationship between digit ratio and obesity measure (Fink *et al.,* 2003; Finks *et al.*, 2006; Danborno *et al.,* 2008; Kyriakidis *et*

al., 2010; Abba *et al*., 2012; Oyeyemi *et al*., 2014;Oyeyemi *et al*., 2016). According to the study of Oyeyemi *et al*.(2014) on Nigerians, digit ratio (2D:4D) in both hands failed to show any significant correlations with NC in female subjects, but a significant relationship was recorded in male. Also, BMI, WC and WHtR were significantly correlated with both right and left digit ratio digit in males and females. WHtR showed the highest significant correlation with right digit ratio in both males and females when compared with BMI, NC and WC. In the same study, the correlation of right digit ratio with other measures of body adiposity was stronger when compared to the left. A similar but weaker association was observed for the females. This difference was more pronounced in right digit ratios than the left. This was similarly reported by previous studies (Zhao *et al.*, 2012). Right hand digit ratio is believed to be a better predictor of intrauterine testosterone levels (Manning *et al.*, 1998; Williams *et al.*, 2000). Thus, sex difference in the right hand digit ratio is more pronounced than that in the left hand. Invariably, right hand show stronger correlation with predicted variables than that in the left hand (Manning, 2002). This assertion is however not a unanimous contention as there are other studies showing the correlation of the left digit ratio with important biological traits to be stronger than the right digit ratio. Indeed Danborno *et al*.(2008) revealed the left digit ratio to correlate better with birth weight, a testosterone linked sexually dimorphic feature. Also, the study of Fink *et al.* (2003) found that BMI was strongly and positively correlated with the left 2nd:4th digit length ratio in males.

2.8 Relationships of Body Adiposity Measures with Metabolic Syndrome

Although studies have indicated the harmful metabolic effect of high amounts of visceral adipose tissue, evidence suggests that subcutaneous fat is not without harm (Ross *et al.*, 2002; Goodpaster *et al.*, 2003). Visceral and subcutaneous fat tissue is associated with inflammatory markers and metabolic risk (Pou *et al.*, 2007). High levels of subcutaneous fat can also contribute to insulin resistance (Tchoukalova *et al.*, 2008). Moreover, WC is more highly correlated with subcutaneous fat tissue than with visceral adipose tissue (Fox *et al.*, 2007). According to the results of previous studies, in some ethnic groups, the structural heterogeneity of tissue in the abdominal region does not allow the use of a unique definition of abdominal obesity or, consequently, MetS.

Several anthropometric indices such as BMI, WC, HC, WHR and WHtR have been proposed to identify individuals who are at risk of MetS and its components (Pischon *et al.*, 2008; MacKay *et al.*, 2009). In recent years, the concept and anthropometric criteria for the MetS have been increasingly discussed. Presently, there are several definitions of the MetS, as proposed by the World Health Organization (Alberti *et al.*, 1998), American Heart Association and National Heart, Lung and Blood Institute (Grundy *et al.*, 2005), the European Group for the Study of Insulin Resistance (Einhorn *et al.*, 2003) and the International Diabetes Federation (IDF, 2006). Most of these definitions take into account various anthropometric measurements found to be germane in the concerned population. Recently, the definition of IDF takes into account ethnic perculiarities. The Japanese Society of Internal Medicine also published similar criteria for the Japanese (Nippon and Gakkai, 2005) which has been widely adopted in Japan. Most of these definitions employ waist circumference as an indicator of central or abdominal obesity. However, several

reports have argued that other indices, for example the waist/height ratio (Hara *et al.*, 2002; Lin *et al.,* 2002; Ho *et al.,* 2003; Hsiehand Muto, 2005; Hsieh and Muto, 2006) and waist/hip ratio (Welborn *et al.,* 2003; Esmaillzadeh *et al.,* 2004) are superior to waist circumference for identifying subjects with cardiovascular risk factors.

Although the indices of truncal obesity were reported to strongly correlate with BMI, it is however not clear whether they can predict cardiovascular diseases better than BMI in all poulation, suggesting that there are some controversial issues around the adiposity markers that better predict cardiovascular risk (Bergman *et al*., 2011a, 2011b). The relatively higher prevalence of DM or hypertension among Indian-Asians who had similar anthropometric dimension and common socio-demographic characteristics with other Indians was solely attributed to higher truncal obesity indices, there is thus, a strong correlation between central obesity and cardiovascular disease (Shaw *et al.*, 2010). Recently a study assessed and compared the strength of association and discriminatory capability of measures of adiposity such as BMI, WC, HC, WHR and WHtR for DM risk in a sub-Saharan African population. From the study,WC was the best predictor and to some extent WHtR in the population, while BMI and WHR were less effective (Mbanya *et al.,* 2015). A comparative study to compare the impact of differences in WC defined according to the International Diabetes Federation (IDF) and the Adult Treatment Panel III (ATP III) and index BMI on cardiovascular disease risk factors in 402 apparently healthy volunteers of European ancestry showed that, prevalence of metabolic syndrome were essentially identical irrespective of the measure of WC used, as were metabolic characteristics of the subjects. Cardiovascular disease risk factor status, therefore, did not vary substantially when subjects

were divided on the basis of WC or BMI and the results indicated that WC and BMI significantly correlated (Marno *et al.,* 2008).

In a study conducted to assess abdominal adiposity and clustering of multiple metabolic syndrome in White, Black and Hispanic Americans, WC appears to be a marker for multiple metabolic syndromes in these ethnic groups. The results of this investigation lend support to the view that waist measurement should be considered as a clinical variable for assessing the risk of cardiovascular diseases (Ike *et al.*, 2000). A descriptive study of metabolic syndrome in a sub-Saharan African setting showed central obesity assessed by WC to be more tightly associated with the other components of the metabolic syndrome (Leopold *et al.,* 2007). Although, WHR measures central fat deposition, it is imperfect, particularly among lean individuals (Wang *et al.,* 2005). Another study has also shown that WC may be a better anthropometric predictor of many components of metabolic syndrome than BMI or WHR (Wang *et al.,* 2003). Indeed, since WC is more strongly associated with stroke and type 2 DM than either BMI or WHR, it may be measuring a different form of adiposity not totally accounted for by BMI or WHR (Molarius *et al.,* 1999).

In contrast, a study aimed at evaluating the associations between different measures of obesity and prevalent cardiovascular disorders in a large population-based cohort discovered that WHR was independently associated with prevalent of the diseases and provided better discrimination than either BMI or WC (Dagenais *et al.,* 2005). The Dallas Heart study illustrated that WHR was stronger associated with the risk of myocardial infarction and atherosclerosis than BMI (See *et al.,* 2007; Yusuf *et al.,* 2010) and was suggested to be the best measurement of adiposity as it differentiates between central and peripheral body adipose tissue distribution (Canoy, 2008). Other studies comparing obesity

measures using mortality and cardiovascular problems as end-points have shown WC and WHR to perform better than BMI. For example, more than 29,000 men were followed-up during a period of 3 years in a study and reported WHR as a stronger predictor of risk compared with BMI (Wang *et al.*, 2005). Similarly, another study followed nearly 8,000 subjects over the course of 4.5 years and reported that although the upper percentiles of BMI, WC and WHR were all associated with increased relative risk for cardiovascular problems, the magnitude of the association was greater for WC and WHR (Dagenais *et al.*, 2005).

Some Studies of clinical relevance have however contested the superiority of WC over BMI (Wang *et al.,* 2003; Ford *et al.,* 2003). This is seen in a study demonstrating the relation between increased abdominal obesity and adverse clinical consequences, which used measurements of WC made at 14 different anatomic sites and showed that measurements made at the 4 most commonly used sites yielded quite different absolute values for WC (Wang *et al.,* 2003). On the basis of this observation, it was deduced that there is no significant difference in the predictive strengths of BMI and waist indices and it does not seem that knowledge of the WC provides any unique clinical insight and that either the BMI or WC can be used by clinicians (Wang *et al.,* 2003). Also a study has observed that the emphasis on the importance of assessment of abdominal obesity by WC to help identify apparently healthy subjects who are more likely to develop cardiovascular disease (CVD) risk is somewhat paradoxical, given the evidence from the National Health and Nutrition Examination Survey showing that measurements of BMI and WC correlated significantly ($r = 0.9$), regardless of age, gender or ethnicity, stressing that if the 2 measures of excess adiposity are so closely related, it is not immediately apparent why one should be

more indicative of cardiovascular risk than the other (Ford *et al.*, 2003). Evidence obtained from some other studies either equates BMI to Truncal obesity indices or upholds BMI (Haffner *et al.,* 1992; Gautier *et al.,* 1999; Tulloch-Reid *et al.,* 2003; Wang *et al;* 2005). For example, a study among Indian population shows that increases in visceral obesity did not correlate with decreases in insulin-mediated glucose disposal in Pima Indians (Gautier *et al.,* 1999). In a similar study, BMI was the estimate of adiposity with the highest hazard ratio in the prediction of type 2 DM (Tulloch-Reidh *et al.,* 2003). Similarly, a prospective study of Mexican-Americans reported that those patients with the highest baseline plasma glucose and insulin values were most likely to develop type 2 DM independent of differences in age, BMI or central obesity (Haffner *et al.,* 1990). In addition, prospective study in predominantly white population concluded that generalized and abdominal adiposity strongly and independently predicts risk of T_2DM (Wang, 2005). A recent extensive review of several ethnic groups by Ashwell *et al*. (2012) suggested that WHtR, WC and BMI are germane in detecting cardiometabolic risk factor in both sexes, but WHtR was considered as the best predictor, although Onat *et al*. (2009) reported that neck circumference (NC) has a better predictive strength compared to WC. Furthermore, study of obesity trend in a multi-ethnic group has shown that BMI is more strongly associated with blood pressure than abdominal obesity (Seidell *et al.,* 1991). The clustering of dyslipidaemia, hyperuricaemia, DM and hypertension described in whites and Africans was most strongly related to BMI, although the magnitude decreased when adjusted for differences in BMI and abdominal obesity (Schmidt *et al.*, 1996).

A cross sectional study conducted in Zaria, northern Nigeria studied the WC, BMI and its correlation with the blood pressure of a sample of women showed that WC was found to

be a better measure in assessing obesity and thus, cardiovascular risk among the subjects. In the same study, a significant positive correlation however exists between the waist indices and BMI (Achie *et al.,* 2012). Additionally, an observational study on the natives of northern Ibadan, Nigeria, investigated the relationship between two anthropometric measurements for obesity – BMI and WHR and the blood pressure of Nigerians aged 15-85 years. The results showed that WHR and BMI had a similar linear relationship with the blood pressure of the participants (Sanya *et al.,* 2009).

The body adiposity index (BAI) is a relatively newer body adiposity measure which was described and subsequently validated (Bergman *et al*., 2011). It estimates percentage of body adipose tissue in both sexes without numerical correction and has the advantage of not requiring a gender-specific calculation making this surrogate index very convenient for practical use. BAI was proposed by Bergman *et al*. (2011) using a study population of 1,700 Mexican-American. BAI was subsequently validated using dual-energy X-ray absorption measurements of percentage body adipose tissue as a gold standard in a cross-sectional study of 223 African-Americans (Bergman *et al*., 2011). The aim of the validation study was to evaluate BAI in its ability to correlate with other anthropometric variables and adipocytokines, serum lipid profile, indicators of blood glucose regulation and blood pressure. Following the discovery of the BAI, there are studies reporting variation in its discriminatory power for metabolic risk factors. Andreas *et al.*(2013) conducted one of the first studies after the discovery of BAI. According to this study, WHtR was superior to other indexes including BAI in estimation of visceral body adipose tissue, while for the prediction of glucose homeostasis, BAI was weakcompared to BMI and WHtR whose predictive powers were comparable. BAI, BMI, WHtR and WHR all had weak predictive

values for serum lipids and blood pressure but BAI was the weakest. BAI was inferior to BMI, WHtR, and WHR in its correlation with plasma adiponectin concentrations.

Schulze *et al.*(2012), studied approximately 36,368 male and female subjects and showed that BAI was associated more with DM risk compared with BMI, while WC was shown to be the strongest predictor. On the other hand, Talaei *et al.*(2013) studied 2981 individuals of the Iranian population for a period of seven years, showed that WHtR and BMI were better than BAI in the prediction of T2DM. Similarly Rafael de *et al.*(2014) revealed from a study conducted on general and Amerindian population in Brazil that BAI may be suggested as a better risk predictor of T2DM than both BMI and WC in the Amerindian population and in men belonging to the general population. However, in women belonging to the general population, WC was superior toBMI and BAI in the prediction of T2DM. Giliane *et al.*(2015) in a study to assess the performance of BAI among Brazilians concluded that, even though the index has good correlation with total body fat, its performance is weak in subjects with morbid obesity.

A study conducted in Enugu, Nigeria to determine the associations of anthropometric markers of adiposity with atherogenic index of plasma (AIP) found BAI to correlate with AIP. However, it was second to BMI and higher than WHtR, WC and WHR in that hierarchical order of correlation (Antoninus and Elias, 2014).

According to Amato *et al.*(2010), increase in visceral adiposity independently correlated with cardiometabolic risk. Another study that evaluated the applicability of VAI in predicting MetS among Peruvian adults has demonstrated its superiority over most adiposity measures (Knowles *et al.,* 2011). This study found significant association of VAI

with all MetS components, with a stronger association for triglyceride and HDL-C in both genders. However, in the same study, the anthropometric measurement that had the strongest correlation to fasting glucose in both sexes was BMI. Additionally, all the anthropometric indices correlated positively with both SBP and DBP, but WC demonstrated the strongest relationship.

Similarly, Heloisa *et al.* (2015) found that in a sample of 221 Brazilians, VAI had the strongest association with TG, HDL-C and BP but its association with serum glucose was weaker when compared to BMI. According to Heloisa *et al.* (2015), BMI in the general population and in females showed a higher correlation with serum glycaemia. On the other hand, while BMI, WC, WHR were all associated with SBP and DBP in females, VAI did not show significant association with BP. For males, SBP was not significantly associated with any adiposity indicator while DBP was correlated with all indicators. In a study of Amato *et al*. (2010) conducted on a sample of European adults, which suggested VAI as an indicator of the role of visceral adipose tissue, cardiometabolic outcomes correlated with BMI, WC and VAI. VAI was the only measure that showed significant and independent association, while WC and BMI have not shown a significant correlation. Another study by Amato *et al.* (2011) on a sample of Caucasian adults has found a positive continuous correlation of VAI with MetS components. Also, Salomon *et al*. (2011), compared WC with sonographically measured visceral fat in terms of their association with MetS components and reported WC to be a stronger predictor in both sexes. Review of literature on the subject matter indicates that ethnicity critically affects the interrelationships between the various body adiposity measures and MetS components. According to Goh *et al.*(2014), central obesity measures of WC and WHR, are better predictors of risk. WHR was reported

to have a stronger predictive ability than WC and BMI in Caucasian women but in European women, BMI was a better indicator of risk. Ethnicity should be incorporated into routine MetS risk assessment since the same anthropometric obesity measure cannot be used across all ethnic groups (Goh *et al.*,2014).

2.6 Anthropometric Cut- off Values for Metabolic Syndrome in Some Ethnic Groups

The cut-off values of adiposity measures for predicting cardiometabolic risk factors have been redefined based on race and ethnicity (Tullocch *et al.,* 2003; Alberti *et al.*,2006) such that no given cut-off value is universally applicable to all ethnic groups. Consequently, many ethnic groups/races currently have cut-off values specific to their population. In Nigeria and most Sub-saharan African countries, European cut off values are still being improvised due to paucity of specific data. Forexample, it is well established that Asians have relatively higher body fat content for the same adiposity measures compared to other races necessitating a much lower reference value for defining obesity and cardiometabolic risk in their population. Similarly, blacks are reported to have a much lower body fat content for similar adiposity measure compared to Caucasians.

Table 2.1: Ethnic specific cut-off values for waist circumference (Alberti *et al.*, 2006).

Country/ Ethnic group		**Waist circumferences**
Europids In the USA, the ATP III values (102 cm male; 88 cm female) are likely to continue to be used for clinical purposes	Male	≥ 94
	Female	≥ 80
South Asians Based on a Chinese, Malay and Asian-Indian population	Male	≥ 90
	Female	≥ 80
Chinese	Male	≥ 90
	Female	≥ 80
Japanese	Male	≥ 90
	Female	≥ 80
Ethnic South and Central Americans	Use South Asian recommendations until more specific data are specific data are available	
Sub-Saharan Africans	Use European data until more specific data are available	
Eastern Mediterranean and Middle East (Arab) population	Use European data until more specific data are available	

Table 2.2: Reference values of WC and WHR among the Asian and European population (Tullocch-Reid *et al.,* 2003)

Central obesity by abdominal circumference*	
Population	Cutoff
Euroamerican men	≥120 cm (40”)
Euroamerican women	≥ 88 cm (35”)
Asian men	≥ 90 cm (35”)
Asian women	≥ 80 cm (32”)
Central obesity by waist–to-hip ratio	
Men	>0.9
Women	>0.85

Table 2.3: Reference values of BMI among the Asian and European populations (Tullocch-Reid *et al.,* 2003)

Category	**Body mass index**
Underweight	≤18.5
Normal weight	18.5-24.99
Overweight	25-29.99
Obesity class I	30-34.99
Obesity class II	≥35

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Study Area

The study was conducted in the metropolis of Kano State, Nigeria representing urban settlement and three local government areas representing rural settlements, which were randomly selected from the north and south geopolitical zones of Kano State. These Local Governments Areas were Dawakin Tofa, Gabasawa and Wudil. This was to ensure adequate representation of the study population from urban and rural settlements which are believed to have different physical activity profiles. Kano State is located on latitude $12^{o}02^{1}$N, longitude $08^{o}30^{1}$E in the north-western region of Nigeria (Fig.2.1) (Ki – Zerbo, 1998). Kano is the most populous state in Nigeria with a population of over 9 million, a metropolis of 137 km^2 area and consisting of 6 Local Government areas with a population of over 2 million (NPC, 2006). The major inhabitants of Kano are of Hausa and Fulani ethnic groups with minority representing virtually all tribes in Nigeria and a minute fraction of foreigners (Dan-Asabe, 2000).

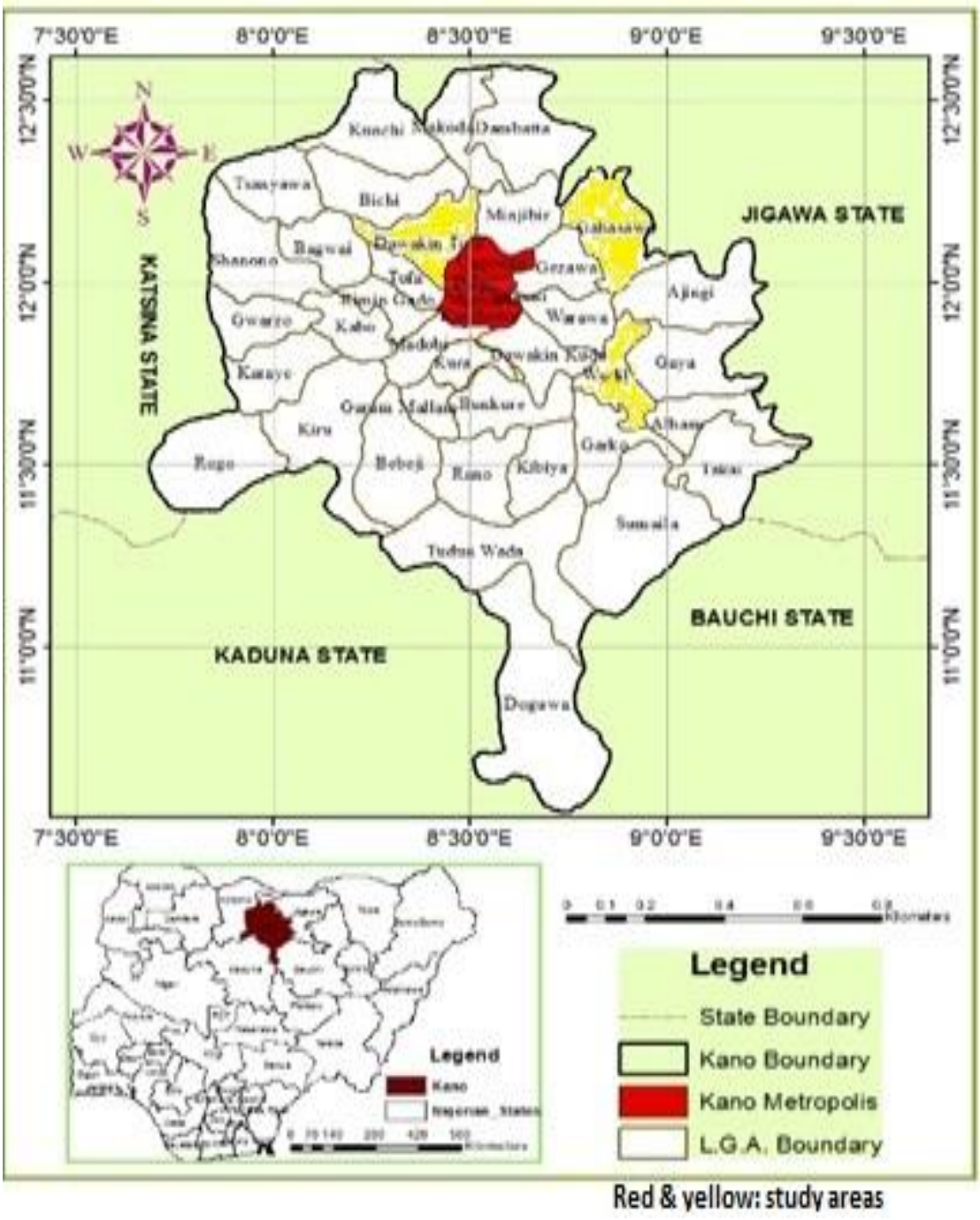


Fig. 3.1: Map of Kano indicating the area of study (Ki - Zerbo, 1998)

3.2 Study Site

The study sites within the metropolis of Kano were the Out Patient Units of the Murtala Muhammad Specialist Hospital (MMSH), Khadija Memorial Hospital and the old campus of Bayero University. For the rural settlements, the study was conducted in the Out Patient Departments of the General Hospitals in the respective Local Government Areas. Murtala Muhammad Specialist Hospital is a secondary health facility that serves the State, Its neighboring States and even some neighboring countries such as Niger, Chad and Cameroon. About 150 patients patronize the Out patient Clinic every working day of the week, while the other General Hospitals are smaller primary or secondary health facilities that serve the surrounding rural communities.

3.3 Study Population

A total of 465 participants who are Hausas of Kano pooled from selected rural and urban communities (based on selection criteria for the study) which comprised of 266 males and 199 females were studied.

In the urban communities, while most males were business men and traders, most of the females were full time house wives. A few subjects belonging to both sexes were however civil servants or students.

In the rural communities, while most males were farmers and cattle rearers, majority of the females were full time house wives. A few subjects belonging to both sexes who were civil servants were either teachers or Local Government workers while a negligible proportion were students.

3.3.1 Inclusion criteria

The inclusion criteria are;

i. Any subject who gave his/her voluntary consent to participate in the study

ii. Subjects must belong to Hausa ethnic origin based on a history of at least 2 parental generation being Hausas of Kano

iii. Subjects must be between the ages of 18 and 68 years. This is to exclude children and elderly subjects, as these may affect anthropometric measurements.

iv. Urban participants must be born in Kano metropolis and must have been living there for at least one decade

3.3.2 Exclusion criteria

The exclusion criteria are;

i. Any subject who refuses to give his/her voluntary consent to participate in the study

ii. Subjects who do not belong to Hausa ethnic origin based on ethnicity criteria

iii. Subjects who are less than 18 years of age and those above 68 years.

iv. Any subject who is on medications known to interfere with any component of the metabolic syndrome.

v. Any subject who is pregnant.

vii. Any subject with pelvic or abdominal space occupying lesion.

viii. Any subject with acquired or congenital structural anomaly of the neck, spine or digits

3.3.3 Informed consent

The procedure, aims and objectives of the study were explained to the participants and a written consent obtained (Appendix II).

3.3.4 Sample size determination

The sample size for study was determined using a standard formula (Lwanga and Lemeshow,1991):

$$n = \frac{Z^2 Pq}{d^2}$$

Where;

n= minimum sample size

Z= standard normal deviation with confidence interval of 95%

p= proportion in the target population (50%) 0.5

q = 1-p, 1-0.5= 0.5

d = sampling error which is 5% (0.05)

$$n = \frac{(1.96)^2 \times 0.5 \times 0.5}{(0.05)^2} = 384$$

384 was therefore the minimum number of subjects needed for the study to allow a meaningful statistical analysis.

3.4 Sampling Technique

The study was a cross-sectional observational study. Systematic random sampling technique was employed in selecting the subjects for this study. During each data collection exercise, the total number of subjects available (daily sample size) was divided by the number of subjects targeted for each day (sample frame) to give a sampling interval. A starting point was then randomly selected and the actual participants were selected by the calculated sample interval. The eligibility of each participant was then assessed using the study selection criteria.

In situations where such subjects were found ineligible, the next eligible subject was recruited. For subjects that were used for serum studies, the procedure for overnight fasting was explained to them and a different appointment was booked for early morning blood sample collection. A semi structured questionnaire wasused to capture biodata, data on sociodemographic characteristics, medical history, blood pressure and anthropometric masurements.

3.5 Ethical Approval

Ethical approval and clearance was obtained from the Ethical Committee of Kano State Health Management Board through the management of Murtala Muhammad Specialist Hospital, Kano in accordance with Helsinki declaration (1952).

3.6 Equipments and Instruments

Digital weighing scale (Seca 769 Digital weighing scale, calibrated in kilograms,USA) was used for measuring body weight.

In-elastic measuring tape (Butterfly model, made in China, graduated in cm, 0-150cm) was used for measuring NC, WC and HC.

Stadiometer (Seca 206IN, Body Meter stadiometer, calibrated in meters, USA) was used for measuring height.

Mercury Sphygmomanometer(SUNMED 420601,USA) was used for blood pressure measurement.

Stethoscope (BOKANG, BK 3003, USA) was used for auscultation of brachial artery

Syringes (5cc) for withdrawing venous blood samples.

Plastic plain sample bottles into which the blood samples were withdrawn.

Ice pack container for preserving the temperature of the blood sample during the period of sample collection and transportation.

Centrifuge (model 800, UK) for centrifuging blood samples.

Micropipette (graduated 0 – 1000 µl, manufactured by HAUWEI, China) for withdrawing and dispensing samples and reagents.

Micropipette (graduated 0 – 100 µl, manufactured by HAUWEI, China) for withdrawing and dispensing samples and reagents.

Microplate reader (NORTEK GENESIS, MR 6000) for reading absorbance.

3.7 Reagents

The reagents/kits used for the estimation of serum glucose, uric acid, adiponectin and lipids were;

Adiponectin kit (manufactured by ELABSCIENCE MED SUPPLIES CORP China) for estimating serum adiponectin.

Spectrum uric acid kit (manufactured by Egyptian Company for Biotechnology, Cairo) for estimating serum uric acid.

Randox glucose kit (manufactured by Randox Laboratory Limited, UK) for estimating serum glucose.

Randox TG kit (manufactured by Randox Laboratory Limited, UK) for estimating serum triglyceride.

Randox HDL-C kit (manufactured by Randox Laboratory Limited, UK) for estimating serum high density lipo-protein cholesterol.

Randox TC kit (manufactured by Randox Laboratory Limited, UK) for estimating serum total cholesterol.

3.8 Methods

3.8.1 Anthropometric measurements

i. **Height**: was measured to the nearest 0.1cm as the vertical distance between the standing surface and the vertex of the head while the subject was standing erect in Frankfort plane and without shoes using a stadiometer (Price *et al.*, 2006) as shown in Plate I

ii. **Weight**: was measured in kilograms using a stadiometer with weighing scale while subject is in light clothes

iii. **Body mass index**: was calculated as body weight divided by the square of the height expressed in meter square

iv. **Waist circumference**: was measured in centimeter with a non-stretchable plastic tape horizontally placed over the abdomen at the narrowest point between the lowest rib and the iliac crest (Lean *et al.*, 1995) as shown in Plate II.

v. **Hip circumference**: was measured while the subject was standing erect with the feet fairly close together; pockets emptied and the tape passed around the point with the maximum circumference over the bottom (Lean *et al.*, 1995) as shown in Plate III.

vi. **Finger length measurements**: Digit lengths was measured on the ventral surface of the hand from the basal crease of the digit to the tip of the finger using a digital sliding caliper (MicroMak, USA) measuring to 0.01mm as shown in plate III and reported on the questionnaire. This measurement has been reported to have high degree of repeatability (Manning *et al*., 1998; Danborno and Danborno, 2015).

vii. **Neck circumference**: was measured in centimeter with a non-stretchable plastic tape horizontally placed over the unclothed neck at the level of the thyroid cartilage (Lean *et al.*, 1995) as shown in Plate IV

Plate I: Technique for measuring height

.

Plate II: Technique for measuring waist and hip circumferences

Body adiposity index was obtained using the formula proposed by Bergman *et al.* (2011). This formula has been shown to be a good measure of central adiposity in some populations (Bergman *et al.*, 2011)

$$\text{Body Adiposity Index (BAI)} = \frac{\text{Hip Circumference (cm)}}{\text{Height (m)}^{1.5}} - 18$$

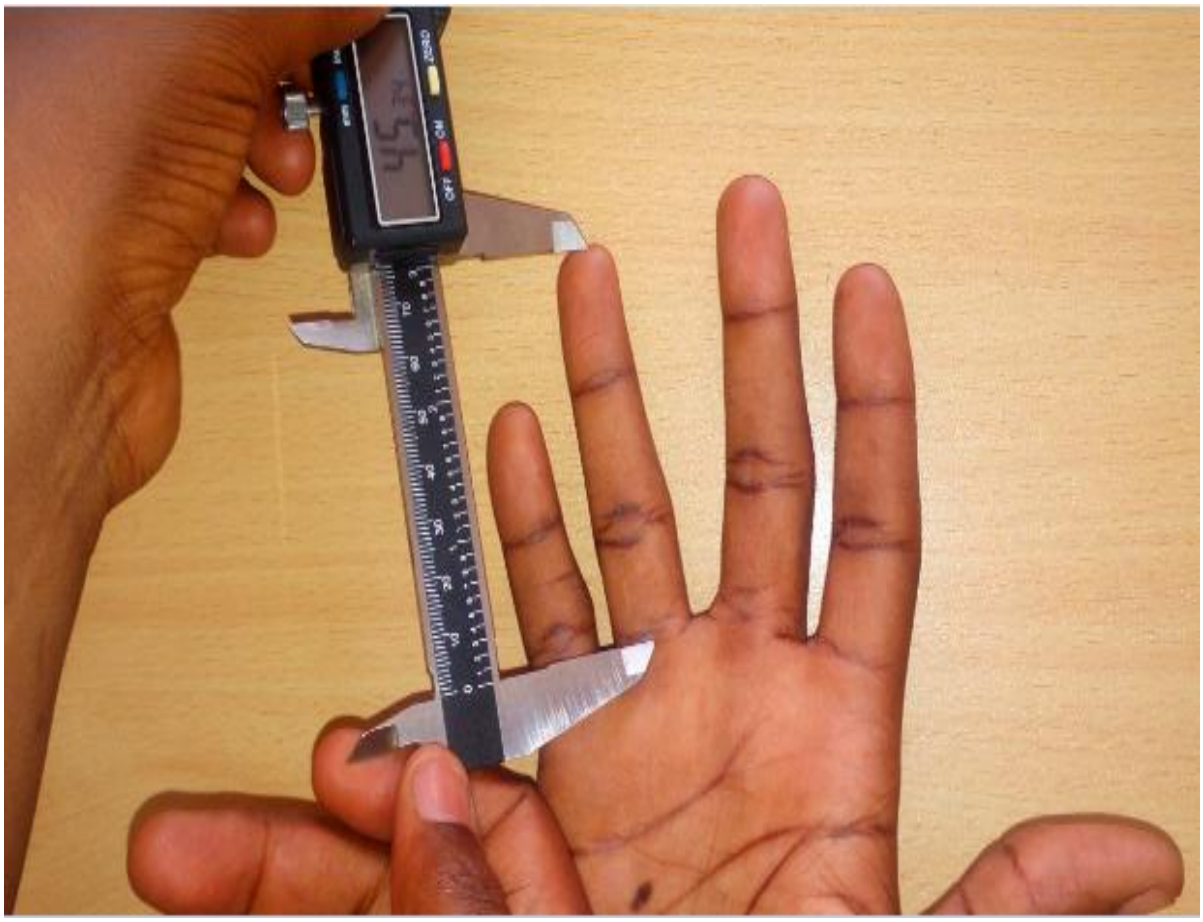


Plate III: Measurement of digit length using digital calliper

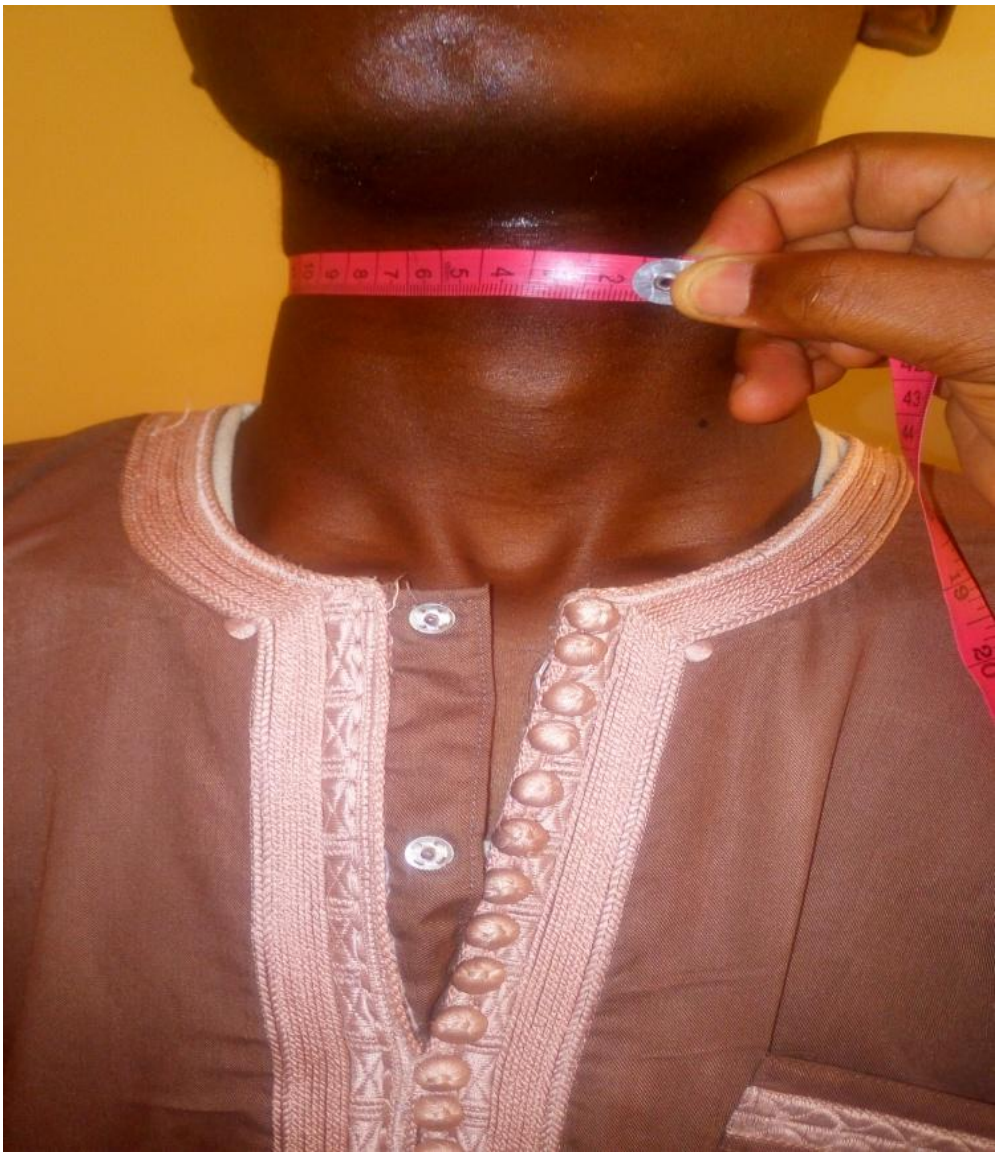


Plate IV: Measurement of neck circumferences

3.9 Measurement of Blood Pressure

A mercury sphygmomanometer was used for measuring blood pressure. Two measurements were taken, and at least 2 minutes was allowed between readings. While the diastolic reading was taken at the level when sounds disappear (Korotkoff phase V), the systolic was taken at the level when it appears (Prisant *et al.*, 1995). The brachial artery was the site of auscultation. Subjects were asked to refrain from smoking or ingesting caffeine for 30 minutes before measurement and the measurement was taken after at least 5 minutes of rest (Haffner *et al.*, 1992).

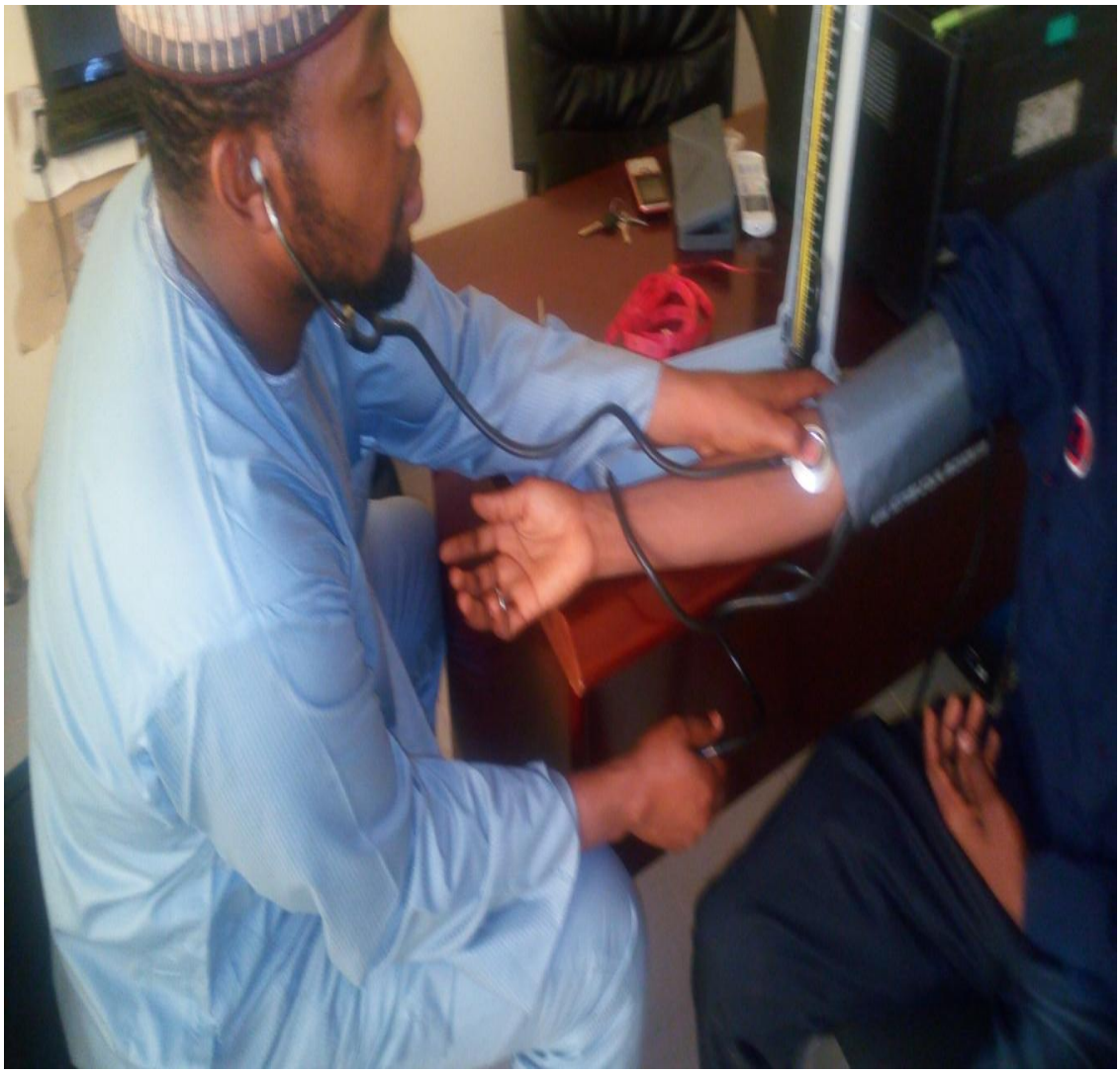


Plate V: Measurement of blood pressure

3.10 Visceral Adiposity Estimation Using Sex Specific Visceral Adiposity Index

Visceral adiposity was estimated as follows (Amato and Giordano, 2014):

$$\boldsymbol{VAI(Male)} = \frac{\boldsymbol{WC}}{39.68 + (1.88 \text{ X BMI})} \times \frac{\boldsymbol{TG}}{\mathbf{1.03}} \times \frac{\mathbf{1.31}}{\boldsymbol{HDL}}$$

$$\boldsymbol{VAI(Female)} = \frac{\boldsymbol{WC}}{36.58 + (1.89 \text{ X BMI})} \times \frac{\boldsymbol{TG}}{\mathbf{0.81}} \times \frac{\mathbf{1.31}}{\boldsymbol{HDL}}$$

Where WC is waist circumference, TG is triglyceride, HDL is high density lipoprotein, BMI is body mass index.

3.11 Assessment of Levels of Physical Activity

The rapid assessment of physical activity (RAPA) questionnaire (Topolski *et al.,* 2006) was administered to participants. Self reported level of PA in the last one year was used to group subjects into seven categories of ascending order of PA. Category I was scored as sedentary, II as under active, III as light PA, IV and V as regular but suboptimal activity, VI and VII as optimal level of PA (see Appendix III).

3.12 Blood Collection and Processing

From each selected subject, 5ml of venous blood sample was collected using a sterile 21G needle fitted with syringe. Blood collection was done during the morning hours to avoid the effect of diurnal variation or circadian rhythm in the blood parameters to be measured. Standard technique of venipuncture and universal safety precaution was employed. Blood sample was transferred into a plain blood specimen bottle and allowed to stand until it was properly clotted. The blood samples were preserved in an ice pack insulating container to preserve the temperature and then transported to the laboratory immediately after each

exercise of sample collection. The samples were then centrifuged at 300 rpm for 5 minutes after which sera were separated and immediately used for assaying blood glucose, lipids (total cholesterol, triglyceride, HDL-C and LDL-C), adiponectin and uric acid. However, on few occasions where the samples could not be analyzed on the same day of collection due to logistic problems, they were kept frozen at -20°C until the following day.

3.13 Laboratory Analytical Methods

3.13.1 Measurement of serum glucose

Serum glucose was measured using enzymatic method of Trinder (1969).

3.13.1.1Principle

Glucose oxidase converts glucose to gluconic acid while peroxidase converts the hydrogen peroxide to water and oxygen which also oxidizes the chromogen (4-aminophenazone) to a pink coloured complex which is measured colorimetrically at 510nm.

$$\text{Glucose} \xrightarrow{\text{Glucose oxidase}} \text{Gluconic acid} + H_2O_2$$

$$H_2O_2 + \text{phenol} \xrightarrow{\text{Hydrogen peroxidase}} H_2O + \text{Oxidised Chromogen}$$

3.13.1.2 Procedure

Into clean test tubes labeled, blank, standard and test, 1ml of glucose reagent was placed. Into the test tubes 10µl of distil water, standard solution and test serum was added to the test tubes respectively. These were then mixed and incubated at 37^0C for 10 minutes, after

which the absorbance (Optical Density) of the test solution and standard was read at 505nm using the blank solution to zero the spectrophotometer.

3.13.1.3 Calculation

The results were calculated as follows:

$$\text{Conc. of test} = \frac{\text{Absorbance of Test} \quad \text{x} \quad \text{Concentration of standard}}{\text{Absorbance of Standard}}$$

Where the concentration of the glucose standard was 5.55 mmol/L (99.9 mg/dl).

3.13.2 Measurement of serum total cholesterol

Serum TC concentrations were measured using enzymatic method by Wybenga *et al.*(1970).

3.13.2.1 Principle

Total Cholesterol (TC) was measured enzymatically in serum in a series of coupled reactions that hydrolyze cholesteryl esters and oxidize the 3-OH group of cholesterol. One of the reaction by-products, H_2O_2 is measured quantitatively in a peroxidase catalyzed reaction that produces a colour. Absorbance was measured at 500 nm. The colour intensity is proportional to cholesterol concentration.

$$\text{Cholesterol ester} \xrightarrow{\text{cholesterol Esteras e}} \text{Cholesterol} + \text{Fatty Acids}$$

$$\text{Cholesterol} + O_2 \xrightarrow{\text{Cholesterol Oxidase}} \text{Cholesterol} - 4\text{en} - 3\text{one} + H_2O_2$$

$$2H_2O_2 + 4\text{AAP} + \text{phenol} \xrightarrow{\text{Peroxides}} \text{Quinoneimine} + 4H_2O \text{ (endpoint) RED}$$

3.13.2.2 Procedure

Three test tubes were labeled as test, standard and blank and to each test tube 1000 µl of the reagent R1 was added. Then 10µl sample was added to test and 10µl standard to standard tube and 10µl distilled water to blank. The content was then mixed well and incubated at room temperature for 15mins. Absorbance was read at a wave length of 530 nm

3.13.2.3 Calculation

The results were calculated as follows:

$$\text{Conc. of test} = \frac{\text{Absorbance of Test}}{\text{Absorbance of standard}} \times \text{Conc. of standard}$$

Where concentration of the total cholesterol standard was 5.17 mmol/L (199mg/dl).

3.13.3 Measurement of serum HDL-cholesterol

Serum HDL-C concentrations were measured using enzymetic method by Wybenga *et al.* (1970).

3.13.3.1 Principle

In the serum chylomicrons, LDL and VLDL are precipitated in the presence of phosphotungustic acid and magnesium chloride and the supernatant is treated as cholesterol.

3.13.3.2 Procedure

Into a clean test tube 0.5ml serum and 0.5 ml HDL reagent were added, mixed and allowed to stand for 10 minutes. It was then centrifuged for 20 minutes at 2000 rpm. Cholesterol reagent, 1ml was dispensed into three cleaned test tubes labeled blank, standard and sample. Supernatant, 50µl was dispensed into sample tube, 50µl of stantadard was dispensed intostandard tube and 50µl of distilled water dispensed into blank tube. All were mixed and incubated at room temperature for 5 min and read at 530 nm.

3.13.3.3 Calculation

The results were calculated as follows:

$$\text{Concentration of test} = \frac{\text{Absorbance of Test} \quad \text{x} \quad \text{Concentration of standard}}{\text{Absorbance of Standard}}$$

Where concentration of the total HDL-cholesterol standard was 1.3 mmol/L (50mg/dl).

3.13.4 Measurement of serum LDL-cholesterol level

Serum LDL-Cholesterol was estimated using Friedewald equation (Friedewald *et al.*, 1972).

3.13.4.1 Procedure

LDL-cholesterol concentrations were calculated from measured values of total cholesterol, triglycerides and HDL-cholesterol according to the Friedewald's equation.

Friedewald Formula:

LDL-Cholesterol =TC-(HDL-C + Triglycerides/2.2) mmol/L.

3.13.5 Measurement of serum triglycerides

Serum TG concentrations were measured using enzymetic method of Wybenga *et al.*(1970).

3.13.5.1 Principle

TG was measured enzymatically using a series of coupled reactions in which triglycerides are hydrolyzed to produce glycerol. Glycerol is then oxidized using glycerol oxidase and H_2O_2, one of the reaction products was then measured as described above for cholesterol. Absorbance was measured at 500 nm.

$$\text{Triglycerides} + H_2O_2 \xrightarrow{\text{Lipoprotein lipase}} \text{Glycerol} + \text{Fatty acid}$$

$$\text{Glycerol} + \text{ATP} \xrightarrow{\text{Glycerol Kinase}} \text{Glycerol} - 3 - \text{phosphate} + \text{ADP}$$

$$\text{Glycerol} - 3 - PO_4 + O_2 \xrightarrow{\text{GPO}} \text{DHAP} + H_2O_2$$

$$H_2O_2 + 4\text{AAP} \xrightarrow{\text{POD}} \text{P} - \text{Chloropheol Red quinoneimine}$$

3.13.5.2 Procedure

Three test tubes were arranged as test, standard and blank tubes. Then 100µl of triglyceride reagent was added into each test tube and 10µl of sample was added into sample tube while 10µl of standard was added into standard tube. The content was mixed and incubated for 5 minutes at 37^0C. The absorbance was read at 520 nm.

3.13.5.3 Calculation

Serum TG concentration was calculated as follows:

$$\text{Concentration of test} = \frac{\text{Absorbance of Test} \quad \text{x} \quad \text{Concentration of standard}}{\text{Absorbance of Standard}}$$

Where concentration of the triglycerides standard was 2.28 mmol/l (201.7mg/dl).

3.13.6 Measurement of serum uric acid

Serum uric acid concentrations were measured using method of Caraway (1955).

3.13.6.1 Principle

Uric acid is oxidized to allantoin and carbon dioxide by phosphotungstic acid in alkaline solution. The phosphotungstic acid is reduced to tungsten blue which is measured at 710nm.

3.13.6.2 Procedure

Into a centrifuge tube, 4ml of water was dispensed followed by 0.5ml of serum, 0.25ml of sulphuric acid and 0.25ml of sodium tungstate. The solution was then mixed and allowed to stand for 5 minutes and then centrifuged. Three tubes were labeled as test, standard and blank and 1.5ml of sample was added to the tube marked- test and 1.5ml working standard into the tube marked- standard. Sodium carbonate, 0.5ml and 0.5ml phosphotungstic acid were added to all test tubes, mixed and allowed to stand for 15 minutes at room temperature and read at 710nm.

3.13.6.3 Calculation

Uric acid concentration was calculated as:

$$\text{Concentration of SUA} = \frac{\text{Absorbance of test} \quad \text{x} \quad \text{Concentration of standard}}{\text{Absorbance of Standard}}$$

Where concentration of the uric acid standard was 0.357mmol/l (6mg/dl)

3.13.7 Measurement of serum adiponectin

Serum adiponectin concentrations were measured using Solid-Phase ELIZA method (Pischon *et al.,* 2003).

3.13.7.1 Principle

The adiponectin assay is a solid – phase ELIZA designed to measure human adiponectin in serum and plasma. It employs the quantitative sandwich enzyme immunoassay principle. The microplate wells which have been coated with an antihuman adiponectin monoclonal antibody and adiponectin in the pretreated sample and in the standardare captured during the first incubation. Washing removes all unbound materials and a biotin conjugated anti-human adiponectin monoclonal antibody binds to the immobilized adiponectin in the wells. After the second wash step, the enzyme streptavidin is added. The addition of O–phenylenediamine as substrate after the third incubation and wash step leads to a calorimetric reaction whose intensity or absorbance is proportional to the adiponectin concentration in the sample.

3.13.7.2 Procedure

First, the sample was pretreated by adding 100µl of protease buffer and 400µl of sample pretreatment buffer to 10µl of sample andthen stirred thoroughly. Dilution buffer, 1ml was added to 10µl of the pretreated sample and then stirred thoroughly under room temperature. Standard and diluted pretreated samples, 50µl each were added to the appropriate wells. The plates were covered with a plate sealer and incubated 1 hour at room temperature. The plates were decanted and stroked against an absorbent towel to remove excess liquid. Washing was done by adding 400µl of wash buffer to each well. The wash buffer was decanted and the plate was stroked against absorbent towel to remove residual liquid. This cycle was repeated for a total of three washes. Biotin labeled monoclonal antibody, 50µl

was then added to each well. The plate was covered with a plate sealer and incubated for 1 hour at room temperature. At this stage, the washing process was repeated and 50µl of the enzyme streptavidin was added to each well and further incubated for 30minutes. The third phase of the wash process was followed immediately. Then,50µl of substrate solution was added to each well and incubated for 10 minutes. Finally, the absorbance was measured within 30 minutes using a microplate reader set at 492nm.

3.14 Statistical Analyses

The data were expressed as mean ± standard deviations.To compare between-group parameters of males and females, left and right hands, mild, moderate and optimal physical activity, variables of urban and rural participants, Student's t-test and one way analysis of variance (ANOVA) were used. For comparism of males and females, left hand and right hand, student t-test was employed while for mild, moderate and optimal PA levels, ANOVA was used. Pearson's correlation was used to test the relationship between the components of the metabolic syndrome with the body adiposity markers and visceral adiposity index. Pearson's correlation was also used to determine the correlation between the digit ratio, obesity indices and MetS components. Regression analyses was employed to generate a model for prediction of components of MetS from adiposity markers and 2D:4D. Receiver operating characteristic (ROC) curves was constructed to determine the cut-off values of the adiposity markers for each MetS components and sensitivity and specificity of the cut-off value determined using the Youden's index. The point classification of area under curve of 1.0-0.9, 0.8-0.7 and 0.6-0.5 were considerd as

excellent, good and poor respectively.SPSS version 20 (IBM Corporation, NY) software was used for statistical analyses and $p < 0.05$ was set as level of significance.

CHAPTER FOUR

4.0 RESULTS

4.1 Sexual Dimorphism in Anthropometric Markers of Adiposity and Digit Ratio

The descriptive statistics (Table 4.1) of the study population in terms of anthropometric indexes of adiposity, digit ratio and BP, showed no statistically significant difference in the mean value of the index of generalized adiposity (BMI) between the male and female subjects. Among the indices of centripetal adiposity, female subjects had significantly ($P < 0.05$) higher HC (88.96cm against 87.01cm, $P < 0.05$), WHtR (0.48 against 0.46 $P < 0.001$). But the BAI and WC showed no statistically significant gender difference. Male subjects had significantly ($P < 0.05$) higher NC (34.9cm to 31.58cm, $P < 0.001$) and WHR (0.89 against 0.85, $P < 0.05$). Both systolic and diastolic componenets of the blood pressure had no statistically significant gender difference. The ratio of the second to fourth digit length was significantly ($P < 0.001$) higher in both hands in females than in males .

Table 4.1: Age, anthropometric indices of adiposity, digit lengths, digit ratio and blood pressure of study participants

	Male (n=266)		**Female (n= 199)**			
Variables	Mean ± SD	Min-max	Mean ± SD	Min-max	t	P Value
Age	34.45± 13.52	18-68	32.06 ± 15.18	18-68	1.79	0.075
Height (cm)	169.15 ± 6.27	142-182.3	158.53 ± 6.83	136.9-175	17.39	<0.0001
Weight (Kg)	63.03 ±12.28	40.5-98.3	55.86 ± 12.99	36-108.9	6.08	<0.0001
BMI (kg/m^2)	21.98 ±3.93	14.52-34.33	22.19 ± 4.70	12.96-39.15	-0.52	0.602
WC (cm)	77.28 ±11.17	57-111	76.02 ± 13.00	51-118.5	1.12	0.261
HC (cm)	87.01 ± 7.80	72.1-109.9	88.96 ± 9.86	65.6-136	-2.38	0.018
NC (cm)	34.99 ± 2.29	30-42	31.58 ± 2.46	26.5-39.5	15.38	<0.0001
W/H	0.89 ± 0.08	0.71-1.11	0.85 ± 0.11	0.65-1.25	3.69	0.00025
W/Ht	0.46 ± 0.06	0.34-0.65	0.48 ± 0.08	0.30-0.72	-3.42	0.00067
BAI	21.60 ± 3.71	13.88-33.90	26.61 ± 4.62	15.38-45.58	-12.95	<0.0001
DBP(mmHg)	82.59 ± 12.37	54-120	84.50 ± 12.99	60-120	-1.61	0.108
SBP(mmHg)	128.07 ± 20.09	90-200	130.66 ± 21.87	95-205	-1.33	0.185
RI (mm)	74.22 ± 5.45	61.17-90.46	67.97 ± 5.02	53.06-79.06	12.64	<0.0001
RII (mm)	72.56 ± 5.09	60.19-87.02	68.94 ± 4.48	55.42-82.09	7.98	<0.0001
RIII (mm)	80.12± 5.44	64.17-97.56	75.53 ± 4.98	63.13-94.26	9.34	<0.0001
RIV (mm)	75.63 ± 5.29	62.84-89.32	69.94 ± 4.51	55.41-85.35	12.21	<0.0001
RV (mm)	62.11 ± 5.31	47.17-85.87	57.60 ± 4.26	44.97-67.32	9.83	<0.0001
R2D:4D	0.96 ± 0.03	0.79-1.05	0.99 ± 0.03	0.86-1.07	-8.39	<0.0001
LI (mm)	74.05 ± 5.36	60.33-87.47	67.77 ± 4.49	55.1-78.83	13.36	<0.0001
LII (mm)	73.32 ± 4.85	60.04-85.81	69.08 ± 4.40	57.19-80.44	9.7	<0.0001
LIII (mm)	80.50 ± 5.61	66.12-96.55	76.23 ±5.56	50.09-98.92	8.15	<0.0001
LIV (mm)	76.03 ± 4.91	62.92-87.81	70.10 ± 4.71	57.45-82.26	13.11	<0.0001
LV (mm)	62.21 ± 5.09	47.46-74.36	57.69 ± 4.88	43.14-75.71	9.63	<0.0001
L2D:4D	0.96 ± 0.03	0.85-1.10	0.99 ± 0.03	0.92-1.09	-7.00	<0.0001

BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, BAI: body adiposity index, DBP: diastolic blood pressure, SBP: systolic blood pressure, I: first digit, II: second digit, III: third digit, IV: fourth digit, V: fifth digit, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio.

The serum concentration (Table 4.2) of adiponectin and uric acid showed no statistically significant sex difference. The fasting serum concentration of glucose, TC, HDL were however significantly higher in female subjects, (FBG $P < 0.002$, TC $P < 0.005$ and HDL $P < 0.002$). For TG and LDL, there was no significant sex difference in their mean values. Visceral adipose tissue measured by VAI was significantly higher in female subjects ($P < 0.002$).

Table 4.2: Serum parameters of MetS and VAI.

Variable	Male (n=120)		Female (n= 41)		t	P value
	Mean ± SD	Min-max	Mean ± SD	Min-max		
Uric Acid (mg/dl)	5.51 ± 1.95	3.1-11.3	6.03 ± 2.42	2.9-10.10	-1.38	0.170
Adiponectin (µg/ml)	23.28 ± 5.96	7.8-33.90	22.55 ± 7.45	14.4-33.9	0.63	0.520
Fasting Glucose (mg/dl)	84.67 ± 24.73	53.6-187.2	100.63 ± 34.90	54.6-176.4	-3.19	0.002
T.Cholesterol (mg/dl)	174.35 ± 32.31	123.7-256.10	187.32 ± 43.85	127.3-290.7	-2.02	0.045
HDL– Cholesterol (mg/dl)	44.10 ± 6.32	28-54.10	47.83 ± 6.71	38.9-60.6	-3.21	0.002
Triglyceride (mg/dl)	117.18 ± 31.76	74.3-196.5	121.83 ± 29.25	80.4-165	-0.83	0.41
LDL– Cholesterol (mg/dl)	106.81 ± 32.44	58.14-192.82	115.12 ± 44.05	54.36-214.46	-1.29	0.200
VAI	3.51 ± 1.71	1.67-9.10	4.46 ± 1.75	2.11-7.56	-3.03	0.003

FBG: fasting blood glucose, TC: total cholesterol, HDL – C: high density lipoprotein cholesterol, TG: triglyceride, LDL – C: low density lipoprotein cholesterol, VAI: visceral adiposity index

4.2 Effect of Urbanization on Adiposity Indices, Digit Ratio and MetS

It was observed (Table 4.3) that significantly ($P < 0.05$) higher measures of anthropometric indices of adiposity, blood pressure and digit ratio were noted in the urban compared to rural settlers. The effect of urbanization on the central measures of adiposity appears higher than that of generalized adiposity in both sexes. Compared to males, it was observed that urbanization had a higher advers effect on the general and central adiposity measures and BP of females.

Table 4.3: Effect of urbanization on anthropometric indices of adiposity, digit lengths, digit ratio and blood pressure

	All			Male			Female		
	Rural	Urban	t	Rural	Urban	t	Rural	Urban	t
Variables	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
Height (cm)	164.23 ± 8.25	164.95 ± 8.48	-0.93	168.59 ± 6.56	169.65 ± 5.98	-1.38	158.61 ± 6.67	158.45 ± 7.01	0.17
Weight (Kg)	54.53 ± 9.94	64.93 ± 13.61	-9.32**	59.1 ± 9.06	66.52 ± 13.66	-5.15**	48.65 ± 7.7	62.72 ± 13.3	-9.08**
BMI	20.16 ± 3.01	23.83 ± 4.5	-10.24**	20.79 ± 3.03	23.04 ± 4.32	-4.86**	19.34 ± 2.81	24.91 ± 4.53	-10.37**
WC (cm)	69.7 ± 7.91	83.18 ± 11.46	-14.63**	71.38 ± 7.4	82.52 ± 11.36	-9.35**	67.53 ± 8.06	84.09 ± 11.6	-11.64**
HC (cm)	86.26 ± 7.46	89.29 ± 9.63	-3.77**	85.53 ± 6.47	88.33 ± 8.62	-2.97*	87.22 ± 8.52	90.63 ± 10.77	-2.47*
NC (cm)	32.47 ± 2.58	34.5 ± 2.85	-8.02**	34.15 ± 1.71	35.73 ± 2.49	-5.93**	30.3 ± 1.76	32.8 ± 2.41	-8.31**
W/H	0.81 ± 0.06	0.93 ± 0.07	-18.95**	0.83 ± 0.05	0.93 ± 0.07	-13.31**	0.78 ± 0.07	0.93 ± 0.08	-14.47**
W/Ht	0.42 ± 0.05	0.51 ± 0.07	-14.45**	0.42 ± 0.04	0.49 ± 0.07	-9.11**	0.43 ± 0.05	0.53 ± 0.07	-12.28**
BAI	23.14 ± 4.33	24.3 ± 5.15	-2.61*	21.14 ± 3.32	22.01 ± 3.99	-1.92	25.72 ± 4.14	27.45 ± 4.91	-2.70*
DBP (mmHg)	75.66 ± 8.4	90.49 ± 11.73	-15.54**	75.88 ± 9.27	88.54 ± 11.74	-9.67**	75.37 ± 7.16	93.18 ± 11.22	-13.27**
SBP (mmHg)	114.87 ± 10.59	142.25 ± 19.35	-18.67**	115.42 ± 12.31	139.28 ± 18.97	-12**	114.16 ± 7.85	146.35 ± 19.21	-15.33**
RI (mm)	70.9 ± 5.59	72.14 ± 6.5	-2.19*	72.86 ± 5.46	75.42 ± 5.17	-3.93**	68.37 ± 4.69	67.59 ± 5.31	1.1
RII(mm)	70.74 ±5.5	71.25 ± 4.81	-1.07	72.16 ± 5.67	72.91 ± 4.51	-1.2	68.92 ± 4.71	68.96 ± 4.26	-0.07
RIII(mm)	77.86 ± 5.97	78.43 ± 5.47	-1.08	79.47 ± 6.11	80.7 ± 4.71	-1.86	75.78 ± 5.12	75.28 ± 4.86	0.71
RIV(mm)	73.74 ± 6.01	72.7 ± 5.38	1.98*	76.28 ± 5.73	75.06 ± 4.81	1.89**	70.48 ± 4.64	69.43 ± 4.34	1.64*
RV(mm)	59.9 ± 5.28	60.43 ± 5.45	-1.07	61.47 ± 5.48	62.67 ± 5.1	-1.85	57.87 ± 4.23	57.34 ± 4.29	0.87
R2D:4D	0.96 ± 0.04	0.98 ± 0.03	-6.58**	0.95 ± 0.03	0.97 ± 0.03	-6.64**	0.98 ± 0.04	0.99 ± 0.03	-3.45*
LI (mm)	70.52 ± 5.29	72.12 ± 6.3	-2.95*	72.62 ± 5.25	75.31 ± 5.16	-4.22**	67.83 ± 3.98	67.72 ± 4.96	0.17
LII(mm)	71.16 ± 5.42	71.83 ± 4.8	-1.43	72.85 ± 5.45	73.74 ± 4.23	-1.49	68.97 ± 4.55	69.19 ± 4.27	-0.36
LIII(mm)	78.55 ± 6.22	78.79 ± 5.73	-0.42	79.95 ± 6.14	80.98 ± 5.06	-1.5	76.75 ± 5.88	75.75 ± 5.22	1.26
LIV(mm)	73.83 ± 5.95	73.19 ± 5.35	1.21*	76.35 ± 5.58	75.75 ± 4.22	0.99	70.58 ± 4.71	69.65 ± 4.69	1.39
LV(mm)	60.09 ± 5.43	60.44 ± 5.52	-0.7	61.66 ± 5.62	62.69 ± 4.53	-1.66	58.07 ± 4.43	57.34 ± 5.27	1.06
L2D:4D	0.96 ± 0.03	0.98 ± 0.03	-5.78*	0.95 ± 0.04	0.97 ± 0.03	-4.67*	0.98 ± 0.03	0.99 ± 0.03	-4.17*

* P < 0.05, **P < 0.001, BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, BAI: body adiposity index, DBP: diastolic blood pressure, SBP: systolic blood pressure, I: first digit, II: second digit, III: third digit, IV: fourth digit, V: fifth digit, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio. SD: standard deviation

Urbanization was observed (Figures 4.1 to 4.8) to have an adverse effect on all the serum components of MetS and VAI. There were significantly higher values of FBG, TC, TG, and LDL in urban participants compared to subjects from rural areas. Also VAI was observed to be significantly higher in urban dwellers. HDL was however observed to be lower in the urban participants. While SUA was seen to be higher in urban participants, adiponectin was higher in rural subjects. In the general study population as well as in both males and females, SUA was observed to be significantly ($P < 0.001$) higher in the urban participants compared to participants from rural areas.

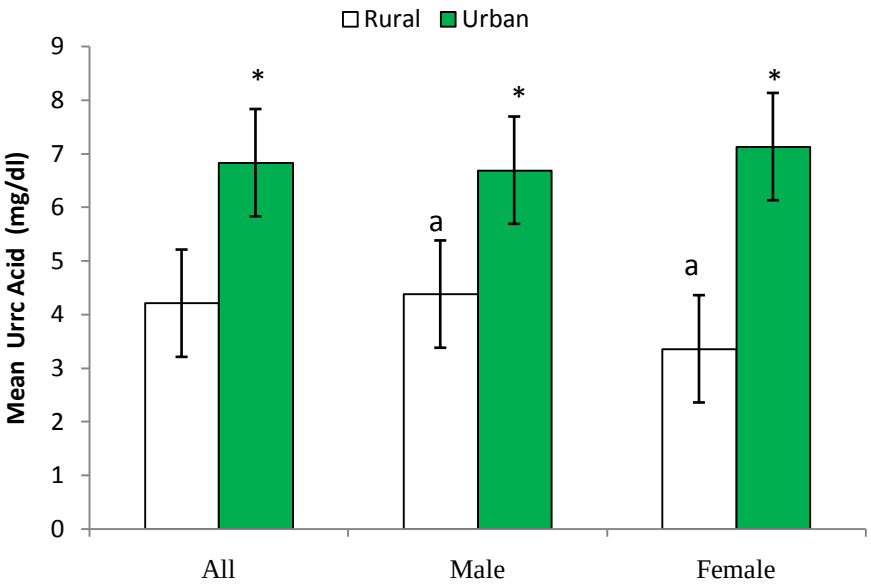


Figure 4.1: Effect of urbanization on the uric acid (* indicates P <0.05 between urban and rural subgroups & similar letter superscript indicates P < 0.05 between sexes for urban and rural groups)

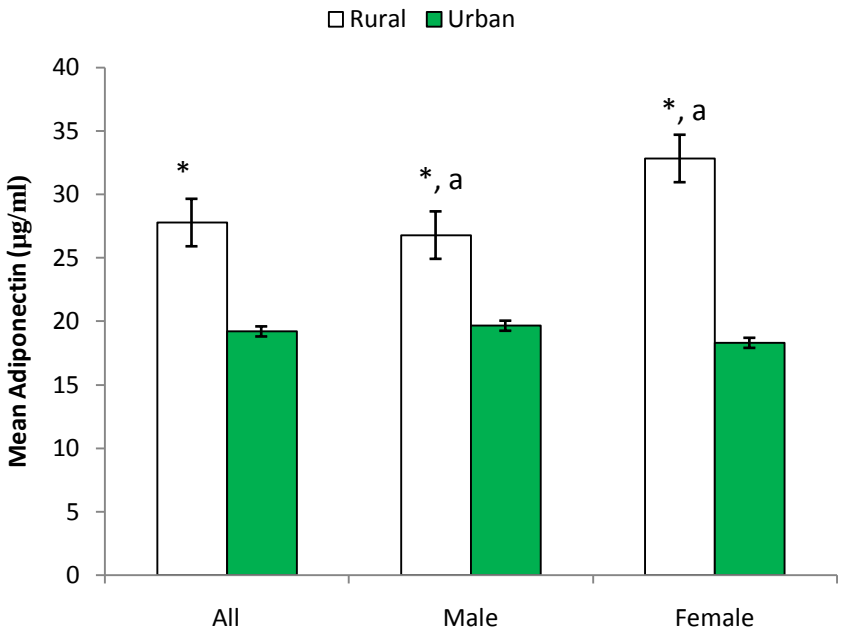


Figure 4.2: Effect of urbanization on serum adiponectin (* indicates P <0.05 between urban and rural subgroups & similar letter superscript indicates P < 0.05 between sexes for urban and rural groups)

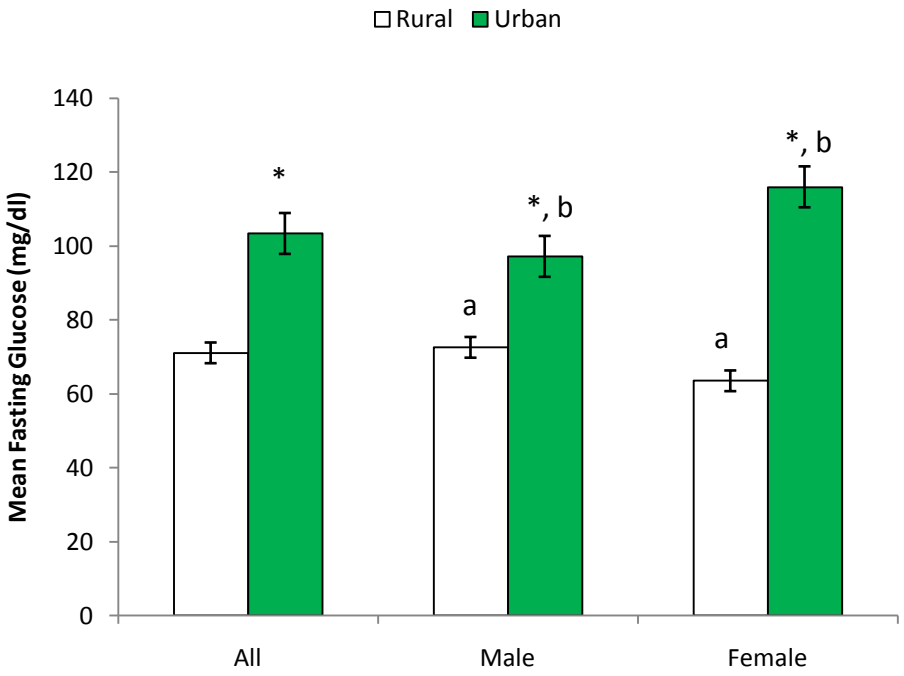


Figure 4.3: Effect of urbanization on serum glucose (* indicates P <0.05 between urban and rural subgroups & similar letter superscript indicates P < 0.05 between sexes for urban and rural groups)

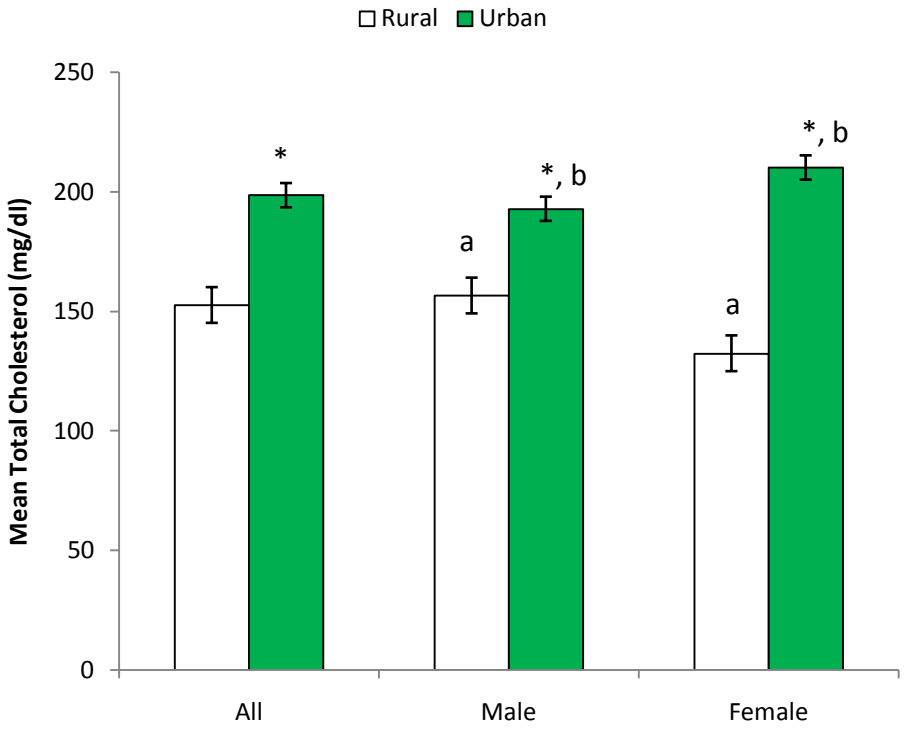


Figure 4.4: Effect of urbanization on serum total cholesterol (* indicates P <0.05 between urban and rural subgroups & similar letter superscript indicates P < 0.05 between sexes for urban and rural groups)

.

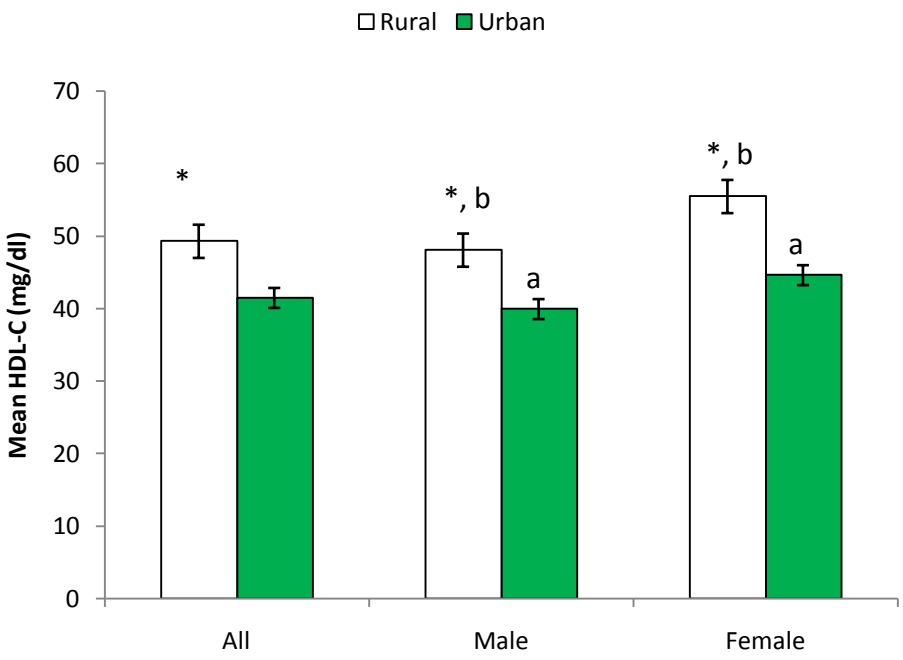


Figure 4.5: Effect of urbanization on serum HDL–C (* indicates P <0.05 between urban and rural subgroups & similar letter superscript indicates P < 0.05 between sexes for urban and rural groups)

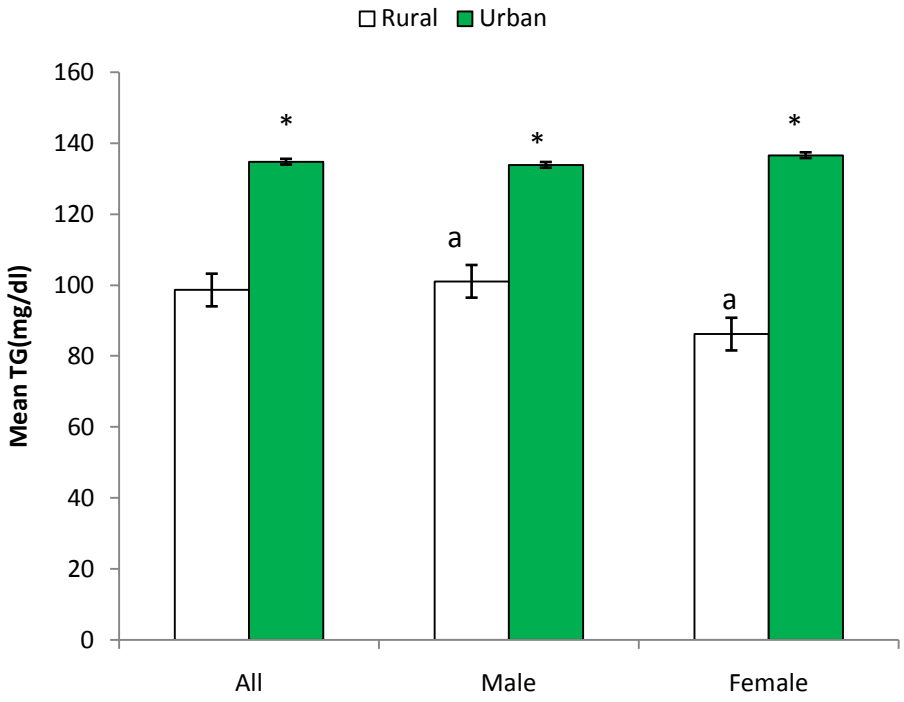


Figure 4.6: Effect of urbanization on serum TG (* indicates P <0.05 between urban and rural within subgroups & similar letter superscript indicates P < 0.05 between sexes for urban and rural groups)

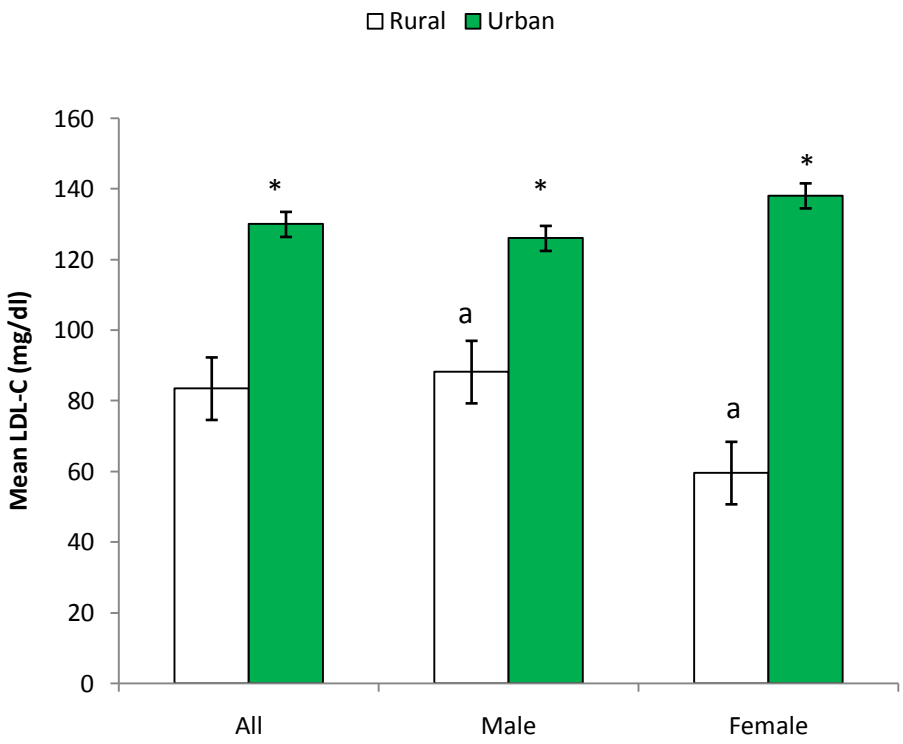


Figure 4.7: Effect of urbanization on serum LDL–C (* indicates P <0.05 between urban and rural subgroups & similar letter superscript indicates P < 0.05 between sexes for urban and rural groups)

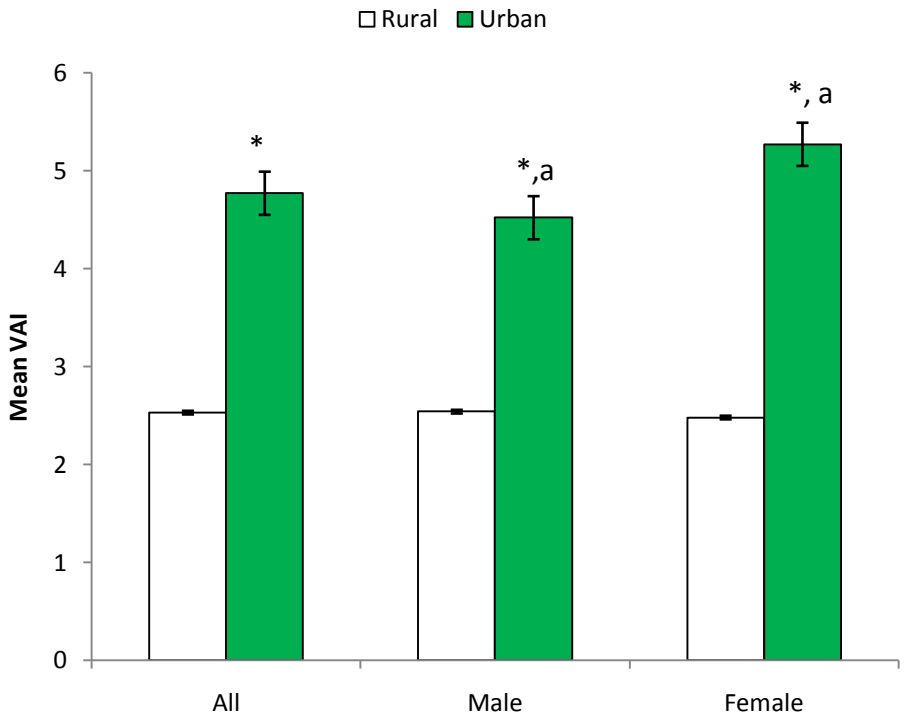


Figure 4.8: Effect of urbanization on the visceral adiposity index (VAI) (* indicates P <0.05 between urban and rural subgroups & similar letter superscript indicate P < 0.05 between sexes for urban and rural groups)

4.3 Correlation Analyses

Among the anthropometric indices of adiposity (Table 4.4), BMI showed a positive and significant correlation with all the serum components of MetS (r = 0.31, 0.43, 0.39 0.42) for FBG, TC, TG and LDL respectively, except HDL with which it showed a negative but significant correlation (r = - 0.28). Its correlation with the biomarkers of MetSwas positive for serum uric acid (r = 0.31) and negative for adiponectin (r = - 0.39). However, both were stastically significant ($P < 0.05$). BMI correlated positively and significantly with both SBP (r = 0.42) and DBP (r = 0.46). The pearsons coefficient (r) showed that, among the serum parameters of MetS, BMI had the strongest correlation with TC (r = 0.43) and LDL-C (r = 0.42) and weakest correlation with HDL-C. Its strength of correlation was similar for both components of BP and for SUA and adiponectin.BMI also correlated positively with VAI (r = 0.38)

Compared to BMI, WC showed a stronger but similar pattern of correlation with all MetS components. It had a strong positive and significant correlation with all the serum componenets of MetS. (r = 0.5, 0.62, 0.58, 0.61) for FBG, TC, TG and LDL respectively, but HDL showed a negative and significant correlation (r = - 0.48). Its correlation with the biomarkers of MetS was positive for serum uric acid (r = 0.54) and negative for adiponectin (r = - 0.58). WC correlated possitively and significantly with both SBP (r = 0.57) and DBP (r = 0.57). For the serum parameters of MetS, WC also had the strongest correlation with TC while the weakest correlation was with HDL-C. Pearsons correlation coefficient of WC with BP was similar for SBP and DBP and was also similar for SUA and adiponectin. WC also had a stong and positive correlation with VAI (r = 0.64).

BAI, HC and NC relatively showed weaker correlation with MetS components. The weakest was HC which showed a very weak correlation with DBP (r = 0.20), SBP (r = 0.14), TC (r = 0.16). No significant correlation was observed between HC and SUA, adiponectin, FBG, HDL, TG, and LDL. The correlation of HC with VAI was also weak (r = 0.19). BAI had no significant correlation with serum biomarkers and HDL. Its correlation with FBG, TC, LDL and TG were relatively weak, withits highest coefficient of correlation observed for TC (r = 0.20). Its correlation with VAI (r = 0.26) was also weak when compared with BMI and WC. NC like HC and BAI showed a weak correlation with MetS parameters, but its correlation coefficient with all the components of MetS was higher than observed for BAI and HC. WHtR correlated positively and strongly with DBP, SBP and all serum parameters except HDL and adiponectin with which it showed significant negative correlation. The correlation coeficient of WHtR with MetS components was slightly higher than that of WC except for HDL and DBP where the correlation of WC was stronger.WHtR showed a positive and significant correlation with VAI and its strength of correlation with VAI (r = 0..67) was similar to that of WC (r = 0.64).

Putting all the anthropometric adiposity indices together, WHR showed the strongest correlation with pressure and serum components of MetS. Higher and similar correlations of WHR were observed for SUA (r = 0.84), adiponectin (r = -0.83), TC (r = 0.83), LDL (r = 0.84) and VAI (r =0.83). Comparing the index of visceral adiposity with all the anthropometric indexes, higher correlation coefficients were observed between VAI and all the parameters of MetS. However, the correlation strength of WHR was close to that of

VAI. Digit ratio showed a significant positive correlation with DBP, SBP, SUA, FBG, TC, TG and LDL but a negative correlation was observed for adiponectin and HDL. The correlation of digit ratio with MetS componenets was weaker compared to WC, WHtR and WHR. However, in terms of its correlation with MetS biomarkers, it was slightly stronger than that for WC and WHtR but slightly weaker than WHR. Digit ratio also showed stronger correlations with MetS compared to BMI, NC, HC and BAI but BMI had a stronger correlation with both SBP and DBP.Significant positive correlation of digit ratio with VAI was also observed in both hands. This correlation was stronger than observed for BMI, NC, HC and BAI but weaker than for WC, WHtR and WHR. Comparing the correlation coefficients of the digit ratio of both hands, the R2D:4D showed stronger correlation with BP, MetS biomarkers, FBG and HDL compared to L2D:4D.

Table 4.4: Correlation between anthropometric and visceral markers of adiposity, digit length and digit ratio with MetS components in the general population

Variables	DBP (mmHg)	SBP (mmHg)	SUA (mg/dl)	Adiponectin (µg/ml)	FBG (mg/dl)	TC (mg/dl)	HDL–C (mg/dl)	TGR (mg/dl)	LDL–C (mg/dl)	VAI
Age (years)	0.393**	0.572**	0.604**	-0.594**	0.640**	0.593**	-0.489**	0.534**	0.592**	0.592**
Height(cm)	0.062	-0.058	-0.103	0.073	-0.190*	-0.110	-0.080	-0.104	-0.078	-0.15
Weight (Kg)	0.443**	0.352**	0.257**	-0.337**	0.214**	0.362**	-0.310**	0.330**	0.363**	0.296**
BMI (kg/m^2	0.468**	0.427**	0.314**	-0.397**	0.318**	0.434**	-0.287**	0.396**	0.420**	0.380**
WC (cm)	0.573**	0.578**	0.540**	-0.582**	0.502**	0.626**	-0.482**	0.586**	0.615**	0.644**
HC (cm)	0.208**	0.114*	0.0458	-0.114	0.061	0.166*	0.004	0.139	0.141	0.199*
NC (cm)	0.303**	0.270**	0.294**	-0.364**	0.177*	0.357**	-0.502**	0.399**	0.381**	0.318**
W/H	0.638**	0.739**	0.841**	-0.834**	0.760**	0.837**	-0.791**	0.805**	0.845**	0.834**
W/Ht	0.561**	0.609**	0.558**	-0.593**	0.553**	0.643**	-0.442**	0.602**	0.622**	0.675**
BAI	0.142**	0.139**	0.098	-0.141	0.172*	0.205**	0.058	0.178*	0.164*	0.261**
RI (mm)	0.060	-0.033	-0.054	-0.037	-0.119	-0.037	-0.148	-0.022	-0.005	-0.086
RII(mm)	0.077	-0.004	0.101	-0.199*	0.011	0.079	-0.232**	0.055	0.11	0.028
RIII(mm)	0.011	-0.083	0.0005	-0.049	-0.131	-0.057	-0.083	-0.076	-0.029	-0.092
RIV(mm)	-0.105*	-0.203**	-0.203**	0.131	-0.285**	-0.208**	0.0299	-0.192*	-0.181*	-0.256**
RV(mm)	0.028	-0.066	-0.046	-0.045	-0.111	-0.102	-0.118	-0.125	-0.059	-0.15
R2D:4D	0.373**	0.425**	0.596**	-0.634**	0.588**	0.563**	-0.494**	0.485**	0.572**	0.563**
LI (mm)	0.093*	0.012	0.0425	-0.108	-0.053	0.011	-0.217**	0.027	0.046	-0.022
LII(mm)	0.070	0.008	0.0781	-0.178*	-0.017	0.065	-0.224**	0.050	0.098	0.010
LIII(mm)	-0.018	-0.093*	0.014	-0.089	-0.080	-0.032	-0.121	-0.038	-0.002	-0.06
LIV(mm)	-0.091*	-0.180**	-0.170*	0.094	-0.272**	-0.208**	-0.013	-.173*	-0.176*	-0.252**
LV(mm)	0.032	-0.050	-0.038	-0.066	-0.098	-0.056	-0.129	-0.093	-0.01	-0.127
L2D:4D	0.345**	0.420**	0.535**	-0.572**	0.560**	0.594**	-0.428**	0.485**	0.591**	0.574**
VAI	0.795**	0.866**	0.886**	-0.854**	0.860**	0.901**	-0.809**	0.937**	0.891**	
DBP (mmHg)		0.791**	0.811**	-0.822**	0.785**	0.771**	-0.714**	0.725**	0.779**	0.795**
SBP (mmHg)	0.791**		0.889**	-0.882**	0.897**	0.838**	-0.788**	0.789**	0.849**	0.866**

*** P <0.05, ** P <0.001**,BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, BAI: body adiposity index, DBP: diastolic blood pressure, SBP: systolic blood pressure, I: first digit, II: second digit, III: third digit, IV: fourth digit, V: fifth digit, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio, FBG: fasting blood glucose, TC: total cholesterol, HDL – c: high density lipoprotein cholesterol, TG: triglyceride, LDL – c: low density lipoprotein cholesterol, VAI: visceral adiposity index

In both males and females (Tables 4.5 and 4.6), the anthropometric adiposity markers and 2D:4D correlated with MetS components in a similar pattern of varying strength. In that, while all the indices correlated positively with DBP, SBP, FBG, SUA, TC, TG and LDL-C, they showed a negative correlation with adiponectin and HDL-C. HC showed only a weak correlation with both SBP and DBP in males, and with only DBP in females. Its correlation with DBP is stronger in males. The correlation of BMI with all MetS parameters was stronger in females. Also, in female subjects, the WC had higher correlation with TC, TG and LDL while in males, it had higher correlation with SUA, adiponectin, FBG and HDL-C. The correlation of WC with VAI was similar in both sexes. The correlation coefficient of NC for the MetS indicators was similar for males and females. However, it had a slightly higher correlation with the serum biomarkers in males. Also, NC had no significant correlation with FBG in female subjects. While WHR showed comparable correlation with MetS in both sexes, WHtR showed higher correlation among females. In both sexes, BAI correlated weakly with some of the MetS components. Correlating with DBP in females, in males, BAI correlated with SBP, TC, and TG. VAI showed weak and similar correlation with BAI in both sexes. Comparison of the correlation of digit ratio with MetS between males and females shows that the R2D:4D in both sexes had similar correlation strength with HDL-C, FBG and VAI. However, its correlation with the serum biomarkers, TC, TG and LDL-C was stronger in female subjects. Also, DBP and SBP correlated better with R2D:4D in males. For the L2D:4D, higher correlation with MetS componenets were observed in females, except for the pressure componenets of MetS where the coefficient of correlation was very similar. In each gender, the R2D:4D had higher correlation with MetS

indicators when compared with the L2D:4D. In females, 2D:4D had weaker correlation with body adiposity measure when compared to males.

Table 4.5: Correlation between anthropometric and visceral markers of adiposity, Digit length and digit ratio with MetS components in male subjects

Variables	DBP (mmHg)	SBP (mmHg)	SUA (mg/dl)	Adiponectin (µg/ml)	FBG (mg/dl)	TC (mg/dl)	HDL –C (mg/dl)	TGR (mg/dl)	LDL –C (mg/dl)	VAI
Age (years)	0.263**	0.477**	0.532**	-0.494**	0.540**	0.483**	-0.389**	0.334**	0.533**	0.692**
Height(cm)	0.262*	0.125*	0.082	0.066	0.005	0.105	0.006	0.115	0.093	0.049
Weight (Kg)	0.409**	0.381**	0.262**	-0.272**	0.246**	0.333**	-0.308**	0.331**	0.326**	0.319**
BMI (kg/m^2	0.331**	0.356**	0.289**	-0.300**	0.247**	0.372**	-0.332**	0.379**	0.361**	0.339**
WC (cm)	0.543**	0.611**	0.552**	-0.573**	0.522**	0.590**	-0.600**	0.600**	0.587**	0.635**
HC (cm)	0.229**	0.225**	0.069	-0.129	0.071	0.133	-0.142	0.173	0.126	0.175
NC (cm)	0.402**	0.396**	0.446**	-0.474**	0.443**	0.503**	-0.489**	0.505**	0.497**	0.512**
W/H	0.657**	0.777**	0.830**	-0.802**	0.774**	0.816**	-0.823**	0.789**	0.819**	0.844**
W/Ht	0.486**	0.595**	0.573**	-0.591**	0.524**	0.615**	-0.616**	0.631**	0.609**	0.648**
BAI	0.061	0.138*	0.107	-0.158	0.068	0.181*	-0.167	0.230*	0.168	0.193*
RI (mm)	0.215**	0.0879	-0.048	-0.027	-0.047	-0.051	-0.016	-0.044	-0.038	-0.011
RII(mm)	0.200**	0.127*	0.229*	-0.286**	0.212*	0.150	-0.214*	0.101	0.171	0.174
RIII(mm)	0.139*	0.049	0.104	-0.138	0.040	0.006	-0.071	-0.028	0.025	0.0278
RIV(mm)	-0.033	-0.143*	-0.098	0.061	-0.122	-0.132	0.120	-0.152	-0.125	-0.131
RV(mm)	0.211**	0.081	0.055	-0.134	0.045	-0.022	-0.054	-0.100	0.008	-0.021
R2D:4D	0.461**	0.544**	0.574**	-0.606**	0.586**	0.493**	-0.585**	0.446**	0.518**	0.535**
LI (mm)	0.259**	0.149*	0.074	-0.126	0.048	0.021	-0.112	0.023	0.038	0.085
LII(mm)	0.189**	0.133*	0.185*	-0.258**	0.185*	0.135	-0.194*	0.092	0.154	0.151
LIII(mm)	0.136*	0.0262	0.106	-0.157	0.078	0.023	-0.081	-0.002	0.039	0.053
LIV(mm)	-0.009	-0.099	-0.067	0.020	-0.077	-0.118	0.079	-0.126	-0.108	-0.104
LV(mm)	0.202**	0.054	0.075	-0.146	0.087	0.021637	-0.060	-0.069	0.046	0.0115
L2D:4D	0.366**	0.432**	0.489**	-0.545**	0.508**	0.491**	-0.526**	0.423**	0.508**	0.492**
VAI	0.777**	0.877**	0.905**	-0.870**	0.910**	0.908**	-0.917**	0.944**	0.898**	
DBP		0.801**	0.789**	-0.804**	0.809**	0.746**	-0.770**	0.690**	0.758**	0.777**
SBP (mmHg)	0.801**		0.891**	-0.884**	0.897**	0.831**	-0.875**	0.777**	0.846**	0.877**

*** P <0.05, ** P <0.001,** BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, BAI: body adiposity index, DBP: diastolic blood pressure, SBP: systolic blood pressure, I: first digit, II: second digit, III: third digit, IV: fourth digit, V: fifth digit, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio, FBG: fasting blood glucose, TC: total cholesterol, HDL–C: high density lipoprotein cholesterol, TG: triglyceride, LDL–C: low density lipoprotein cholesterol, VAI: visceral adiposity index

Table 4.6: Correlation between anthropometric and visceral markers of adiposity, digit length and digit ratio with MetS components in female subjects

Variables	**DBP (mmHg)**	**SBP (mmHg)**	**SUA (mg/dl)**	**Adiponectin (µg/ml)**	**FBG (mg/dl)**	**TC (mg/dl)**	**HDL–C (mg/dl)**	**TGR (mg/dl)**	**LDL –C (mg/dl)**	**VAI**
Age (years)	0.273**	0.482**	0.504**	-0.394**	0.550**	0.473**	-0.389**	0.334**	0.692**	0.492**
Height(cm)	-0.001	-0.196**	0.017	0.030	-0.119	0.122	0.157	-0.006	0.098	0.062
Weight (Kg)	0.572**	0.387**	0.287	-0.488**	0.249	0.482**	-0.272	0.367*	0.472**	0.356*
BMI (kg/m^2)	0.616**	0.501**	0.328*	-0.596**	0.359*	0.508**	-0.397*	0.431**	0.509**	0.387*
WC (cm)	0.621**	0.555**	0.490**	-0.612**	0.399**	0.662**	-0.472**	0.563**	0.656**	0.611**
HC (cm)	0.177*	-0.004	-0.081	-0.059	-0.138	0.121	0.081	0.015	0.106	0.072
NC (cm)	0.458**	0.355**	0.302	-0.394*	0.177	0.534**	-0.343*	0.473**	0.521**	0.519**
W/H	0.679**	0.758**	0.872**	-0.901**	0.792**	0.902**	-0.825**	0.866**	0.908**	0.875**
W/Ht	0.636**	0.624**	0.551**	-0.705**	0.499**	0.702**	-0.592**	0.637**	0.704**	0.668**
BAI	0.184**	0.114	-0.116	-0.108	-0.065	0.049	-0.033	0.022	0.052	0.036
RI (mm)	-0.023	-0.121	0.109	-0.176	0.111	0.262	-0.065	0.187	0.246	0.169
RII(mm)	-0.018	-0.133	0.001	-0.141	-0.049	0.195	0.049	0.053	0.179	0.046
RIII(mm)	-0.089	-0.218**	-0.121	0.104	-0.253	-0.014	0.260	-0.157	-0.033	-0.124
RIV(mm)	-0.147*	-0.282**	-0.358*	0.274	-0.359*	-0.201	0.350*	-0.290	-0.215	-0.274
RV(mm)	-0.165*	-0.238**	-0.130	0.072	-0.103	-0.068	0.139	-0.132	-0.071	-0.155
R2D:4D	0.252**	0.289**	0.632**	-0.718**	0.547**	0.681**	-0.532**	0.600**	0.679**	0.562**
LI (mm)	0.002	-0.088	0.219	-0.234	0.176	0.316*	-0.104	0.230	0.299	0.209
LII(mm)	0.001	-0.095	0.026	-0.134	-0.083	0.195	0.049	0.066	0.178	0.053
LIII(mm)	-0.153*	-0.203**	-0.075	-0.006	-0.154	0.056	0.142	-0.068	0.043	-0.049
LIV(mm)	-0.131	-0.270**	-0.293	0.220	-0.367*	-0.213	0.351*	-0.288	-0.227	-0.293
LV(mm)	-0.107	-0.133	-0.131	0.004	-0.116	0.025	0.124	-0.072	0.016	-0.104
L2D:4D	0.305**	0.417**	0.635**	-0.690**	0.576**	0.790**	-0.611**	0.703**	0.786**	0.686**
VAI	0.824**	0.823**	0.868**	-0.872**	0.761**	0.909**	-0.930**	0.974**	0.917**	
DBP (mmHg)		0.778**	0.862**	-0.881**	0.745**	0.822**	-0.822**	0.837**	0.832**	0.824**
SBP (mmHg)	0.778**		0.888**	-0.902**	0.906**	0.851**	-0.865**	0.844**	0.866**	0.823**

*** P <0.05, ** P <0.001,** BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, BAI: body adiposity index, DBP: diastolic blood pressure, SBP: systolic blood pressure, I: first digit, II: second digit, III: third digit, IV: fourth digit, V: fifth digit, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio, FBG: fasting blood glucose, TC: total cholesterol, HDL –C: high density lipoprotein cholesterol, TG: triglyceride, LDL-C: low density lipoprotein cholesterol, VAI: visceral adiposity index

Digit ratio of both hands (Table 4.7) showed a positive and weak correlation with overall adiposity indicator (BMI) and all the indices of central adiposity except neck circumference. However, its correlation with the central adiposity indices was stronger compared to BMI. 2D:4D of both hands showed comparable correlation powers with the body adiposity measures.

In male subjects (Table 4.8), the R2D:4D showed higher correlation with both generalized and central adiposity indices compared to L2D:4D. Also, there was no significant correlation between BAI with both R2D:4D and L2D:4D in males. In females (Table 4.9), a weak correlation was observed between digit ratio and indices of adiposity. Only WHR correlated with R2D:4D while WHR and WHtR correlated with L2D:4D. Similarly, no significant correlation was observed between BAI and digit ratio.

Table 4.7: Correlation between digit length and digit ratio with anthropometric measures of adiposity in the general population

Variables	**RI (mm)**	**RII (mm)**	**RIII (mm)**	**RIV (mm)**	**RV (mm)**	**R2D:4D**	**LI (mm)**	**LII (mm)**	**LIII (mm)**	**LIV (mm)**	**LV (mm)**	**L2D:4D**
Age (years)	-0.069	-.0177**	-0.199**	-0.229**	-0.152**	0.139	-0.0292	-0.141**	-0.202**	-0.221	-0.187**	0.197
Height(cm)	0.622**	0.583**	0.645**	0.631**	0.592**	-0.192**	0.655**	0.629**	0.597**	0.650**	0.592**	-0.151**
Weight (Kg)	0.353**	0.327**	0.320**	0.281**	0.310**	0.044	0.400**	0.368**	0.295**	0.317**	0.325**	0.048
BMI(kg/m^2)	0.068	0.067	0.027	-0.009	0.039	0.150**	0.103*	0.087	0.026	0.020	0.061	0.130**
WC (cm)	0.154**	0.131**	0.096*	0.018	0.098*	0.218**	0.201**	0.159**	0.069	0.041	0.105*	0.233**
HC (cm)	0.130**	0.158**	0.132**	0.099*	0.096*	0.098*	0.151**	0.156**	0.117*	0.101*	0.122**	0.089
NC (cm)	0.428**	0.370**	0.367**	0.395**	0.360**	-0.113	0.456**	0.423**	0.360**	0.428**	0.375**	-0.082
W/H	0.100*	0.039	0.019	-0.066	0.052	0.218**	0.149**	0.083	-0.008	-0.036	0.034	0.251**
W/Ht	-0.052	-0.061	-0.116*	-0.191**	-0.100*	0.285**	-0.016	-0.048	-0.126**	-0.175**	-0.090	0.287**
BAI	-0.302**	-0.250**	-0.312**	-0.334**	-0.309**	0.214**	-0.304**	-0.284**	-0.292**	-0.345**	-0.286**	0.177**

*** P <0.05, ** P <0.001,** BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, BAI: body adiposity index, I: first digit, II: second digit, III: third digit, IV: fourth digit, V: fifth digit, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio

Table 4.8: Correlation between digit length and digit ratio with anthropometric measures of adiposity in males

Variables	**RI (mm)**	**RII (mm)**	**RIII (mm)**	**RIV (mm)**	**RV (mm)**	**R2D:4D**	**LI (mm)**	**LII (mm)**	**LIII (mm)**	**LIV (mm)**	**LV (mm)**	**L2D:4D**
Age (years)	-0.104	-0.235**	-0.263**	-0.348**	-0.186**	0.230**	-0.053	-0.222**	-0.289**	-0.332**	-0.252**	0.184**
Height(cm)	0.502**	0.451**	0.534**	0.404**	0.455**	0.088	0.559**	0.469**	0.534**	0.425**	0.472**	0.093
Weight (kg)	0.343**	0.236**	0.257**	0.124*	0.224**	0.220**	0.398**	0.277**	0.249**	0.192**	0.235**	0.159**
BMI (kg/m^2)	0.167**	0.071	0.066	-0.033	0.053	0.205**	0.204**	0.108	0.059	0.039	0.062	0.125*
WC (cm)	0.258**	0.119	0.089	-0.068	0.125*	0.373**	0.307**	0.154*	0.088	-0.009	0.106	0.300**
HC (cm)	0.302**	0.149*	0.158**	0.084	0.130*	0.129*	0.335**	0.182**	0.153*	0.118	0.143*	0.120
NC (cm)	0.297**	0.225**	0.211**	0.115	0.162**	0.217**	0.321**	0.289**	0.265**	0.207**	0.190**	0.155*
W/H	0.116	0.044	-0.008	-0.192**	0.075	0.473**	0.166**	0.069	-0.006	-0.133*	0.031	0.369**
W/Ht	0.133*	0.002	-0.046	-0.179**	0.005	0.362**	0.169**	0.035	-0.049	-0.121*	-0.017	0.283**
BAI	-0.011	-0.130*	-0.164**	-0.164**	-0.149*	0.071	-0.012	-0.109	-0.171**	-0.142*	-0.146*	0.055

*** P <0.05, ** P <0.001,** BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, BAI: body adiposity index, I: first digit, II: second digit, III: third digit, IV: fourth digit, V: fifth digit, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio

Table 4.9: Correlation between digit length and digit ratio with anthropometric measures of adiposity in females

Variables	**RI (mm)**	**RII (mm)**	**RIII (mm)**	**RIV (mm)**	**RV (mm)**	**R2D:4D**	**LI (mm)**	**LII (mm)**	**LIII (mm)**	**LIV (mm)**	**LV (mm)**	**L2D:4D**
Age (years)	-0.166*	-0.205**	-0.246**	-0.268**	-0.240**	0.122	-0.135	-0.156*	-0.200**	-0.284**	-0.234**	0.313**
Height(cm)	0.392**	0.576**	0.583**	0.582**	0.500**	0.002	0.397**	0.601**	.0490**	0.567**	0.473**	0.011
Weight (Kg)	0.145*	0.293**	0.219**	0.255**	0.233**	0.076	0.194**	0.315**	0.184**	0.242**	0.256**	0.125
BMI (kg/m^2)	0.006	0.095	0.008	0.049	0.058	0.089	0.051	0.106	0.012	0.039	0.097	0.139
WC (cm)	0.013	0.126	0.074	0.071	0.028	0.113	0.068	0.150*	0.017	0.046	0.076	0.218**
HC (cm)	0.124	0.292**	0.239**	0.302**	0.201**	-0.011	0.148*	0.276**	0.186**	0.267**	0.232**	-0.015
NC (cm)	0.048	0.215**	0.142*	0.210**	0.160*	0.015	0.064	0.195**	0.123	0.147*	0.178*	0.086
W/H	-0.086	-0.093	-0.104	-0.165*	-0.137	0.142*	-0.033	-0.043	-0.141*	-0.169*	-0.111	0.294**
W/Ht	-0.085	-0.0178	-0.075	-0.078	-0.098	0.121	-0.032	0.001	-0.107	-0.099	-0.042	0.226**
BAI	-0.107	-0.041	-0.105	-0.037	-0.093	-0.009	-0.088	-0.075	-0.101	-0.065	-0.042	-0.019

*** P <0.05, ** P <0.001,** BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, BAI: body adiposity index, I: first digit, II: second digit, III: third digit, IV: fourth digit, V: fifth digit, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio

4.4 Effects of Physical Activity on Anthropometric Measures of Adiposity, Digit Ratio and Blood Pressure

From (Table 4.10) the overall effect of PA on the anthropometric measures of adiposity, BP and 2D:4D, was statistically significant as evidenced by progressive reduction in mean values of all the measured parameters with exception of BAI in males and HC in females

Multiple comparison (Table 4.10 and 4.11) of differences in the mean body adiposity measures, BP and digit ratio along the PA ladder show that the body adiposity measures and BP significantly decreased on moving from lower levels of physical activity to higher levels but such difference was not observed for digit ratio. An exception to this trend was observed for WC, NC and BAI. In females WC measure, there was no significant difference between subjects in moderate and optimal levels of PA. For NC, significant reduction was only observed between inactive and mild levels of PA while moderate and optimal PA levels did not yield significant reduction in the mean value. There was no observed significant reduction between groups of all the levels of PA for BAI in both sexes.

Table 4.10: Effect of physical activity on anthropometric measures of adiposity, 2D:4D and blood pressure in male subjects

	Inactive (n=68)	Mild PA (n=40)	Moderate PA (n=86)	Optimal PA (n=72)		
Variables	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	F	P value
Height (cm)	169.97 ± 5.73	170.09 ± 6.37	169.28 ± 5.86	167.70 ± 7.01	2.01	0.11
Weight (Kg)	68.82 ± 14.24	66.90 ± 12.84	59.94 ± 10.02	59.12 ± 9.65	11.93	<0.001
BMI (kg/m2)	23.72 ± 4.37[a,b]	23.04 ± 3.82[d,e]	20.92 ± 3.46[a,d]	21.03 ± 3.36[b,e,]	9.8	<0.001
WC (cm)	85.79 ± 11.45[a,b]	81.49 ± 10.60[d,e]	74.73 ± 8.70[a,d,f]	69.97 ± 6.96[b,e,f]	38.07	<0.001
HC (cm)	88.49 ± 9.77[a]	88.41 ± 7.91	87.04 ± 6.84	84.81 ± 6.19[b]	3.24	0.022
NC (cm)	36.51 ± 2.72[a,b]	35.47 ± 1.96[d,e]	34.16 ± 1.92[a,d]	34.26 ± 1.56[b,e,]	20.38	<0.001
W/H	0.97 ± 0.06[a,b,c]	0.92 ± 0.06[a,d,e]	0.86 ± 0.05[b,d,f]	0.82 ± 0.05[c,e,f]	98.5	<0.001
W/Ht	0.50 ± 0.07[a,b]	0.48 ± 0.06[d,e]	0.44 ± 0.05[a,d,f]	0.42 ± 0.04[b,e,f]	33.86	<0.001
BAI	21.96 ± 4.37	21.89 ± 3.60	21.58 ± 3.41	21.15 ± 3.45	0.65	0.58
DBP (mmHg)	94.38 ± 11.88[a,b,c]	87.30 ± 11.15[a,d,e]	79.48 ± 5.89[b,d,f]	72.56 ± 8.31[c,e,f]	72.65	<0.001
SBP (mmHg)	149.32 ±19.92[a,b,c]	136.88 ±14.15[a,d,e]	121.24 ± 9.71[b,d,f]	111.26 ± 9.47[c,e,f]	104.15	<0.001
RI (mm)	75.43 ± 5.80	75.32 ± 4.60	73.36 ± 5.27	73.49 ±5.55	2.85	0.038
RII (mm)	73.45 ± 4.85	73.54 ± 3.86	72.23 ± 5.05	71.57 ± 5.79	2.24	0.084
RIII (mm)	81.03 ± 5.02	80.72 ± 4.12	79.88 ± 5.50	79.21 ± 6.26	1.54	0.20
RIV (mm)	75.06 ± 5.40	75.77 ± 3.88	75.76 ± 5.30	75.93 ± 5.88	0.36	0.78
RV (mm)	62.96 ± 4.46	62.53 ± 6.24	62.31 ± 5.04	60.82 ± 5.66	2.16	0.092
R2D:4D	0.98 ± 0.03[a,b]	0.97 ± 0.03[d,e]	0.95 ± 0.03[a,d]	0.94 ± 0.03[b,e,]	18.82	<0.001
LI (mm)	75.67 ± 5.76	74.79 ± 4.66	73.49 ± 4.95	72.76 ± 5.47	4.17	0.007
LII (mm)	74.30 ± 4.21	74.84 ± 3.79	73.08 ± 5.01	71.85 ± 5.36	4.68	0.003
LIII (mm)	81.14 ± 5.26	81.09 ± 4.85	80.54 ± 5.53	79.53 ± 6.34	1.17	0.32
LIV (mm)	75.56± 4.66	77.14 ± 3.72	76.06 ± 5.11	75.83 ± 5.44	0.93	0.42
LV (mm)	62.86 ± 4.59	62.51 ± 4.72	62.56 ± 5.00	61.00 ± 5.70	1.94	0.12
L2D:4D	0.98 ± 0.03[a,b]	0.97 ± 0.02[c]	0.96 ± 0.04[a]	0.95 ± 0.03[b,c]	15.54	<0.001

BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, BAI: body adiposity index, I: first digit, II: second digit, III: third digit, IV: fourth digit, V: fifth digit, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio, DBP: diastolic blood pressure, SBP: systolic blood pressure

Table 4.11: Effect of physical activity on anthropometric measures of adiposity, 2D:4D and blood pressure in female subjects

	Inactive (n=65)	Mild (n=31)	Moderate (n=76)	Optimal (n=21)		
Variables	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	F	P value
Height (cm)	157.52 ± 7.37	158.54 ± 7.82	159.07 ± 5.19	159.41 ± 8.32	0.78	0.51
Weight (Kg)	64.66 ± 14.44	56.11 ± 11.11	51.06 ± 9.49	47.93 ± 6.56	22.14	<0.001
BMI (kg/m2)	25.92 ± 4.62[a,b,c]	22.32 ± 4.19[a,d,e]	20.11 ± 3.20[b,d]	18.94 ± 2.73[c,e]	34.53	<0.001
WC (cm)	86.85 ± 12.12 [a,b,c]	77.25 ± 10.38 [a,d,e]	69.94 ± 8.90 [b,d]	65.67 ± 7.65 [c,e]	43.25	<0.001
HC (cm)	91.11 ± 11.28	87.14 ± 8.68	88.30 ± 9.71	87.77 ± 7.10	1.64	0.18
NC (cm)	33.08 ± 2.42 [a,b,c]	31.63 ± 2.47 [a]	30.70 ± 1.90 [b]	30.37 ± 2.14 [c]	16.83	<0.001
W/H	0.95 ± 0.07 [a,b,c]	0.89 ± 0.10 [a,d,e]	0.79 ± 0.07 [b,d,f]	0.75 ± 0.05[e,c,f]	80.41	<0.001
W/Ht	0.55 ± 0.07 [a,b,c]	0.49 ± 0.06 [a,d,e]	0.44 ± 0.05 [b,d]	0.41 ± 0.05 [c,e]	55.06	<0.001
BAI	28.08 ± 4.95	25.71 ± 4.25	26.02 ± 4.45	25.74 ± 3.98	3.46	0.017
DBP (mmHg)	98.29 ± 9.32 [a,b,c]	84.58 ± 8.55 [a,d,e]	77.38 ± 6.55 [b,d,f]	71.22 ± 7.45 [e,c,f]	109.82	<0.001
SBP (mmHg)	154.34 ± 18.41 [a,b,c]	132.97 ± 11.29 [a,d,e]	116.95 ± 8.20 [b,d]	109.63 ± 7.10 [c,e]	128.19	<0.001
RI (mm)	66.65 ±5.46	69.84 ± 5.19	68.38 ± 3.98	67.87 ± 5.72	3.2	0.024
RII (mm)	67.98 ± 4.12	70.54 ± 5.51	69.28 ± 4.25	68.47 ± 4.22	2.62	0.052
RIII (mm)	74.15 ± 4.79	77.37 ± 6.64	75.77 ± 4.40	76.04 ± 4.03	3.34	0.02
RIV (mm)	68.58 ± 4.41	70.94 ± 5.25	70.36 ± 4.07	70.89 ± 4.45	3.22	0.024
RV (mm)	56.25 ± 4.29	59.59 ± 3.83	57.77 ± 4.30	58.10 ± 3.60	4.88	0.0027
R2D:4D	0.99 ± 0.02 [a]	0.99 ± 0.03[b]	0.98 ± 0.03	0.97 ± 0.05[a,b]	4.89	0.0027
LI (mm)	66.66 ± 4.72	69.94 ± 5.23	68.15 ± 3.42	66.89 ± 4.89	4.46	0.0047
LII (mm)	68.15 ± 4.18	70.74 ± 5.20	69.38 ± 4.27	68.60 ± 3.82	2.72	0.046
LIII (mm)	74.78 ± 5.57	77.36 ± 6.01	76.70 ± 4.95	77.11 ± 6.19	2.36	0.073
LIV (mm)	68.41 ± 4.57	71.63 ± 5.45	70.72 ± 4.34	70.69 ± 4.22	4.71	0.0034
LV (mm)	56.64 ± 5.95	58.49 ± 4.48	58.07 ± 4.13	58.24 ± 4.19	1.57	0.198
L2D:4D	1.00 ± 0.03 [a,b]	0.99 ± 0.03	0.98 ± 0.03 [a]	0.97 ± 0.03[b]	6.75	0.0002

BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, BAI: body adiposity index, I: first digit, II: second digit, III: third digit, IV: fourth digit, V: fifth digit, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio

It was observed (Figures 4.9 – 4.15) that although the serum components of MetS, biomarkers and visceral adipose tissue had higher or similar baseline values in females when compared to male subjects, the rate of drop following PA was also more drastic in females and reached a lower value at the highest level of PA when compared to males. However, HDL-C and adiponectin remained higher in females even at optimal PA level.

The effect of PA levels on the biomarkers showed that SUA levels decreased significantly ($P < 0.05$) and progressively. However, SUA levels did not show any significant reduction between moderate and optimal PA in both sexes. Effect of physical activity on serum adiponectin showed increased levels from lower to higher PA. However serum concentration of adiponectin did not also increase significantly ($P > 0.05$) between moderate and optimal PA in males. The effect of PA on FBG (Fig. 4.11) showed that though significant reduction occurred in FBG level with increased PA, no significant reduction was observed between moderate and optimal PA in both sexes. Serum TC (Fig. 4.12) level decreased significantly ($P < 0.05$) with increasing PA. However, no significant reduction between inactive and mild PA level in occurred in females as well as between moderate optimal PA in both sexes.

Significant ($P < 0.05$) reduction in serum HDL-C (Fig. 4.13) was observed as PA increased to a higher level except between moderate and optimal PA, where the decrease was not significant in both sexes. Significant ($P < 0.05$) reduction in serum TG (Fig. 4.14) was observed from a lower level of PA to a higher one except between moderate and optimal PA, where the decrease was not significant in both sexes.

Significant ($P < 0.05$) reduction in serum LDL-C (Fig. 4.15) was observed on moving from a lower level of PA to a higher one except between inactive and mild PA in females, and between moderate and optimal PA in both sexes.

The effect of PA on VAI (Fig. 4.16) showed that though significant reduction in visceral adipose tissue occured with increase in PA, no significant reduction was observed between moderate and optimal PA in both sexes. It was also observed that no significant change in VAI occured between inactive and mild PA in females

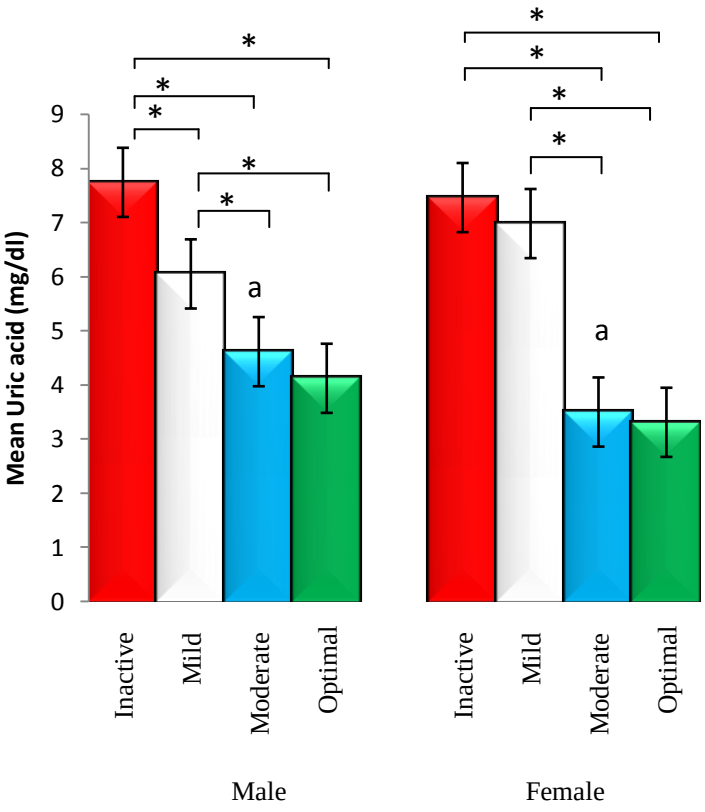


Figure 4.9: Effect of physical activity on serum uric acid level (* indicates P <0.05 between categories of PA within sexes & similar letter superscript indicate P < 0.05 between sexes for each category of PA)

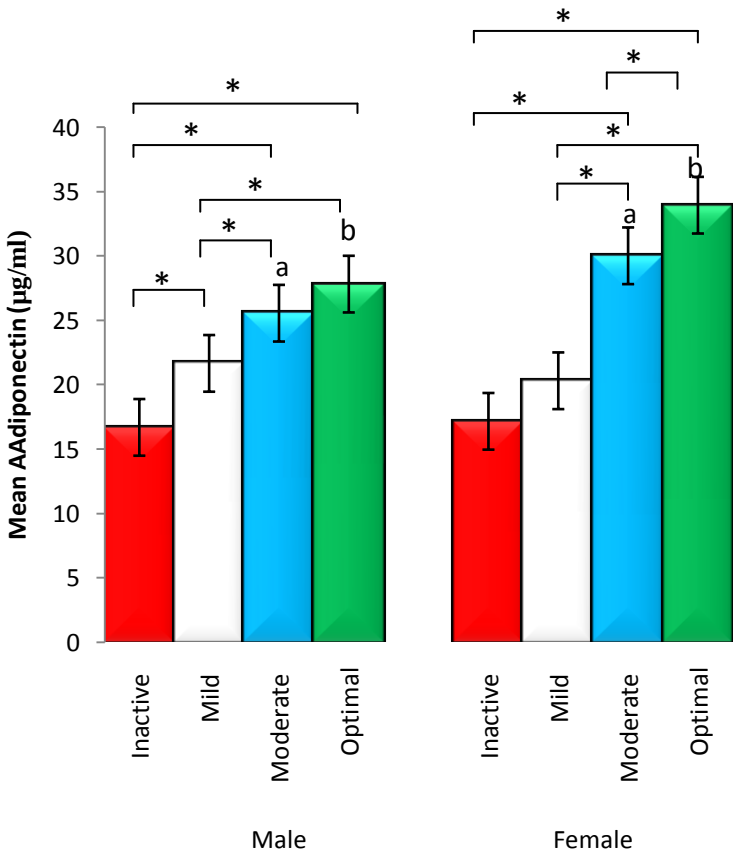


Figure 4.10: Efeect of physical activity on serum adiponectin (* indicates P <0.05 between categories of PA within sexes & similar letter superscript indicate P < 0.05 between sexes for each category of PA)

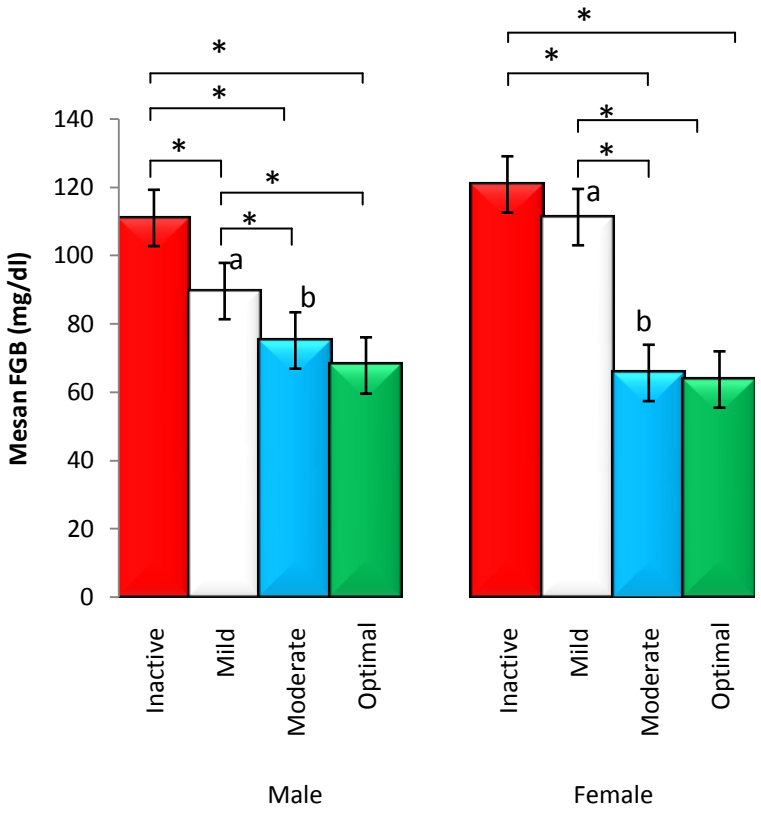


Figure 4.11: Effect of physical activity on sreum glucose level (* indicates P <0.05 between categories of PA within sexes & similar letter superscript indicate P < 0.05 between sexes for each category of PA)

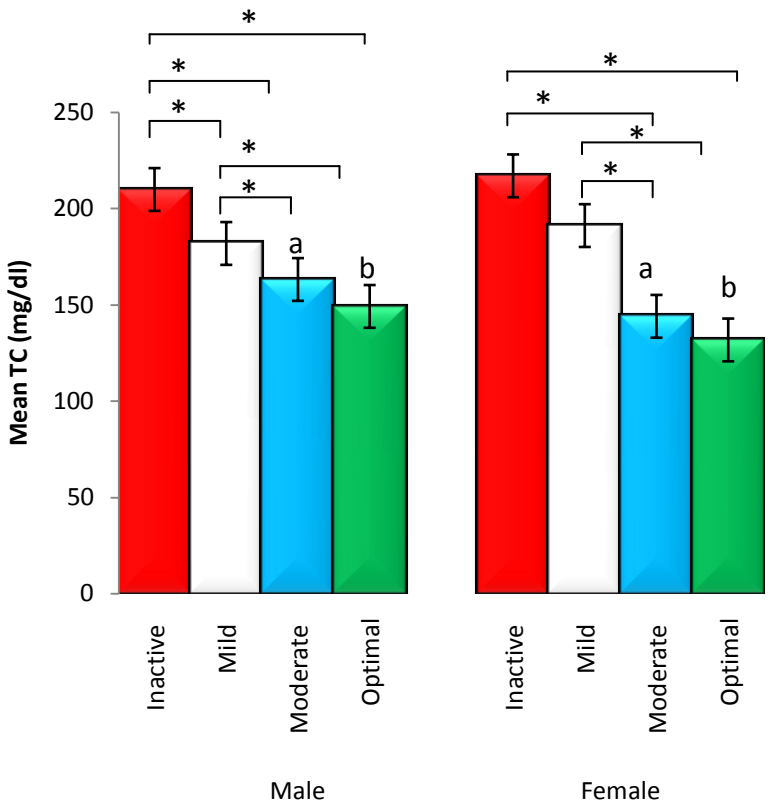


Figure 4.12: Effect of physical activity on serum TC level (* indicates P <0.05 between categories of PA within sexes & similar letter superscript indicate P < 0.05 between sexes for each category of PA)

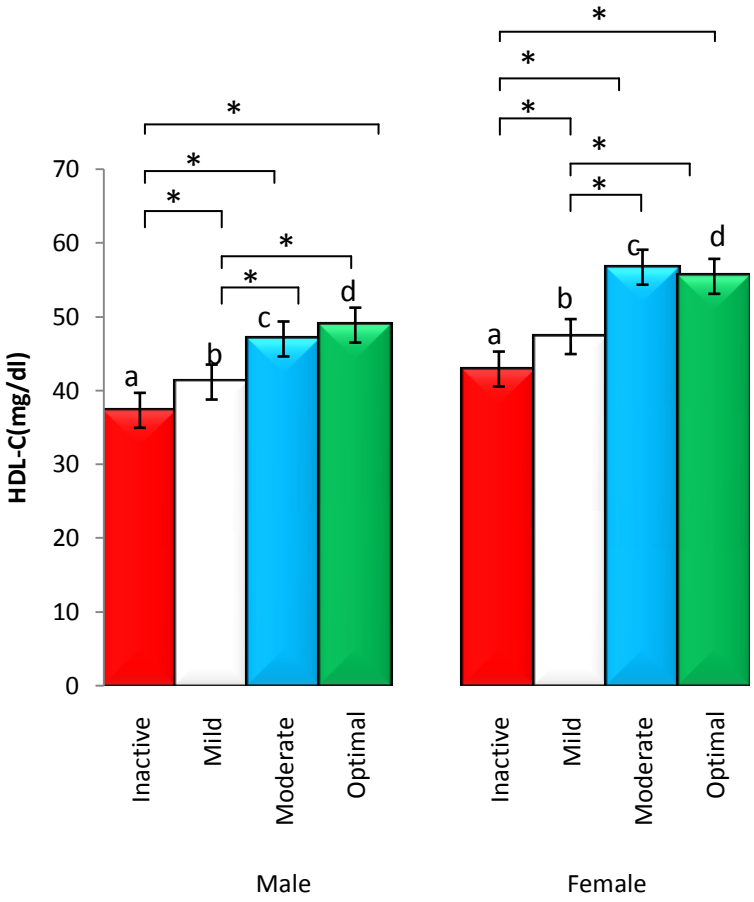


Figure 4.13: Effect of physical activity on serum HDL-C level (* indicates P <0.05 between categories of PA within sexes & similar letter superscript indicate P < 0.05 between sexes for each category of PA)

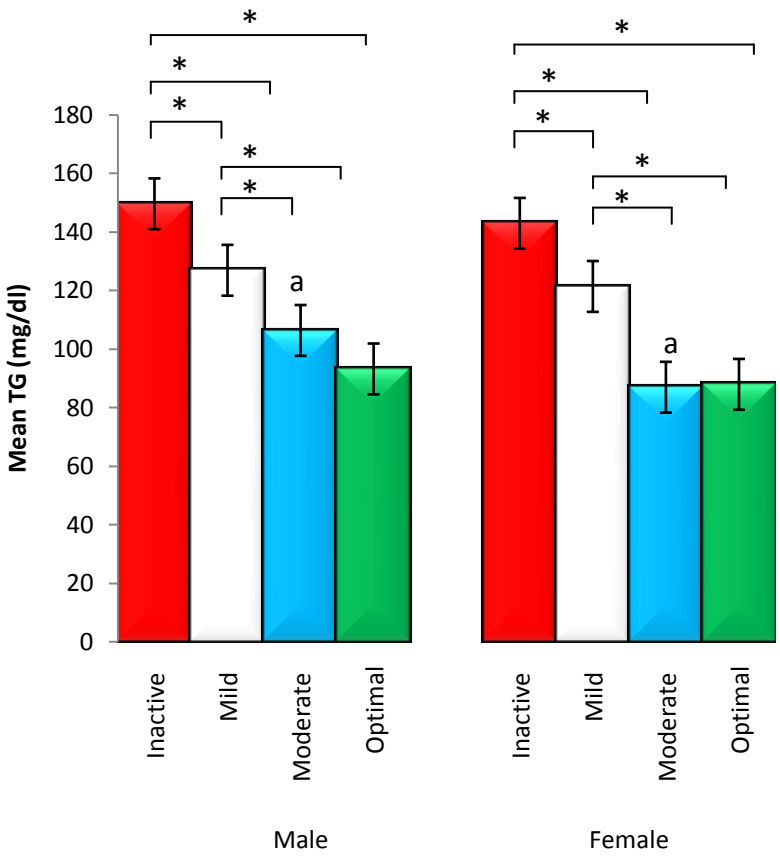


Figure 4.14: Effect of physical activity on serum TG level (* indicates P <0.05 between categories of PA within sexes & similar letter superscript indicate P < 0.05 between sexes for each category of PA)

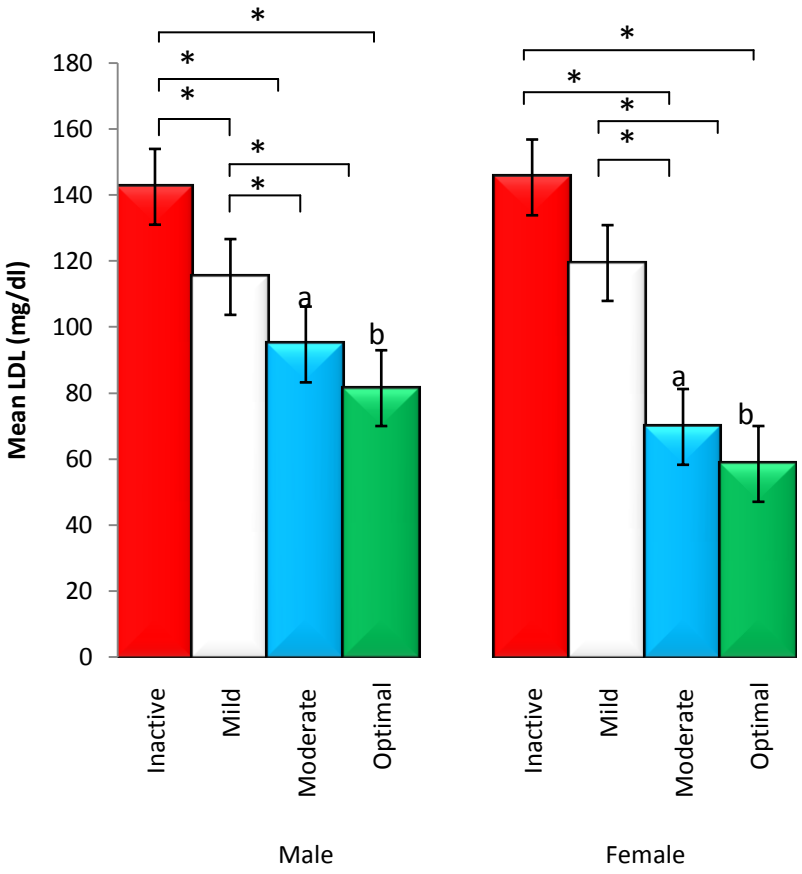


Figure 4.15: Effect of physical activity on serum LDL–C level (* indicates P <0.05 between categories of PA within sexes & similar letter superscriptindicate P < 0.05 between sexes for each category of PA)

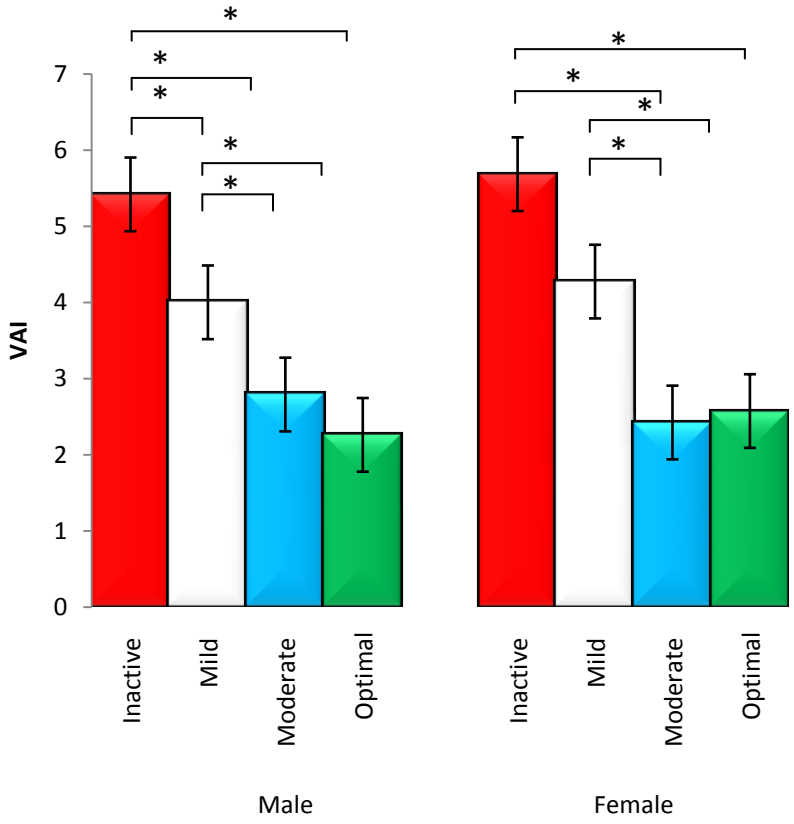


Figure 4.16: Efeect of physical activity on VAI (* P < 0.05)

.

4.5 Prediction of Serum Components of MetS from Anthropometric Variables

Stepwise multiple linear regression (Tables 4.12 and 4.13) for predicting componenets of MetS showed that WHR was the strongest predictor of all the componenets of MetS and for visceral adiposity but with varying percentage of accuracy. For visceral adipose tissue estimation, WHR had 71% and 77% contribution to estimation in males and females respectively. For the serum components, the highest contribution of WHR in female was observed for LDL –C and TC (81% and 82% respectively) while the lowest was for FBG in males (63%). For males WHR had the highest estimation ability for HDL-C (68%) and the lowest for FBG (60%). There was however little contribution from R2D:4D in FBG estimation for males and contribution from L2D:4D in LDL –C and TC estimation in females. For BP prediction, there were also contributions from digit ratio, digit length and other anthropometric indices.

Table 4.12: Stepwise multiple linear regression for estimation of serum component of MetS from anthropometric measurements in males

Variables	Model	R	R^2	SEE	F	P Value
FBG (mg/dl)	1. FBG= 260.32 (W/H) + (-147.43)	0.77	0.6	15.71	176.83	<0.0001
	2. FBG= 266.07 (W/H) + 106.79(R2D:4D) +(-219.54)	0.78	0.62	15.47	93.59	<0.0001
TC (mg/dl)	1. TC= 358.48 (W/H) + (-145.26)	0.82	0.67	18.74	235.64	<0.0001
	2. TC= 358.53 (W/H) + (-38.83)	0.82	0.68	18.51	122.8	<0.0001
HDL-C (mg/dl)	1. HDL-C =70.74(W/H) + 107.17	0.82	0.68	3.6	248.5	<0.0001
TG (mg/dl)	TG= 340.51(W/H) + (-186.41)	0.79	0.62	19.6	194.32	<0.0001
	TG= 340.56(W/H) + (0.69)(Height) + (-70.41)	0.8	0.64	19.33	102.11	<0.0001
LDL-C (mg/dl)	1. LDL= 361.12(W/H) + (-215.15)	0.82	0.67	18.69	240.57	<0.0001
VAI	VAI= 19.56 (W/H) + (-13.90)	0.844	0.71	0.92	291.81	<0.0001
DBP (mmHg)	1. DBP=104.64 (W/H)+(-10.14)	0.66	0.43	9.34	200.78	<0.0001
SBP (mmHg)	1. SBP= 200.94(W/H) + (-50.00)	0.78	0.6	12.66	403.44	<0.0001
	2. SBP= 173.15(W/H) + 133.66(R2D:4D)+(-153.57)	0.8	0.64	12.02	238.47	<0.0001

FBG: fasting glucose, TC: total cholesterol, HDL-C: high density lipoprotein, TG: triglyceride, LDL-C: low density lipoprotein, VAI; Visceral adiposity index , SBP; systolic blood pressure, DBP; systolic blood pressure, W/H: waist-to-hip ratio, R2D:4D; right second to forth digit ratio,L2D:4D; left second to forth digit ratio, SEE: standard error of estimate, F:ratio of variation between sample means: variation within the sample

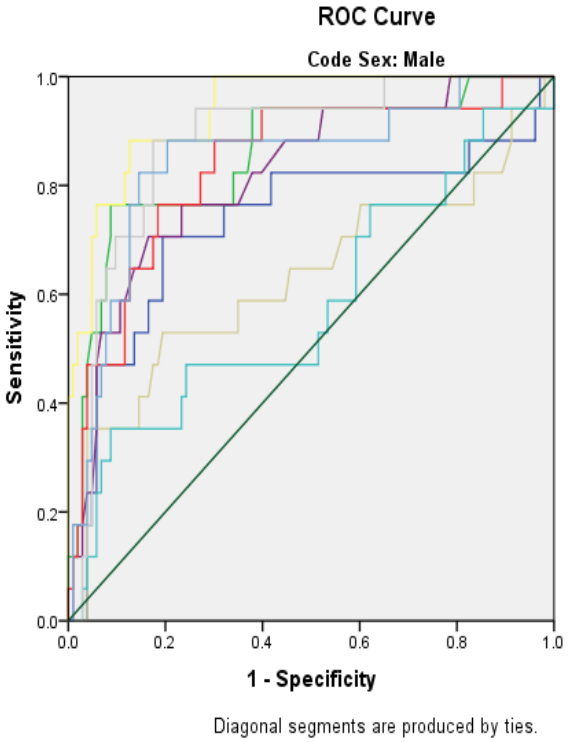
Table 4.13: Stepwise multiple linear regression for estimation of serum component of MetS from anthropometric measurements in females

Variables	Model	R	R^2	SEE	F	P Value
FBG (mg/dl)	1. FBG= 326.05 (W/H) + (-191.68)	0.792	0.63	21.59	65.53	<0.0001
TC (mg/dl)	1. TC= 466.70 (W/H) + (-231.10)	0.9	0.81	19.18	170.09	<0.0001
	2. TC= 354.95 (W/H) + 405.41(L2D:4D) (-533.76)	0.93	0.86	16.79	117.34	<0.0001
HDL- (mg/dl)	1. HDL-C =65.30(W/H) + 106.37	0.83	0.68	3.84	82.87	<0.0001
TG (mg/dl)	TG= 299.08(W/H) + (-146.30)	0.87	0.75	14.79	117.41	<0.0001
LDL-C (mg/dl)	1. LDL= 472.19(W/H) + (-308.21)	0.91	0.82	18.66	183.84	<0.0001
	2. LDL= 366.03(W/H) + 385.1(L2D:4D)+ (-595.72)	0.93	0.87	16.47	124.02	<0.0001
VAI	VAI= 18.06 (W/H) + (-11.74)	.875b	0.77	0.86	127.37	<0.0001
DBP (mmHg)	1. DBP=81.83 (W/H)+ 14.58	0.68	0.46	9.56	168.22	<0.0001
	2. DBP=59.16 (W/H)+ 0.99(BMI) +12.14	0.74	0.55	8.72	121.38	<0.0001
	3. DBP=56.75 (W/H)+ 0.98(BMI) + 62.06(R2D:4D) + (-46.95)	0.76	0.58	8.52	88.43	<0.0001
	4. DBP=47.18 (W/H)+ 1.46(BMI) + 59.70(R2D:4D) + (-0.54)(BAI)+ (-32.66)	0.77	0.59	8.38	70.24	<0.0001
SBP (mmHg)	1. SBP= 153.98(W/H) + (-0.90)	0.76	0.58	14.29	266.53	<0.0001
	2. SBP= 141.32(W/H) + 158.99(L2D:4D)+(-146.87)	0.79	0.62	13.62	157.3	<0.0001
	3. SBP= 138.48(W/H) + 163.26(L2D:4D)+(-0.44) (Height) (-79.30)	0.8	0.63	13.32	112.89	<0.0001
	4. SBP= 121.99(W/H) + 165.36(L2D:4D)+(-0.45) (Height) + 0.71(BMI)+ (-80.43)	0.81	0.65	13.05	90.6	<0.0001
	11. SBP= 226.38(W/H) + 120.64(L2D:4D) + 7.63(BMI)+ (-2.62) (Weight) + (-7.68)(BAI) + 561.75(W/Ht) + 1.26(NC) + (51.20)	0.84	0.71	12.08	65.39	<0.0001

FBG: fasting glucose, TC: total cholesterol, HDL-C: high density lipoprotein, TG: triglyceride, LDL-C: low density lipoprotein, VAI; Visceral adiposity index , SBP; systolic blood pressure, DBP; systolic blood pressure, W/H: waist-to-hip ratio, R2D:4D; right second to forth digit ratio,L2D:4D; left second to forth digit ratio, SEE: standard error of estimate, F:ratio of variation between sample means: variation within the sample

4.6 Cut-off Values with Sensitivity and Specificity of Anthropometric Variables for Each MetS Component

The ROC curve (Fig 4. 17–4.30) showed that most of the anthropometric indices were above the reference line for prediction. The index with the highest area under the curve was WHR while the indexes with the lowest were BAI and HC which were slightly above or below the reference line for prediction of components of MetS. The cut off value of most of the anthropometric measures for the different MetS componenets were higher in males compared to females except for BAI and WHtR which was higher in females. For the digit ratio, the values were very similar but did not show a constant pattern. WHR was the anthropometric index that had the highest sensitivity and specificity at its cut off values for the various MetS indices. It was observed also that, in terms of optimal combination of both measures of the validity of a screening tool (sensitivity and specificity) at cut off points, BAI, HC and NC were weaker compared to other anthropometric measures.

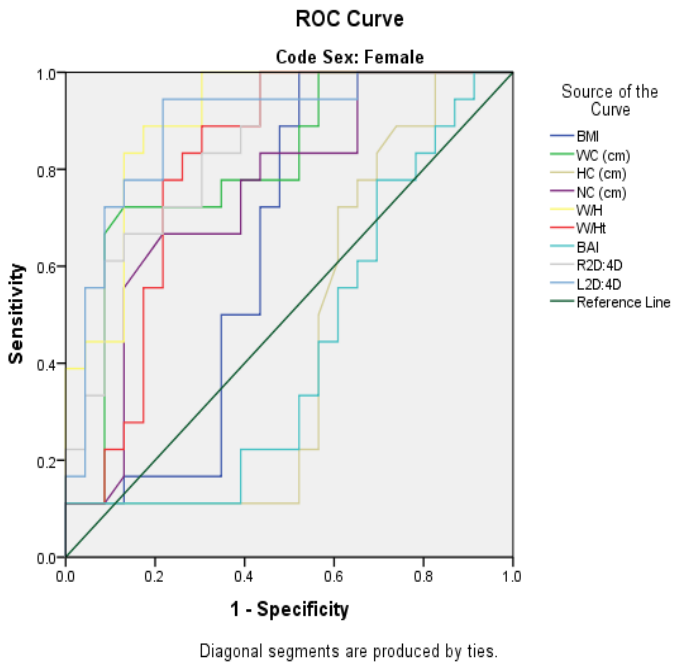


Source
Cu
BMI
WC (c
HC (c
NC (c
W/H
W/Ht
BAI
R2D:4
L2D:4
Refer

Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit.	Specif.	YI
BMI	0.73	0.08	0.002	0.573	0.888	24.10	0.71	0.81	1.51
WC (cm)	0.856	0.054	<0.0001	0.751	0.962	87.65	0.76	0.91	1.68
HC (cm)	0.628	0.087	0.091	0.458	0.798	93.95	0.53	0.81	1.34
NC (cm)	0.819	0.056	<0.0001	0.71	0.928	37.00	0.71	0.83	1.54
W/H	0.937	0.026	<0.0001	0.886	0.988	0.95	0.88	0.87	1.76
W/Ht	0.837	0.056	<0.0001	0.727	0.946	0.48	0.88	0.70	1.58
BAI	0.581	0.083	0.284	0.419	0.743	26.57	0.35	0.91	1.27
R2D:4D	0.879	0.042	<0.0001	0.798	0.961	0.98	0.88	0.83	1.71
L2D:4D	0.845	0.057	<0.0001	0.734	0.956	0.99	0.88	0.80	1.68

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

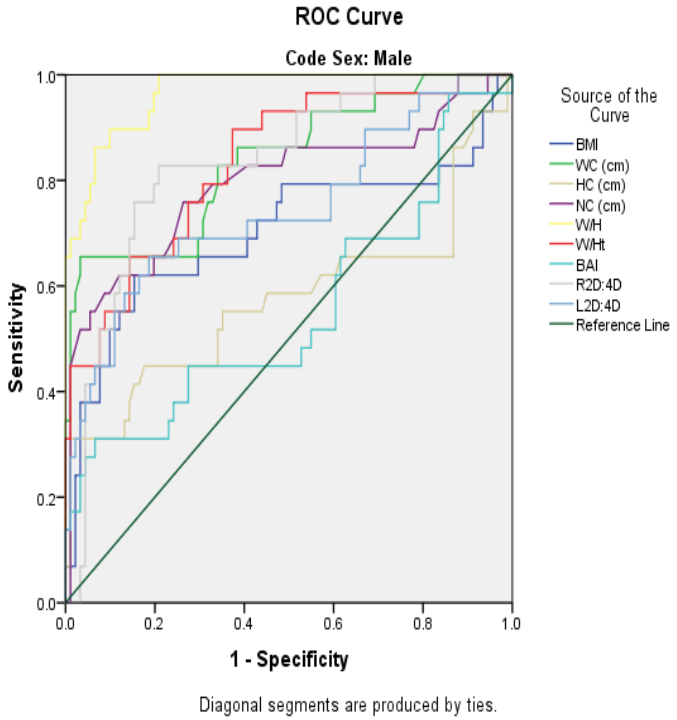
Figure 4.17: ROC curve for determination of cut off value of the anthropometric indices for fasting blood glucose in males.



Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit.	Specif.	YI
BMI	0.643	0.090	0.121	0.467	0.818	21.82	1.00	0.48	1.48
WC (cm)	0.806	0.071	0.001	0.667	0.944	87.35	0.72	0.87	1.59
HC (cm)	0.446	0.095	0.554	0.259	0.633	80.90	1.00	0.17	1.17
NC (cm)	0.748	0.078	0.007	0.595	0.900	32.95	0.67	0.78	1.45
W/H	0.903	0.047	0.000	0.811	0.996	0.93	0.89	0.83	1.71
W/Ht	0.807	0.070	0.001	0.669	0.944	0.53	0.89	0.70	1.58
BAI	0.428	0.092	0.431	0.247	0.608	35.20	0.11	1.00	1.11
R2D:4D	0.848	0.059	0.000	0.732	0.964	0.97	1.00	0.57	1.57
L2D:4D	0.889	0.054	0.000	0.784	0.994	0.99	0.94	0.78	1.73

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

Figure 4.18: ROC curve for determination of cut off value of the anthropometric indices for fasting blood glucose in females.

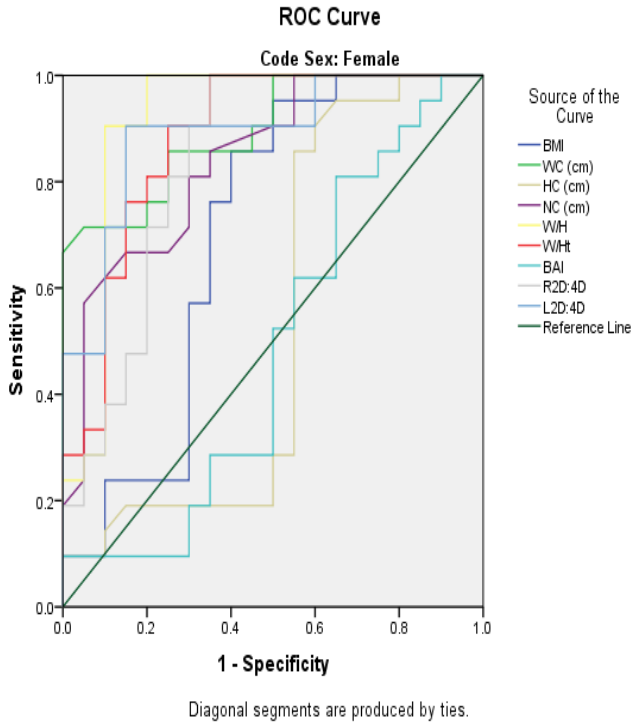


Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit.	Specif.	YI
BMI	0.70	0.07	0.0011	0.57	0.83	24.10	0.62	0.85	1.47
WC (cm)	0.84	0.05	0.0000	0.75	0.93	87.65	0.66	0.97	1.62
HC (cm)	0.58	0.07	0.2237	0.43	0.72	100.15	0.31	0.99	1.30
NC (cm)	0.79	0.06	0.0000	0.68	0.90	37.00	0.62	0.88	1.50
W/H	0.97	0.01	0.0000	0.94	0.99	0.94	0.90	0.90	1.80
W/Ht	0.84	0.04	0.0000	0.75	0.92	0.46	0.90	0.63	1.52
BAI	0.55	0.07	0.3925	0.42	0.69	26.57	0.31	0.93	1.24
R2D:4D	0.83	0.04	0.0000	0.75	0.92	0.98	0.83	0.79	1.62
L2D:4D	0.75	0.06	0.0001	0.63	0.86	0.99	0.66	0.81	1.47

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

Figure 4.19: ROC curve for determination of cut off value of the anthropometric indices for serum TC in males

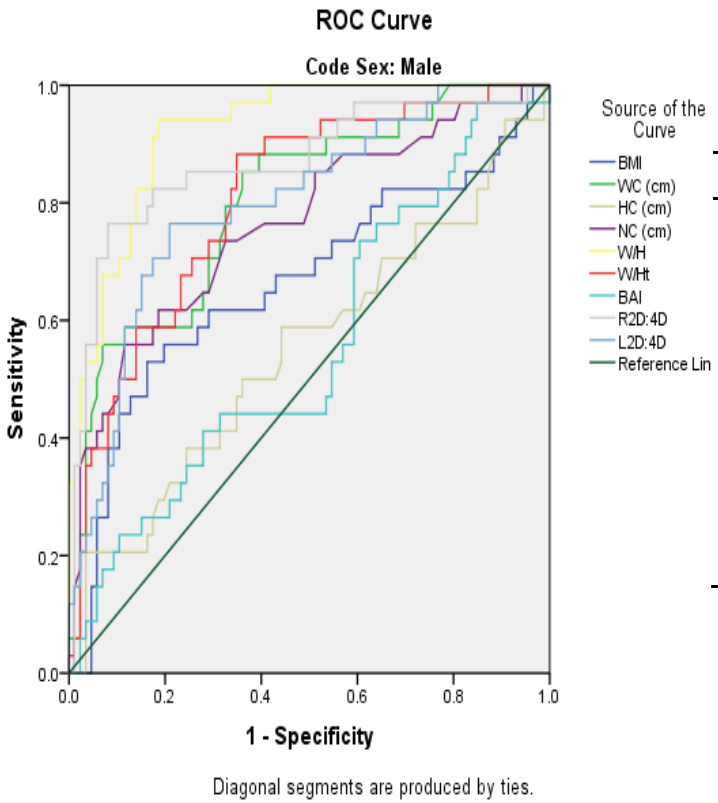
.



Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit.	Specif.	YI
BMI	0.70	0.09	0.0266	0.53	0.87	22.82	0.86	0.60	1.46
WC (cm)	0.90	0.05	0.0000	0.80	0.99	87.65	0.67	1.00	1.67
HC (cm)	0.53	0.10	0.7346	0.34	0.73	89.80	0.86	0.45	1.31
NC (cm)	0.84	0.06	0.0002	0.72	0.96	33.20	0.57	0.95	1.52
W/H	0.92	0.05	0.0000	0.82	1.00	0.90	0.90	0.90	1.80
W/Ht	0.88	0.05	0.0000	0.77	0.99	0.53	0.90	0.75	1.65
BAI	0.49	0.09	0.8756	0.30	0.67	26.61	0.81	0.35	1.16
R2D:4D	0.84	0.07	0.0002	0.71	0.97	0.97	1.00	0.65	1.65
L2D:4D	0.89	0.05	0.0000	0.79	0.99	0.99	0.90	0.85	1.75

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

Figure 4.20: ROC curve for determination of cut off value of the anthropometric indices for serum TC in females

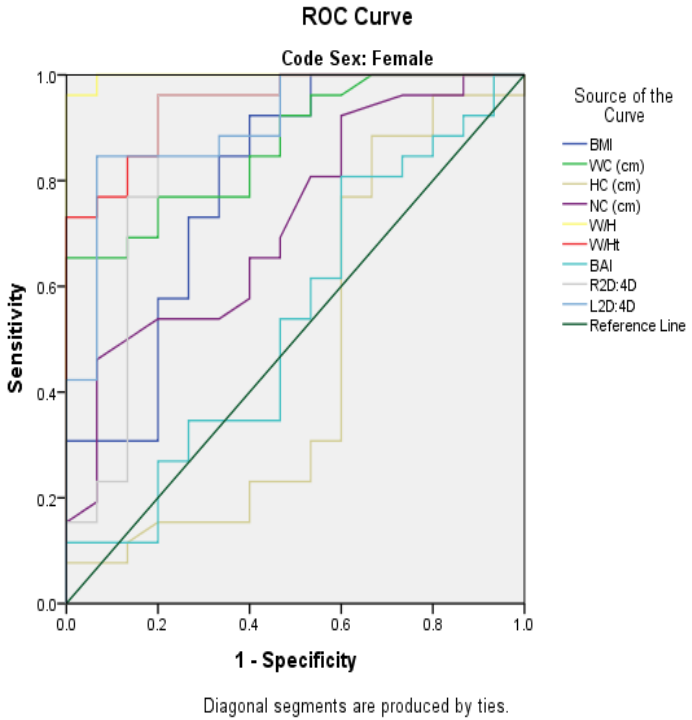


Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit	Specif	YI
BMI	0.66	0.06	0.0053	0.54	0.78	24.10	0.53	0.84	1.37
WC (cm)	0.80	0.04	0.0000	0.72	0.89	78.95	0.85	0.64	1.49
HC (cm)	0.55	0.06	0.3871	0.43	0.67	100.15	0.21	0.97	1.17
NC (cm)	0.76	0.05	0.0000	0.66	0.86	37.00	0.56	0.88	1.44
W/H	0.92	0.02	0.0000	0.88	0.97	0.91	0.94	0.81	1.76
W/Ht	0.81	0.04	0.0000	0.72	0.89	0.46	0.88	0.65	1.53
BAI	0.55	0.06	0.3514	0.44	0.67	23.34	0.41	0.72	1.13
R2D:4D	0.87	0.04	0.0000	0.79	0.95	0.98	0.76	0.92	1.68
L2D:4D	0.80	0.05	0.0000	0.71	0.89	0.98	0.76	0.79	1.56

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

Figure 4.21: ROC curve for determination of cut off value of the anthropometric indices for HDL-C in males

.

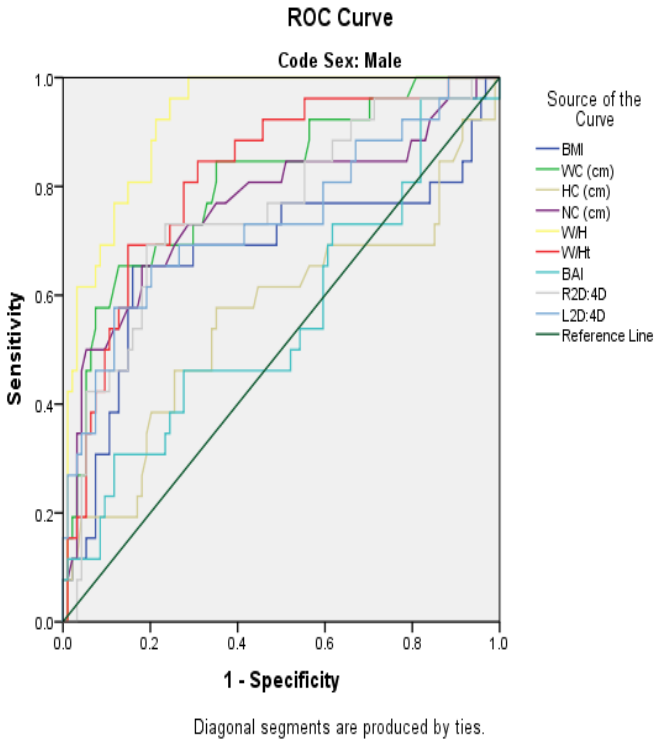


Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit	Specif	YI
BMI	0.79	0.08	0.0019	0.64	0.95	21.82	0.92	0.60	1.52
WC (cm)	0.87	0.05	0.0001	0.76	0.97	87.25	0.65	1.00	1.65
HC (cm)	0.46	0.11	0.6947	0.26	0.67	88.50	0.88	0.33	1.22
NC (cm)	0.72	0.08	0.0192	0.56	0.88	33.20	0.46	0.93	1.39
W/H	1.00	0.00	0.0000	0.99	1.00	0.86	0.96	1.00	1.96
W/Ht	0.95	0.03	0.0000	0.88	1.00	0.52	0.96	0.80	1.76
BAI	0.54	0.10	0.6847	0.35	0.73	26.61	0.81	0.40	1.21
R2D:4D	0.87	0.07	0.0001	0.72	1.00	0.97	0.96	0.80	1.76
L2D:4D	0.91	0.05	0.0000	0.81	1.00	0.99	0.85	0.93	1.78

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

Figure 4.22: ROC curve for determination of cut off value of the anthropometric indices for HDL-C in females.

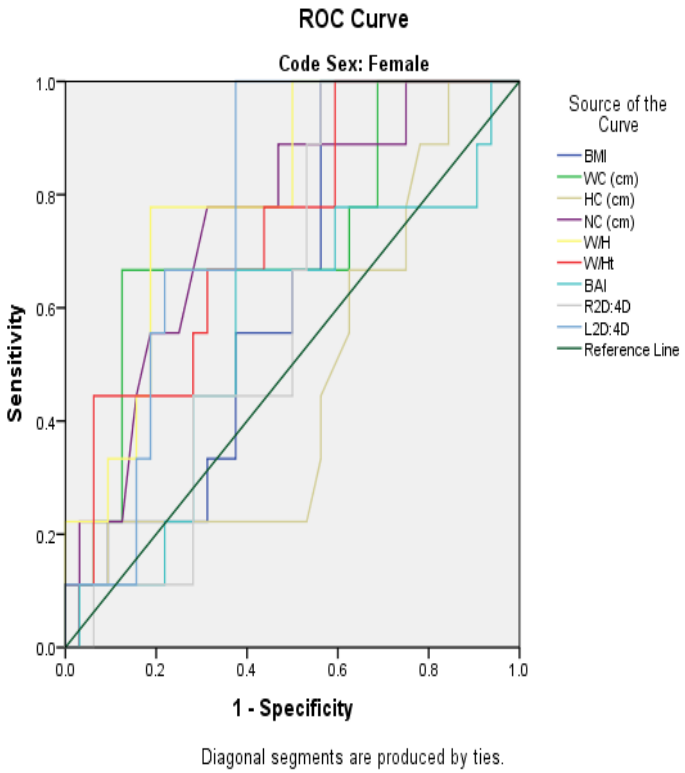
.



Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit	Specif	YI
BMI	0.68	0.07	0.0064	0.53	0.82	24.10	0.65	0.84	1.49
WC (cm)	0.81	0.05	0.0000	0.71	0.91	86.60	0.65	0.87	1.53
HC (cm)	0.56	0.07	0.3361	0.42	0.70	90.10	0.58	0.65	1.23
NC (cm)	0.76	0.06	0.0000	0.64	0.88	36.35	0.65	0.82	1.47
W/H	0.92	0.02	0.0000	0.88	0.97	0.91	0.96	0.76	1.72
W/Ht	0.82	0.05	0.0000	0.73	0.91	0.50	0.69	0.85	1.54
BAI	0.56	0.07	0.3524	0.43	0.69	26.26	0.31	0.88	1.19
R2D:4D	0.75	0.06	0.0001	0.64	0.86	0.98	0.69	0.81	1.50
L2D:4D	0.74	0.06	0.0002	0.62	0.86	1.00	0.58	0.88	1.46

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

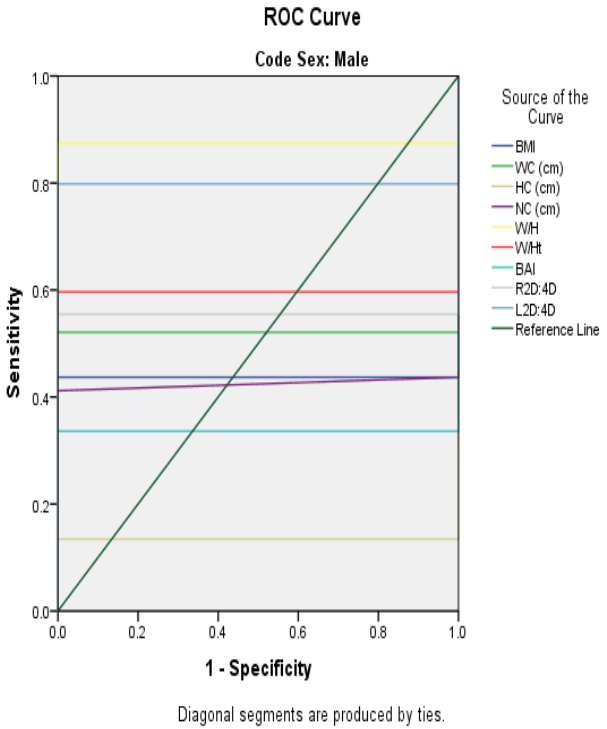
Figure 4.23: ROC curve for determination of cut off value of the anthropometric indices for TG in males



Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit	Specif	YI
BMI	0.63	0.09	0.2568	0.45	0.80	22.73	1.00	0.44	1.44
WC (cm)	0.72	0.10	0.0508	0.51	0.92	89.05	0.67	0.88	1.54
HC (cm)	0.47	0.11	0.7768	0.25	0.68	82.90	1.00	0.16	1.16
NC (cm)	0.75	0.09	0.0243	0.57	0.92	32.95	0.78	0.69	1.47
W/H	0.80	0.08	0.0068	0.65	0.95	0.97	0.78	0.81	1.59
W/Ht	0.73	0.09	0.0376	0.55	0.90	0.52	1.00	0.41	1.41
BAI	0.56	0.11	0.6143	0.34	0.77	29.74	0.67	0.63	1.29
R2D:4D	0.61	0.09	0.3289	0.43	0.78	0.97	1.00	0.44	1.44
L2D:4D	0.77	0.07	0.0128	0.63	0.92	1.00	1.00	0.63	1.63

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

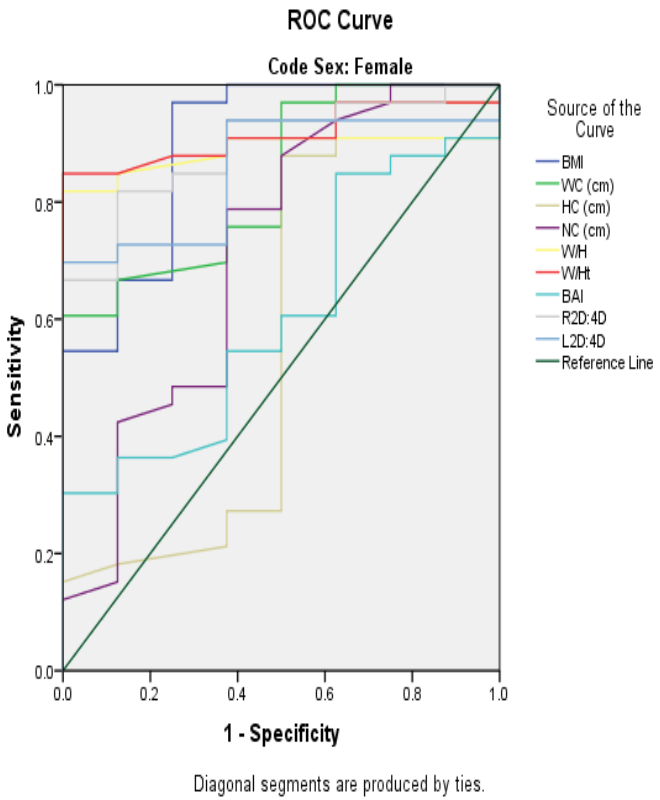
Figure 4.24: ROC curve for determination of cut off value of the anthropometric indices for TG in females



Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit	Specif	YI
BMI	0.44	0.05	0.829	0.35	0.53	22.79	0.44	1.00	1.44
WC (cm)	0.52	0.05	0.942	0.43	0.61	78.65	0.52	1.00	1.52
HC (cm)	0.13	0.03	0.209	0.07	0.20	96.70	0.13	1.00	1.13
NC (cm)	0.42	0.05	0.795	0.33	0.51	35.25	0.41	1.00	1.41
W/H	0.87	0.03	0.199	0.81	0.93	0.82	0.87	1.00	1.87
W/Ht	0.60	0.04	0.740	0.51	0.68	0.45	0.60	1.00	1.60
BAI	0.34	0.04	0.573	0.25	0.42	23.32	0.34	1.00	1.34
R2D:4D	0.55	0.05	0.851	0.47	0.64	0.96	0.55	1.00	1.55
L2D:4D	0.80	0.04	0.305	0.73	0.87	0.95	0.80	1.00	1.80

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

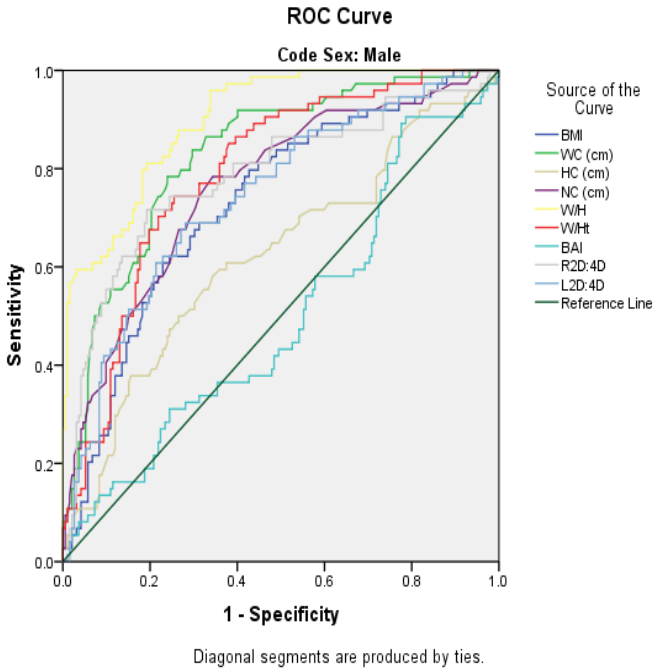
Figure 4.25: ROC curve for determination of cut off value of the anthropometric indices for LDL-C in males.



Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit	Specif	YI
BMI	0.90	0.07	0.001	0.77	1.00	20.76	0.97	0.75	1.72
WC (cm)	0.84	0.07	0.003	0.70	0.97	85.00	0.61	1.00	1.61
HC (cm)	0.58	0.14	0.500	0.31	0.85	88.50	0.88	0.50	1.38
NC (cm)	0.71	0.11	0.063	0.49	0.94	30.85	0.79	0.63	1.41
W/H	0.89	0.05	0.001	0.78	0.99	0.83	0.82	1.00	1.82
W/Ht	0.91	0.04	0.000	0.83	1.00	0.52	0.85	1.00	1.85
BAI	0.60	0.10	0.366	0.40	0.80	32.01	0.30	1.00	1.30
R2D:4D	0.89	0.05	0.001	0.79	1.00	0.97	0.82	0.88	1.69
L2D:4D	0.86	0.06	0.002	0.74	0.98	0.99	0.70	1.00	1.70

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

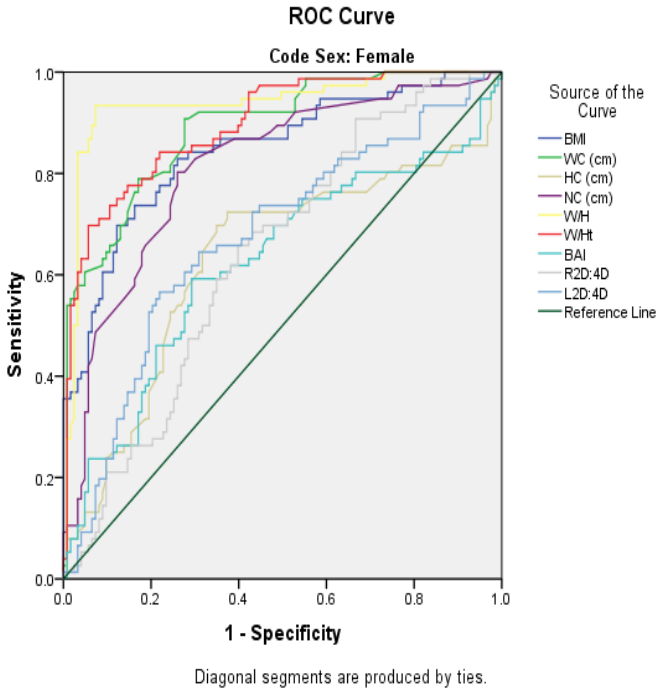
Figure 4.26: ROC curve for determination of cut off value of the anthropometric indices for LDL-C in females



Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit	Specif	YI
BMI	0.73	0.03	0.0000	0.66	0.80	23.24	0.61	0.77	1.38
WC (cm)	0.83	0.03	0.0000	0.78	0.88	79.45	0.78	0.76	1.54
HC (cm)	0.62	0.04	0.0019	0.55	0.70	88.05	0.58	0.66	1.24
NC (cm)	0.76	0.03	0.0000	0.70	0.83	34.95	0.78	0.66	1.44
W/H	0.90	0.02	0.0000	0.87	0.94	0.87	0.96	0.66	1.62
W/Ht	0.79	0.03	0.0000	0.73	0.85	0.47	0.74	0.74	1.49
BAI	0.50	0.04	0.9433	0.42	0.58	18.20	0.91	0.21	1.12
R2D:4D	0.78	0.03	0.0000	0.72	0.85	0.97	0.72	0.81	1.52
L2D:4D	0.74	0.03	0.0000	0.68	0.81	0.97	0.69	0.72	1.41

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

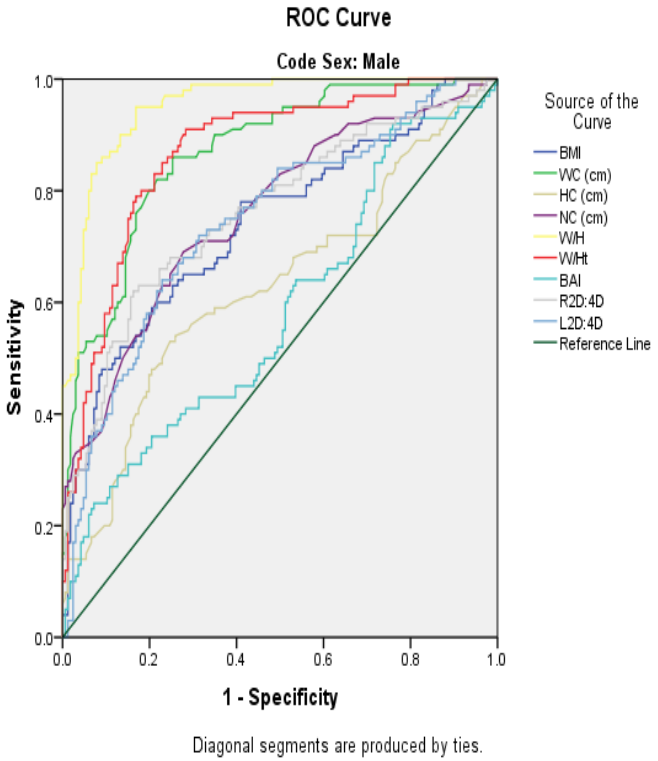
Figure 4.27: ROC curve for determination of cut off value of the anthropometric indices for DBP in males



Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit	Specif	YI
BMI	0.85	0.03	0.0000	0.79	0.90	23.32	0.70	0.88	1.58
WC (cm)	0.89	0.02	0.0000	0.84	0.94	72.15	0.91	0.72	1.63
HC (cm)	0.61	0.04	0.0019	0.55	0.72	88.05	0.72	0.63	1.35
NC (cm)	0.81	0.03	0.0000	0.75	0.87	31.25	0.80	0.74	1.54
W/H	0.94	0.02	0.0000	0.90	0.98	0.87	0.93	0.93	1.86
W/Ht	0.90	0.02	0.0000	0.85	0.94	0.43	0.97	0.47	1.45
BAI	0.62	0.04	0.0035	0.54	0.71	27.52	0.59	0.71	1.30
R2D:4D	0.64	0.04	0.0011	0.56	0.71	0.98	0.66	0.60	1.26
L2D:4D	0.67	0.04	0.0000	0.60	0.75	0.99	0.57	0.78	1.35

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

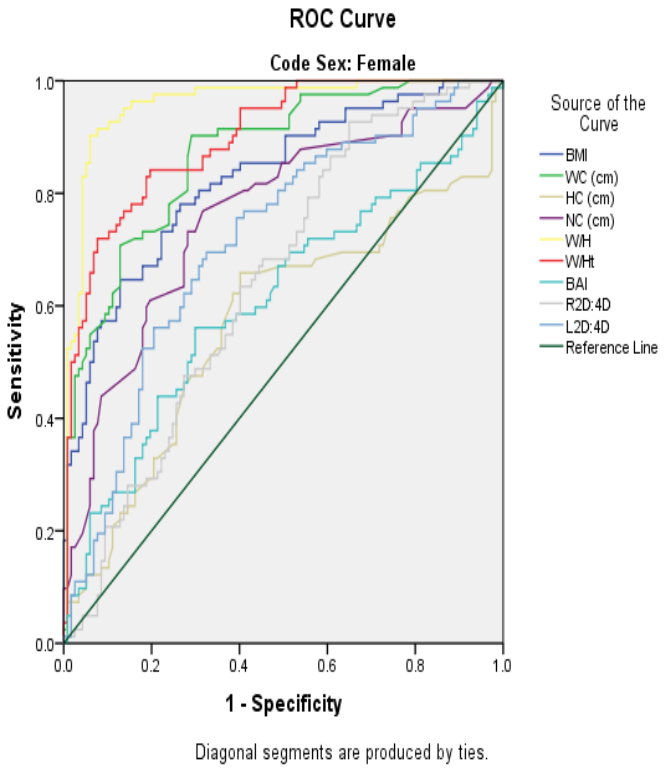
Figure 4.28: ROC curve for determination of cut off value of the anthropometric indices for DBP in females



Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit	Specif	YI
BMI	0.74	0.03	0.0000	0.68	0.80	24.10	0.48	0.91	1.39
WC (cm)	0.87	0.02	0.0000	0.83	0.91	76.65	0.86	0.75	1.61
HC (cm)	0.63	0.04	0.0004	0.56	0.70	89.30	0.53	0.75	1.28
NC (cm)	0.76	0.03	0.0000	0.70	0.82	35.05	0.69	0.72	1.41
W/H	0.95	0.01	0.0000	0.93	0.98	0.89	0.95	0.83	1.78
W/Ht	0.87	0.02	0.0000	0.82	0.91	0.45	0.91	0.72	1.63
BAI	0.58	0.04	0.0256	0.51	0.65	26.15	0.24	0.93	1.17
R2D:4D	0.76	0.03	0.0000	0.70	0.82	0.97	0.62	0.84	1.46
L2D:4D	0.75	0.03	0.0000	0.68	0.81	0.98	0.64	0.77	1.41

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

Figure 4.29: ROC curve for determination of cut off value of the anthropometric indices for SBP in males



Variables	Area	SE	Sig	Lower CI	Upper CI	Cut off	Sensit	Specif	YI
BMI	0.83	0.03	0.0000	0.77	0.89	23.32	0.65	0.87	1.52
WC (cm)	0.87	0.03	0.0000	0.82	0.92	71.95	0.90	0.71	1.61
HC (cm)	0.57	0.04	0.0840	0.49	0.66	88.05	0.66	0.60	1.26
NC (cm)	0.76	0.04	0.0000	0.69	0.83	31.05	0.77	0.68	1.45
W/H	0.96	0.01	0.0000	0.93	0.99	0.87	0.90	0.94	1.84
W/Ht	0.90	0.02	0.0000	0.86	0.94	0.43	0.99	0.48	1.47
BAI	0.61	0.04	0.0080	0.53	0.69	27.52	0.56	0.70	1.26
R2D:4D	0.65	0.04	0.0005	0.57	0.72	0.97	0.93	0.35	1.28
L2D:4D	0.71	0.04	0.0000	0.64	0.79	0.98	0.70	0.68	1.37

BMI: body mass index, WC: waist circumferences, HC: hip circumferences, NC; neck circumferences, W/H: waist to hip ratio, WHt: waist to height ratio, R2D:4D: right second to fouth digit ratio, L2D:4D: left second to fouth digit ratio, sensit: sensitivity, specif: specificity, SE: standard error, YI: Youden's index, CI:confidence interval

Figure 4.30: ROC curve for determination of cut off value of the anthropometric indices for SBP in females

CHAPTER FIVE

5.0 DISCUSSION

This cross sectional study was conducted to determine the effect of body adiposity indices, 2D:4D ratio and level of physical activity on MetS in a sample of urban and rural populace of Hausa ethnic group in Kano, Nigeria. The significantly higher 2D:4D ratio observed in the female subjects of this study is in keeping with previous studies (Manning *et al*., 1998; Manning *et al.,* 2002; Putz *et al.,* 2004; McIntyre *et al*., 2006; Trivers *et al*., 2006; Danborno *et al.,* 2010; Oyeyemi *et al*., 2014; Xu and Zheng, 2015; Oyeyemi *et al*., 2016). This difference has been widely attributed to the differential effects of androgen and oestrogen on the ring and index fingers during intrauterine development (Manning *et al.,* 1998; Malas *et al.,* 2006; Trivers *et al.,* 2006; .Galis *et al.,* 2010; Manning, 2010; Zhao *et al.,* 2012). It is note worthy from the present study that even though the sexual dimorphism observed in 2D:4D agrees with previous studies, the observed mean values were higher than the suggested normal range of 0.947 ± 0.029 and 0.965 ± 0.026 in males and females respectively (Loehlin *et al.,* 2012).

It is documented that ethnicity (Manning *et al*., 2004; 2007) and geographical factors (Loehlin *et al*., 2006) significantly affect the digit ratio and that ethic variation even exceeds the sexual differences (Manning *et al*., 2004; 2007). This means that the difference in geographical location and ethnicity may partly explain the variation observed in this study. Also, considering that some of the subjects of the present study were pooled from a clinic, a higher number of subjects compared to the general population may be harbouring some MetS indices and excessive adipose tissue, and since adiposity measures have been

shown to be positive correlates of 2D:4D (Danborno *et al.*, 2008; Oyeyemi *et al.*, 2014; Umut *et al.,* 2015), higher digit ratio may characterize some of the subjects of this study.

The observation from the present study that HC and WHtR were significantly higher in female than in males subjects is also in agreement with previous studies (Zhang *et al.*, 2013b; Ahmad *et al.*, 2015). For the HC, this difference is likely linked to the fat distribution effect of oestrogen, in that; there is preferential deposition of fats in the hip and thigh region in females (Lemieux *et al.*, 1993; Kuke *et al.*, 2005). WHtR is a fraction with body height as denominator and since studies revealed that the mean height of males is significantly higher than that of females (Zhang *et al.*, 2013b; Mousa and Fares, 2015), this may explain why the mean WHtR of females is higher than that of males as observed in our study. The mean values of BMI and BAI of females were reported to be higher than those in males, while that of WC was higher in males than in females (Andreas *et al.*, 2013; Zhang *et al.*, 2013b; Ahmad *et al.*, 2015). In the present study, there was no significant difference in these indices.

BMI as an index of body adiposity is reported to have limitations in certain individuals including younger and older people (Camhi *et al.*, 2011; Freedman *et al.*, 2012) and since this study included some teenagers and older adults who represents such age group in whom BMI was reported to be less effective, this may explain why sexual dimorphism in BMI was not observed in this study. Moreover, body adiposity measures are tightly linked with metabolic parameters (Akuyam *et al.*, 2009; Anyanwu *et al.*, 2011; Zhang *et al.*, 2013) especially visceral adiposity to which WC is a pointer (Lemieux *et al.*, 1999; Després *et al.*, 2000; Lara-Castro *et al.,* 2002) consequently, the presence and distribution of this metabolic parameters among the subjects of the study may affect sexual dimorphism in

these adiposity measures. Furthermore, considering the fact that the subjects recruited for this study included subjects from Outpatient Departments of hospitals, some of whom were newly diagnosed hypertensives, diabetics or having hypertension–diabetes co–morbidity, this may affect the body adiposity trend and may be the reason why BMI and WC did not show sexual dimorphism in this study. Additionally, the age group of the women in this study included women of reproductive age, expectedly, many would be multiparous and this could cause laxity of the anterior abdominal wall muscles leading to higher measurements of WC in females. The significantly higher NC and WHR observed for males of this study are in concordance with previous studies (Fink *et al.*, 2003; Fink *et al.*, 2006;Neelambika and Sowmya, 2015). This finding may not be unconnected with the fact that testosterone encourages fat deposition in the upper trunk (Lemieux *et al.*, 1993).

The significantly higher mean serum concentrations of FBG and TC observed in females of this study is a pointer to the higher incidence of adverse metabolic profile in the females compared to males. This impression is strengthened by the higher mean values of visceral adiposity in females as measured by VAI which has been shown to be the hallmark of MetS phenotype (Bay, 2011). Similar to this study, many previous studies reported higher mean values for HDL–C in females when compared to males (Sabir *et al.*, 2013; Mousa and Fares, 2015).

The observation from the present study that VAI was higher in females slightly deviates from previous studies (Kuke *et al.*, 2005; Amato *et al.*, 2010; Amato and Giordano, 2014) which were conducted on other populations that differ from those of the present study in terms of race, ethnicity and environmental influence. These variations in the characteristics of the study population may be the basis for this observed deviation. Salomon *et al*. (2011)

reported that differences in methods employed for visceral fat estimation may yield different results. Therefore, since various observers employed different technique, this may account for differences in findings. Also, as noted earlier, the female subjects of our study were likely to have laxed anterior abdominal wall muscles resulting from pregnancies and deliveries and as such likely to have raised WC measurement. Since WC is a component of the sex specific model employed in this study for estimating visceral fat, this may account for the higher values of VAI observed in females of this study and may probably represent an inherent drawback in the model proposed by Amato and Giordano (2014). This means that the accuracy of this model may be limited in some subjects exemplified by multiparous women in whom factors other than intra-abdominal visceral fat may contribute to the value of WC measurement. In keeping with the present study however, Andreas *et al.*(2015) used VAI as the tool for visceral adipose tissue estimation and showed the mean value to be higher in females.

In the present study, unlike many studies comparing the mean values of uric acid and adiponectin in males and females, the levels of these analytes showed no significant difference in their mean values. As independent biomarkers of MetS, SUA have been shown to be higher in males (Zheng *et al.*, 2013), while adiponectin was higher in females (Pedersen *et al.,* 2004; Mattsson and Olsson, 2007). In this study, there was a slight deviation from this trend in that, no significant difference was observed in the mean values of SUA and adiponectin. The lower levels of SUA in females reported in many studies is attributed to the uricosuric effect of oestrogen (Nicholls *et al.,* 1973) and the higher level of adiponectin in females was also thought to be associated with levels of circulating oestrogen (Pedersen *et al.,* 2004; Mattsson and Olsson, 2007). Since the level of oestrogen

significantly drops post-menopausally (Lovejoy *et al.,* 2008; Keller *et al.,* 2010), body functions driven principally by this sex hormone may demonstrate a trend reversal. Considering the age group of subjects recruited for this study, women falling within the post menopausal age range were included and this may explain the absence of significant sexual dimorphism observed for SUA and adiponectin in this particular study. Furthermore, since the indicators of adverse metabolic profile especially the VAI was significantly higher in females, it means the serum levels of protective biomarker (adiponectin) will likely decrease, while that of SUA will increase in females. This may explain the seemingly reversed trend of SUA and adiponectin seen in this study.

The positive correlation between the indices of body adiposity and components of MetS observed in the present study is in keeping with many studies (Mathieu *et al.,* 2009; Whitlock *et al.,* 2009; Eckel *et al.,* 2010; Simmons *et al.,* 2010; Okamkpa *et al.,* 2016). Similarly, the positive correlation between body adiposity measures and SUA and their negative correlation with adiponectin as observed in this study is also in conformity with previous findings (Hu *et al.,* 1996; Hotta *et al.,* 2000; Weyer *et al*., 2001; Hotta *et al.,* 2001 and Stefan *et al*., 2002).

The positive correlation of SUA with MetS as observed in the present study agrees with previous studies (Billiet *et al.,* 2014), and is believed to have an evolutionary basis resulting from uricase mutation in order to confer a survival advantage by helping to maintain blood pressure (BP), stimulate salt-sensitivity, induce insulin resistance (IR) and obesity, thereby helps promote survival during a period of famine or stress (Johnson *et al.,* 2008). Studies have also shown that hyperuricaemia is an independent predictor of MetS (Kadiri and Salako 1997; Billiet *et al.,* 2014). Also since many studies have demonstrated the protective

effect of adiponectin against MetS (Hu *et al.,* 1996; Arita *et al.,* 1999; Hotta *et al.,*2000; Weyer *et al.,* 2001), it therefore means that, as obtained in this study, all adverse metabolic indicators are expected to correlate inversely with adiponectin and positively with SUA. The antagonistic effect of adiponectin against MetS which may be the basis for the inverse correlation observed in the present study was reported to result from its anti-atherogenic (Okamoto *et al.,* 2002; Ouchi *et al.,* 2001), anti-diabetic (Yamauchi *et al.,* 2002; Stefan *et al.,* 2003) and anti-inflammatory (Maeda *et al.,* 2002; Engeli *et al.,* 2003) effects. Therefore, similar to the result obtained in this study, low plasma levels of adiponectin is reported to characterize higher measures of body adiposity and adverse metabolic parameters (Engeli *et al.,* 2003). In this study, one of the serum components of MetS, HDL correlated negatively with body adiposity measures. This finding is also similar to those of many studies (Bergman *et al.,* 2006). Consequent to this inverse relationship, unlike other serum components, lower levels of HDL characterize obesity and MetS (Bergman *et al.,* 2006). Also, significant correlation between anthropometric measures of adiposity and VAI observed in this study is in line with documented reports showing positive correlation between various measures of visceral adiposity and anthropometric measures (Lemieux *et al.,* 1999; Després *et al.,* 2000; Lara-Castro *et al.,* 2002).

Comparing the pattern of correlations observed in this study to those of previous studies, while close similarities were observed for some of the indices, wide variations were noted in others. These variations are not unexpected as there is currently an ongoing controversy on the adiposity measure with the highest discriminatory power for MetS because of conflicting reports from different ethnicity and populations (Lin *et* al., 2002; Hsieh *et al.,* 2003; Tulloch-Reid *et al.,* 2003; Shao *et al.,* 2010). The relatively weak correlation of BMI

with MetS indices and VAI when compared with indices of centripetal adiposity as found in this study is supported by many other studies (Alberti *et al.,* 1998; Einhorn *et al.,* 2003; Grundy *et al.,* 2005; Pischon *et al.,* 2008; MacKay *et al.,* 2009).

There is increasing number of publications pointing at the probable superiority of central measures of adiposity compared to BMI (Einhorn *et al.,* 2003; Grundy *et al.,* 2005; Pischon *et al.,* 2008; MacKay *et al.,* 2009). This is mainly because of its reported tight association with intra–abdominal visceral fat which is a critical determinant of MetS (Yki-Jarvinen and Westerbacka, 2005; Adiels *et al.,* 2008; Korenblat *et al.,* 2008). Also, the unique anatomic location of visceral adipose tissue (Kraegen *et al.,* 1991), difference in structural and functional characteristics between visceral and subcutaneous adipocytes (Matsuzawa, 2008; Mathieu *et al.,* 2009; Browning*et al.,* 2010), differernce in pattern of vascularisation (Bergman *et al.,* 2001; Bélanger *et al.,* 2002) are additional theories that have been put forward to explain these findings of central adiposity measures correlating with MetS better than BMI.

Additionally, in the case of the present study which included adults of advanced age, since elderly people are more likely to be physically inactive and physical inactivity has been shown to preferentially increase visceral adipose reserve (Ross and Janiszewski, 2006) manifesting as increased central adiposity measure, this factor may further contribute to the superiority of central indices over BMI as observed in this study. In line with this, a relatively higher prevalence of diabetes and/or hypertension among Indian-Asians who had similar anthropometric dimension and common socio-demographic characteristics with other Indians was solely attributed to higher truncal obesity indices rather than BMI (Shaw *et al.,* 2010). Contrarily, there are some studies which either showed both to be equivalent

or found BMI to be superior in its discriminatory power for all or some components of MetS. For example, Wang *et al.* (2003) and Ford *et al.* (2003) contested the superiority of waist circumference over BMI. This is seen in a study demonstrating a relation between increased central obesity and adverse clinical consequences, which used measurements of WC made at 14 different anatomic sites and showed that measurements made at the 4 most commonly used sites (mid-point between iliac crest and the lowest rib, superior border of iliac crest, level of umbilicus and minimal circumference between the lower end of xiphoid process and umblicus) yielded quite different absolute values for WC. On the basis of this observation, it was deduced that there is no significant difference in the predictive strengths of BMI and waist indices and it does not seem that knowledge of the WC provides any unique clinical insight and that either the BMI or WC can be used by clinicians (Wang *et al.,* 2003).

Differing from the present study, a study has observed that the emphasis on the importance of measurement of central obesity to help identify apparently healthy subjects who are more likely to develop metabolic disease is somewhat paradoxical, given the evidence from the National Health and Nutrition Examination Survey showing that measurements of BMI and WC correlated highly (r = 0.9), regardless of age, gender, or ethnicity, stressing that if the 2 measures of excess adiposity are so closely related, it is not immediately apparent why one should be more indicative of metabolic risk than the other (Ford *et al.,* 2003). Still contrary to the finding of the present study, evidence obtained from some other studies either equates BMI to truncal obesity indices or upholds BMI over the truncal indices (Haffner *et al.,* 1990; Gautier *et al.,* 1999; Tulloch-Reid *et al.,* 2003; Wang *et al;* 2005). For example, a study among Indian population shows that increases in visceral

obesity did not correlate with decreases in insulin-mediated glucose disposal in Pima Indians (Gautier *et al.,* 1999).

In another study, unlike the findings of the the present study, BMI was the estimate of adiposity with the highest hazard ratio in the prediction of type 2 DM (Tulloch-Reid *et al.*, 2003). Also contrary to the observation in the present study, a prospective study of Mexican-Americans reported that those patients with the highest baseline plasma glucose and insulin values were most likely to develop type 2 DM independent of differences in age, BMI or central obesity measures (Haffner *et al.,* 1990). In addition, a prospective study in predominantly white population, deviating from the present study concluded that generalized and central adiposity strongly and independently predicts risk of type 2 DM (Wang, 2005). Furthermore, study of obesity trend in a multi-ethnic group has shown that BMI is more strongly associated with blood pressure than abdominal obesity (Seidell *et al.*, 1991).

However in keeping with the findings of the present study, it is reported that, the clustering of dyslipidaemia, hyperuricaemia, DM and hypertension described in Whites and Africans was most strongly related to BMI, although the magnitude decreased when adjusted for differences in BMI and abdominal obesity (Schmidt *et al*., 1996). Additionally, an observational study on the natives of northern Ibadan, Nigeria investigated the relationship between two anthropometric measurements for obesity – BMI and WHR and the BP of Nigerians aged 15-85 years and the results showed that WHR and BMI had a similar linear relationship with the blood pressure of the participants (Sanya *et al.,* 2009). These wide variation and conflicting reports on the comparison of generalized and central adiposity measure may suggest that there are probably population specific factors that affect and

determine the interrelationship between body adiposity measures and MetS. These factors may include race, ethnicity, diet and physical activity level. For example, in the case of race, it is documented that blacks have lower body fat content for the same adiposity measure when compared to whites (Deurenberg *et al.,* 1998). Since adipose tissue reserve is the main consideration, this has implication on the interrelationship between adiposity and metabolic parameters and it also means that subjects belonging to different races, although may have similar adiposity measures, but the MetS parameters and their pattern of relationship with adiposity may differ.

In case of physical activity, individuals with similar body adiposity measures but different levels of physical activity may have different metabolic profile since PA has been shown to correlate negatively with metabolic parameters independent of adiposity measures (Andersen, 2006; Butte *et al.,* 2007). In any case, the difference between the results of the present study compared to those obtained from different populations on this issue further strengthen the current recommendation that anthropometric criteria for metabolic risk assessment should be population specific (Lear *et al.,* 2007; Lear *et al.,* 2010; Katzmarzyk *et al.,* 2011).

The stronger relationship between centripetal adiposity indices (WC, WHR, WHtR) with visceral adipose tissue measure when compared to BMI, as observed in this study has been similarly reported (Alberti *et al.,* 1998; Einhorn *et al.,* 2003; Grundy *et al.,* 2005; Pischon *et al.,* 2008; MacKay *et al.,* 2009). Interestingly, the result of the present study shows that even the indices of central adiposity do not exhibit the same strength of relationship with MetS indices. WHR in both males and females had the highest correlation with all the components of MetS. This relationship was further validated by WHR showing the

strongest relationship with SUA and adiponectin which have been used as serum biomarkers to test the validity of relationships between body adiposity measures and MetS parameters. In keeping with this finding, a study aimed at evaluating the associations between different measures of obesity and prevalent cardiometabolic disorders in a large population-based cohort discovered that WHR was independently associated with prevalence of the diseases and provided better discrimination than either BMI or WC (Dagenais *et al.*, 2005). Similarly, the Dallas Heart Study illustrated that WHR was more strongly associated with the risk of myocardial infarction and atherosclerosis than BMI (See *et al.*, 2007; Yusuf *et al.*, 2005) and was suggested to be the best measurement of adiposity as it differentiates between central and peripheral body adipose tissue distribution (Canoy, 2008).

In keeping with the present study, previous studies comparing obesity measures using mortality and cardiovascular problems as end points have shown WHR to perform better than other anthropometric indices. For example, more than 29,000 men were followed-up during a period of 3 years in a study, and reported WHR as a stronger predictor of risk than WC and BMI (Wang *et al*., 1995). Similarly, another study followed nearly 8,000 subjects over the course of 4.5 years and reported that although the upper percentiles of BMI, WC and WHR were all associated with increased relative risk for cardiovascular problems, the magnitude of the association was greater for WC and WHR than for BMI (Dagenais *et al.*, 2005). Similarly, Welborn *et al.* (2003) and Esmaillzadeh *et al.* (2004) demonstrated superior performance of WHR compared to WC for identifying subjects with cardiovascular risk factors.

Different from the observation of the result of the present study, there are however studies that have identified other central adiposity measures to perform better than WHR. Recently, a study assessed and compared the strength of association and discriminatory capability of measures of adiposity such as BMI, WC, HC, WHR and WHtR for DM in a sub-Saharan African population, WC was the best predictors and to some extent WHtR in the population, while BMI and WHR were less effective (Mbanya *et al.,* 2015).

Slightly deviating from the present study, which showed WHR to be superior to other anthropometric indices, a study conducted to assess abdominal adiposity and clustering of multiple metabolic syndromes in white, black and Hispanic-Americans, WC appears to be a marker for multiple metabolic syndromes indices in these ethnic groups. An observer, arguing for WC against WHR reported that, although, WHR measures central fat deposition, it is imperfect, particularly among lean individuals (Wang *et al.,* 2005). Another study has also shown that WC may be a better anthropometric predictor of many components of metabolic syndrome than BMI or WHR (Wang *et al.,* 2003) and that since WC is more strongly associated with stroke and type 2 DM than either BMI or WHR, it may be measuring a different form of adiposity not totally accounted for by BMI or WHR (Molarius *et al.,* 1999). This underscores the role of ethnicity in the interrelationships between adiposity markers and MetS.

Recently, a study conducted to predict high BP in South Eastern Nigeria showed that WC was the best predictor of hypertension (Okamkpa *et al.,* 2016). The other measures of central adipose tissue deposit have been reported to perform better than WC and WHtR. A recent extensive review of several ethnic groups by Ashwell *et al*. (2012) suggested that WHtR, WC and BMI are all important predictors of cardiometabolic risk factor in both

sexes, but WHtR was considered as the best predictor, while Onat *et al*. (2009) reported that NC has a better predictive strength compared to WC.

Also different from the present study, a good number of studies conducted on other populations have upheld WHtR to be superior to other anthropometric predictors of MetS (Hara *et al.,* 2002; Lin *et al.*, 2002; Ho *et al.,* 2003; Hsieh and Muto, 2005; Hsieh and Muto, 2006). BAI, a relatively new body adiposity measure which has been shown to have better performance than the BMI (Schulze *et al.,* 2012) and even comparable performance to central indices (Rafael de *et al.,* 2014) was found to be weak in its relationship with MetS and with VAI in the present study. This finding is very similar to that demonstrated by Andreas *et al.* (2013) who conducted one of the first studies after the discovery of BAI. According to Andreas *et al.* (2013), WHtR was superior to other indexes including BAI in estimation of visceral body adipose tissue, while for the prediction of glucose homeostasis; BAI was weak compared to BMI and WHtR whose predictive powers were comparable.

BAI, BMI, WHtR and WHR all had weak predictive values for serum lipids and BP but BAI was the weakest according to Andreas *et al.* (2011) and in the same study BAI was inferior to BMI, WHtR and WHR in its correlation with plasma adiponectin concentrations. Talaei *et al.*(2013) studied 2981 individuals of the Iranian population and reported that WHtR and BMI were stronger than BAI in the prediction of T2DM. Similarly in line with this study, Giliane *et al.*(2015) in a study to assess the performance of BAI among Brazilians concluded that, even though the index has good correlation with total body fat, its performance is weak in subjects with morbid obesity. Also, a study conducted in Enugu, Nigeria to determine the associations of anthropometric markers of adiposity with atherogenic index of plasma (AIP) found BAI to correlate with AIP but it was weaker

compared to BMI (Antoninus and Elias, 2014). The results of the present study, having demonstrated a good relationship between MetS and the anthropometric indices of body adiposity, provides a rationale for a recommendation that these indices should be considered as a clinical variable for assessing the risk of MetS in Hausa populations while giving special considerations to the WHR, which is the adiposity marker that was found to be most germane to this particular Hausa population.

The superiority of VAI over all the anthropometric measures obtained in this study is similar to many reports from different populations (Amato *et al.*, 2010; Amato *et al*., 2011). However, this index, according the present study differed from some studies in terms of its predilection for certain components of MetS. A study that evaluated the applicability of VAI in predicting MetS among Peruvian adults has demonstrated its superiority over the adiposity measures (Knowles *et al.*, 2011). Deviating slightly from the present study which shows the highest predilection of VAI for TC and TG, the study of Knowles *et al.* (2011) found significant association of VAI with all MetS components, but with a stronger predilection for TG and HDL-C in both genders. Similarly, Heloisa *et al.* (2015) found that in a sample of 221 Brazilians, VAI had the strongest association with TG, HDL-C and BP but its association with serum glucose was weaker when compared to BMI. The study of Heloisa *et al.* (2015) differs from the present study in that, even though it showed superior correlation with MetS components compared to anthropometric measures of adiposity like this study, unlike this study, the superiority of VAI did not cut across all the components of MetS because according to Heloisa *et al.* (2015), BMI in the general population and in females showed a higher correlation with serum glycaemia. Still demonstrating the validity of VAI over simple anthropometric measures as obtained in the present study, Amato *et al*.

(2010) conducted a study on a sample of European adults and found that VAI was the only measure that showed significant and independent association with MetS parameters.

From the result of the present study showing the weakest correlation of VAI with DBP and SBP compared to other MetS parameters, it may be speculated that the relationship between BP and visceral adiposity may be weaker compared to other MetS components. This may be due to higher number offactors that come into play in the regulation of BP compared to other MetS components, making the contribution of visceral adipose tissue deposit less in the pathogenesis of hypertension.

Further, the higher mRNA concentrations for angiotensinogen reported for visceral compared to abdominal subcutaneous adipose tissue is thought to be a major pathophysiologic mechanism linking hypertension with visceral adipose tissue (Dusserre *et al.,* 2000). This pathogenic pathway may seem to be longer than those linking visceral adiposity with serum lipids and glucose which often involves direct release of lipid products into the circulation (lipidaemia) or glucose release via hepatic glycogenolysis (Matsuzawa, 2008; Mathieu *et al.*, 2009; Browning *et al.*, 2010).

The availability of contrary reports (Salomon *et al*., 2011; Heloisa *et al.,* 2015) indicates that the superior discriminatory ability of visceral adipose tissue over other adiposity measures is not a unanimous contention and does not follow a uniform trend in all population which demonstrates that factors such as ethnicity may influence the interrelationships between visceral adipose tissue and MetS. Moreover, Goh *et al.* (2014) has reported that ethnicity is a principal determinant of the extent of impact of a particular adiposity measure on MetS componenents. This means that ethnic specific factors may

either up-regulate or down-regulate the relationship. Contrary the present study, Salomon *et al*. (2011), compared WC with sonographically measured visceral fat in terms of their association with MetS components and reported WC to be a stronger predictor in both sexes. Overall, the superior performance of visceral adipose measure observed in the present study may have its explanation rooted to the fact that visceral adipose tissue is tied to overproduction of TG-rich lipoproteins and glucose, leading to the dysglyaecemic and dyslipidaemic states found in viscerally obese subjects (Yki-Jarvinen and Westerbacka, 2005; Adiels *et al.*, 2008; Korenblat *et al.*, 2008).

The positive correlation observed between 2D:4D and anthropometric adiposity measures in the present study were similarly reported by other studies. Digit ratio was found to be correlated with NC among Europeans (Fink *et al.*, 2003; Fink *et al.*, 2006), with WC and HC among Ugandans(Abba *et al.*, 2012), with NC, WC, HC, CC, BMI, WHtR among Nigerians (Danborno *et al.*, 2008; Oyeyemi *et al.*, 2016). The significant correlation of 2D:4D with anthropometric measures of body adiposity as obtained the present study and other cited studies may be explained by the fact that similar to 2D:4D, body adiposity distribution pattern is sexually dimorphic (Manning *et al*., 1998; Manning *et al*., 2002; Putz *et al*., 2004; McIntyre *et al*., 2006; Trivers *et al*., 2006; Danborno *et al.*, 2010; Oyeyemi *et al*., 2014; Xu and Zheng, 2015; Oyeyemi *et al*., 2016) and also significantly influenced by sex hormones (Lemieux, 1993; Kuke *et al.*, 2005). Since 2D:4D has been linked putatively to all testosterone-linked trait (Benderlioglu and Nelson, 2004; Van Anders and Hampson, 2005; Muller *et al.*, 2011; Kangassalo *et al.*, 2011), body fat distribution pattern inclusive (Lemieux, 1993; Kuke *et al.*, 2005), this may explain the close association between the digit ratio and body adiposity measures as observed in the present study. Additionally, the

tendency of humans to accumulate excessive body fat has been traced evolutionarily to certain gene mutation aimed at conserving fats in order to withstand starvation and famine (Konarzewski, 2006).

Since variations in 2D:4D has also been attributed to evolutionary fitness (Medland *et al.*, 2010), it is possible that an individual's tendency to obesity and high 2D:4D may be a consequence of a similar genetic mutation resulting in a positive correlation between the digit ratio and body adiposity measures as observed in the present study. Interestingly, in the present study, 2D:4D also correlated with VAI and the components of MetS. The correlation of 2D:4D with VAI as seen in this study is probably explainable by the same factors linking 2D:4D with anthropometric measures of adiposity. Moreover, the anthropometric indices have been shown to strongly correlate with visceral measures of adiposity (Alberti *et al.,* 1998; Einhorn *et al.,* 2003; Grundy *et al.,* 2005; Pischon *et al.*, 2008; MacKay *et al.*, 2009).

If 2D:4D correlates with body adiposity measures as observed in the present study and other studies (Danborno *et al.,* 2008; Abba *et al.,* 2012; Oyeyemi *et al.*, 2016), then its correlation with BP and serum components of MetS which are tightly linked to adiposity is not out of scope. 2D:4D relationship with MetS parameters as observed in this study is also validated by its observed strong correlation with serum adiponectin and uric acid which are independent biomarkers that are also sexually dimorphic in their normal mean serum values. In keeping with this study, in north india, Ranvider and Manju (2016) conducted a cross sectional observational study on 200 subjects to assess the relationship between digit length and digit ratio with hypertension and revealed a positive and significant correlation. Contrarily, Pınar *et al.*(2015) recruited 137 female subjects in turkey for a study to assess

the relationship of 2D:4D with WC, BP, FBG, HDL and TG and found no significant association with all these measured parameters. The smaller sample size of the above cited study could explain the absence of correlation between 2D:4D and the measured MetS parameters. More so, in the same study, it was shown that 2D:4D did not show any correlation with all the anthropometric measures of adiposity which contradicts the vast majority of reports in the body of literature on the subject matter (Fink *et al.,* 2003; Fink *et al.,* 2006; Danborno *et al.,* 2008; Abba *et al.,* 2012; Oyeyemi *et al.,* 2016). Additionally, the study of Pınar *et al.* (2015) whose findings are in conflict with the present study recruited only female subjects and since 2D:4D has been shown to be sexually dimorphic in measurement and sometimes in relationship with body traits (Fink *et al.,* 2003; Oyeyemi *et al.,* 2016), generalization of such results to both sexes may not be appropriate. Moreover, in the present study, unlike the above cited study, the validity of the relationships between 2D:4D and MetS components was tested using biomarkers. It is also possible that the prevalence of obesity and obesity-related metabolic derangement is so low in the population studied by Pınar *et al.* (2015) and this may possibly affect the likelihood of a significant statistical correlation between 2D:4D and adiposity measures or MetS indices.

World Health Organisation (WHO, 2014) has reported that the global prevalence of obesity shows a very wide variation from extremely low in some communities to very high in others. It therefore implies that; finding relationships between obesity measures and any other body characteristics in populations with extremely low prevalence may not yield a reliable result. The smaller sample size (137) of the study of Pınar *et al.* (2015) is another possible reason for the differences observed between their study and the present study. Moreover the study was conducted on a population of different ethnicity and ethnicity has

been reported to affect the interrelationship between anthropometric measures and MetS (Lear *et al.,* 2007; Lear *et al.,* 2010; Katzmarzyk *et al.,* 2011).

Another interesting finding in the present study is that 2D:4D showed a much stronger correlation with the actual indices of MetS (serum lipid profile, glycaemic level and BP) than with adiposity measures. This relationship even attracts more attention considering that it also correlated better with serum biomarkers of MetS, putting emphasis on the probable validity of 2D:4D as a surrogate marker of MetS. The reason why its correlation with MetS indices seem to be stronger than with adiposity measures is not clear. However, it is possible that the pathophysiologic mechanism linking 2D:4D with MetS may be similar to but not exactly the same as those linking body adiposity measures with MetS. For example, it is well established that the susceptibility of an individual to MetS is determined by both modifiable and non-modifiable factors (Shoback *et al.,* 2011). While the non-modifiable factors are mainly genetic and not amenable to environmental influence, the modifiable ones can be influenced by life style (Wannamethee *et al.,* 2005).

2D:4D being established *in utero* and remains unchanged throughout life (Çelik*et al.,* 2010; Umut *et al.,* 2015), its determinants may similarly constitute a genetic variant having MetS as its manifesting feature in latter life. While the above hypothetical link between 2D:4D and MetS may not be significantly influenced by life style, body adiposity measures even though have some genetic components too, factors such as diet (Paniagua *et al.,* 2007; Romaguera *et al.,* 2009) and physical activity (Van Harmelen *et al.,* 1997; Ross and Janiszewski, 2006) have been shown to significantly influence it. Furthermore, prenatal androgen level, the major determinant of 2D:4D has been shown to enhance the development of cardiovascular system (English *et al.,* 2000; Pokrywka *et al.,* 2005). Since

a high testosterone level leads to development of a longer ring finger and a lower 2D:4D, this also implies that individuals with lower 2D:4D are likely to have a well developed cardiovascular system and thus normal cardiovascular function. On the other hand, persons with higher 2D:4D may have a poorly developed cardiovascular system and may be more likely to manifest features of poor cardiovascular function exemplified by systemic hypertension.

Inferentially, since BP is a hallmark of cardiovascular function, this may partly explain why 2D:4D was found to correlate with BP as observed in the present study and as reported by Ranvider and Manju (2016). Further to this, the correlation of 2D:4D with birth weight as demonstrated by Danborno *et al.* (2010) also strengthens the likelihood of an association between 2D:4D and MetS since low birth weight has been shown to be a good predictor of some important components of MetS such as hypertension, DM and obesity in adulthood (Baker 1998; Huxley *et al*., 2000; Anazawa *et al*., 2003).

In both males and females, the results of the present study indicate that the R2D:4D is a better correlate of MetS indices. The reason for this asymmetry is not very clear but development of digit ratio appears to be a function of androgen sensitivity related to X-linked androgen receptor gene on the digit rather than the androgen concentration (Romano *et al.,* 2006). If the alleles in the androgen receptor (AR) genes have more CAG, then it makes the AR gene insensitive to the testosterone while it is compensated by producing more testosterone in the embryo (Romano *et al.,* 2006). It is possible that these androgen receptors are unevenly distributed with a higher concentration on the right hand. In support of this study, Oyeyemi *et al.*(2014) reported that the correlation of right 2D:4D with other measures of body adiposity was stronger when compared to the left. This is also in

agreement with some previous studies (Hönekopp *et al.*, 2010; Zhao *et al.*, 2012). Right hand 2D:4D is believed to be a better predictor of intrauterine testosterone levels (Manning *et al.*, 1998; Williams *et al.*, 2000; Hönekopp *et al.*, 2010). Thus, sex difference in the right hand 2D:4D is more pronounced than that in the left hand. Invariably, the right hand shows stronger correlation with predicted variables than that of the left hand (Manning, 2002). This assertion is, however, not generally agreed upon as there are other studies showing the correlation of the left 2D:4D with important biological traits to be stronger than the right 2D:4D. Danborno *et al.*(2010) reported the left 2D:4D to correlate better with birth weight which has been reported to be a testosterone-linked sexually dimorphic feature (Danborno and Afegbua 2006). Also, the study of Fink *et al.*(2003) found that BMI was better correlated with the left 2D:4D in males.

The adverse effect of urbanization on body measures of adiposity and BP demonstrated by a negative correlation as observed in the present study has been reported by previous studies. For example, a group of observers reported that urbanization is an important contributor to rising global obesity prevalence and its attendant MetS (Abubakari *et al.*, 2008; Ramachandran *et al*., 2008; Mbanya *et al*., 2014). Urbanization is also identified as a substantial contributor to the difference in adiposity and metabolic characteristics of different communities (Abubakari *et al.*, 2008; Ramachandran *et al*., 2008; Mbanya *et al*., 2014). These factors may as well explain the differences in the adiposity measures and BP of participants from urban and rural areas of the present study. This finding may also be related to the fact that urban participants might be less active and consume unhealthy food containing more saturated fat and high calorie diet, while rural participants eat the

traditional high carbohydrate, low protein and low fat diet as documented in the literature (Amuna and Zotor, 2008).

Urbanization appears to be associated with extreme changes in dietary habits, psychological stress and physical inactivity (Taro *et al.,* 2001; Nyenwe *et al.,* 2003; Amuna and Zotor, 2008; Sabir *et al.,* 2013). The observed higher adverse impact of urbanization on central adiposity indices compared to generalized index may mean that sedentary life style which characterizes urban dwellers may enhance preferential visceral fat deposition compared to subcutaneous adipose tissue. Since visceral adipose tissue is reported to be the hallmark of MetS phenotype and the major link between adiposity and MetS (Després and Lemieux, 2006). This may further explain why visceral adipose measure and MetS indices are also higher in urban than in rural subjects of the present study. The observation from this study that the adverse effect of urbanization are more on females compared to males is probably due to males being more likely to live an active life style compared to females. This means that even in urban setting where sedentary life style is common, women have a higher tendency of being sedentary.

Since it is a well established concept that 2D:4D once established *in utero* around the 14^{th} – 15^{th} week, the ratio remains fairly stable throughout life (Çelik*et al.,* 2010; Umut *et al.,* 2015), it is not clear why 2D:4D in the present study, like body adiposity measures was observed to be higher in urban participant. It is, however, possible that environmental factors actually influence the development of urban or rural 2D:4D variant during embryogenesis and not after birth. This may also be the explanation for the finding in the literature where 2D:4D is documented to vary due to environmental influence and geographical location (Loehlin *et al*., 2006).

The observed significantly higher values of all serum components of MetS with the exception of HDL, and higher body adiposity measures in urban participants of the present study are similar to previous reports. Sabir *et al.* (2013) conducted a study to compare the adiposity profile of a rural and urban settlement in Nigeria and showed that the mean values of WC, BMI, WHR, DBP and SBP were higher for the urban inhabitants. Sabir *et al.*(2013) also found that the TC was significantly higher in urban than rural participants. Deviating slightly from the present study, Sabir *et al.*(2013) observed that there was no significant difference in the mean serum LDL-C and TG concentrations in the urban than rural inhabitants. Mean serum HDL-C was also insignificantly higher in the rural than in urban participants.

In line with the result of the present study, Adediran *et al.*(2012) conducted an observational study on rural and urban settlements of Abuja, Nigeria to compare the distribution of MetS parameters among the people in both communities and found that WC, WHR, BMI, DBP and SBP were significantly lower in rural settlements, while TC, LDL and TG similar to the present study were all higher in urban settlement and HDL-C was higher in rural settlements. Differing slightly from the result of the present study where the impact of urbanization on the indices were similar, Adediran *et al.*(2012) observed that while the impact of urbanization on BMI, WC, DBP, SBP, HDL and TG were all significant and comparable, the impact on LDL, TC and FBG was much less.

Another slightly different report by Obirikorang *et al.*(2015) who conducted a comparative study to look at the adiposity and metabolic trends in rural and urban communities in Ghana, the results suggested that among serum and BP components of MetS, significant differences were only observed in DBP, TC, LDL and FBG. However, in the

anthropometric measures of adiposity, significantly higher values were recorded for all indices for participants in the urban area.

Overall comparison of the result of the present study and other studies demonstrates a similar adverse effect of urbanization on body adiposity measures and MetS indices but with little variation in terms of the magnitude of impact on the different indices. These differences could be due to variations in the extent of exposure to urban life style in the subject of the different studies or individual differences in the inherent mechanism of metabolizing food nutrients. The adverse effects posed by urban life style on the anthropometric and visceral measures of body adiposity is supported by the observation from the present study that SUA levels are higher in the urban area and adiponectin is higher in rural area. Since adiponectin which is known to be a negative correlate of MetS (Hu *et al.,* 1996; Arita *et al.,* 1999; Hotta *et al.,* 2000; Weyer *et al.,* 2001) was observed to be higher in the rural area and SUA, a positive correlate of MetS (Kadiri and Salako 1997; Billiet *et al.,* 2014) to be higher in urban areas, this probably validates the difference in the metabolic and adiposity profile of the urban and rural participants of the present study.

The significant effect of PA on MetS indices as demonstrated by significant reduction in measures of adiposity and serum components observed in the present study indicates that PA confers protection against MetS. Also, the pattern of change observed in the serum biomarkers supports this notion in that while SUA decreased with increasing levels of PA, adiponectin increases. Also, HDL–C, a component of lipid profile whose increased levels indicates a lower metabolic risk (Andreas *et al.,* 2013; Sabir *et al.,* 2013) was also observed to rise with increasing PA. In keeping with this result, previous studies have shown the inverse relationship between physical activity and adverse metabolic parameters, thus

indicating its protective effect against MetS (Franks *et al.,* 2004; Ekelund *et al.,* 2007; Healy*et al.,* 2008). It has also been reported that PA can have a profound effect on reducing body and visceral adiposity and therefore reduces the risk of MetS (Pattyn *et al.,* 2013; Vissers *et al.,* 2013). Increased PA, especially that which is associated with reduced fat mass, corrects the dysfunction in adipokine and cytokine expression so that expression of adiponectin is increased in adipose tissue and production of inflammatory cytokines is reduced (Bradley *et al.,* 2008; Kim *et al.,* 2013).

Some reports suggest that the beneficial effect of PA as observed in the present study is partly mediated through changes in the adipokines profile, that is, by increasing anti-inflammatory cytokines and decreasing proinflammatory ones (Bruunsgaard *et al.,* 2005; Petersen and Pedersen, 2005).This effect has been described at the levels of gene expression, protein ligands and receptor bindings (Moldoveanu *et al.,* 2001). For instance, PA increases insulin sensitivity through reduction of resting levels of TNF-α and augmentation of adiponectin levels (Kasapis *et al.,* 2005). Also, the observation in this study that certain measures of body adiposity such as HC in females and BAI in males do not change significantly following PA may suggest that the various anatomic sites of body adipose tissue reserve may respond differently to PA. This view may be buttressed by the observation in the present study that, even in the adiposity indices which changed significantly with PA, the extent of change varied following exposure to the same type of PA. This finding may be of utmost significance in the selection of individualized therapeutic exercise regimen for various adiposity phenotypes. Moreover, it is documented that increased physical activity, especially that which is associated with reduced fat mass, corrects the dysfunction in adipokine and cytokine expression so that expression of

adiponectin is increased in adipose tissue and production of inflammatory cytokines is reduced (Bradley*et al.,* 2008; Kim *et al.,* 2013).

The reason why 2D:4D ratio was observed in this study to decrease with PA is not very clear. This is considering the fact that the ratio is a stable, hormonally and genetically determined congenital variable (Çelik *et al.,* 2010; Umut *et al.,* 2015). However, since the ratio has been shown to be a marker of behaviour (Manning, 2002a) and has been associated with behavioural characteristics such as type of sexual behaviour (McFadden and Champlin, 2000; Robinson and Manning, 2000), assertiveness (Manning, 2002a), aggression (Bailey and Hurd 2005; Millet and Dewitte 2007) and even sport performance (Manning and Taylor, 2002), it is possible that the likelihood of an individual to adopt an active or sedentary life style is a biologic trait which is also genetically and congenitally predetermined and may manifest phenotypically in the digit ratio, behaviourally in the form of individual's desire for PA and physiologically as threshold of PA tolerance. This means that the digit ratio may provide a clue to an individual's PA personality or behaviour.

The observation from this study that WC in females, VAI, FBG, TC, TG and LDL all decreased with increasing PA levels but did not show any significant decrease after moderate PA may suggest that PA brings about reduction in measures of MetS indices and also suggests that the effect of PA on MetS indices probably has a threshold in that moderate PA may be enough to combat most adverse metabolic parameters and higher levels of PA may be higher threshold and thereby not conferring additional benefit. Interestingly, the biomarkers also demonstrated corresponding changes in that they remained relatively stable after moderate activity level. This finding is particularly important because adiposity and MetS markers have been reported to increase with age

(Lemieux *et al.,* 1999; Després *et al.,* 2000; Lara-Castro *et al.,* 2002) making most victims to fall in the older age group. Since elderly people are also more likely to have other age related co–morbid conditions like ischaemic heart disease and arthritic changes which makes high levels of PA unfit for them, this implies that exposure of this group of individuals to such high PA levels in order to combat adiposity and MetS may be unnecessary. Notably, some serum parameters like TC and LDL in females did not show significant change after only mild PA indicating that very low levels of PA may be inadequate to significantly reduce these indices. These findings underscore the importance of regimenting PA therapy based on its desired metabolic effect. The slight sex difference observed in the metabolic response to PA as noted for WC, TC and LDL and the observation that the rate of drop in the serum parameters was more drastic in females when compared to males suggest that there is sexual dimorphism in the interrelationship between PA, adiposity and MetS and that such gender peculiarity should be considered in exercise therapy for adiposity and MetS. Supporting this observation, some evidences exist to suggest that there is gender discrepancy in exercise-induced insulin sensitivity, in that females respond better than males for age-matched counterparts following the same dose and duration of aerobic PA (Lee, 2012).

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

It can be concluded from the findings of this study that:

i. 2D:4D, NC, HC, WHtR, WHR, VAI are sexually dimorphic, with higher 2D:4D, VAI, HC and WHtR in females and higher NC and WHR in males while, BMI and WC did not show sexual dimorphism

ii. Females had higher TC, HDL and FBG while, SBP, DBP, TG, LDL, SUA and adiponectin were similar in both sexes.

iii. Body adiposity measures, DBP, SBP, 2D:4D were higher in urban than in rural dwellers and this difference was more marked in the central adiposity indices and in females. For serum parameters, only HDL-C and adiponectin were higher in rural areas, others were higher in urban areas. This may imply that rural dwellers have better protection against cardiovascular diseases

iv. The adiposity indices, 2D:4D correlated positively with MetS parameters and SUA but negatively with HDL-C and adiponectin. This means that higher digit ratio and adiposity measures are MetS risk predictors

v. Among the anthropometric indices, WHR showed strongest correlation with metabolic indices but VAI was stronger than all other indices and that BAI and HC showed the

weakest correlation. This implies that VAI is more strongly associated with MetS when compared with other adiposity measures.

vi. VAI correlated better with serum components compared to blood pressure components of MetS. This implies that VAI is more strongly associated with serum components of MetS when compared with blood pressure components

vii. Anthropometric adiposity indices and 2D:4D correlated strongly with VAI.

viii. The R2D:4D was a better correlate of metabolic indices compared to L2D:4D.

ix. In females, 2D:4D had weaker correlation with body adiposity measure when compared to males.

x. Adiposity indices, serum parameters of MetS and 2D:4D were lower in physically active individuals while HDL-C and adiponectin were higher in physically active individuals and PA showed the lowest impact on HC and BAI. This means that PA increases serum levels of protective biomarkers.

xi. The metabolic profile of females showed higher responsiveness to PA compared to males.

xii. The impacts of moderate and optimal physical activity on MetS indices were very similar.

xiii. Both blood pressure and serum componenets of MetS are predictable from 2D:4D and anthropometric adiposity indices.

xiiii. WHR showed the highest percentage contribution to the prediction of all MetS components in both sexes. This indicates that WHR is the anthropometric adiposity tool with the strongest relationship with MetS.

xv. Cut-off values of the anthropometric indices for MetS componenets were slightly different from those obtained for other populations and also slightly different in both sexes.

xvi. WHR had the highest sensitivity and specificity and the largest area under the ROC curve.

6.2. RECOMMENDATIONS

It can be recommended from the findings of the study that:

i. 2D:4D may be considered as a surrogate marker of body adiposity and MetS and should be used as an initial screening tool for individuals susceptible to MetS among Hausas of Kano.
ii. measurement of serum adiponectin may be included in the standard protocols for the biochemical evaluation of MetS.
iii. prescription of therapeutic exercise regimen to combat adiposity and MetS may be individualized based on sex, adiposity phenotype and pattern of metabolic indices.
iv. VAI may be used as a cheaper alternative to CT-scan and MRI in the estimation of visceral fat content and metabolic risk stratification in Hausas of Kano and probably elsewhere.
v. WHR may be used as the most sensitive and specific anthropometric predictor of MetS among Hausas of Kano and probably elsewhere.

vi. larger scale multi-ethnic study may be carried out to investigate if the validity of 2D:4D as a metabolic screening tool observed in this study is universally applicable

vii. similar studies on other ethnic groups in Nigeria should be conducted to find out if the anthropometric cut-off values for MetS indicators obtained in this study can be applied on other Nigerians.

6.3 CONTRIBUTION TO KNOWLEDGE

i. The study revealed 2D:4D to be a good correlate of visceral adiposity (for males R2D:4D r = 0.54, L2D:4D r =0.49. $P < 0.001$., for females R2D:4D r = 0.56,L2D:4D r =0.68 $P < 0.001$) and body adiposity (for males R2D:4D r = 0.47, L2D:4D r = 0.37 $P < 0.05$, for females R2D:4Dr =0.14, L2D:4D r = 0.29 $P < 0.05$ as well as MetS components and biomarkers among Husas of Kano (for R2D:4D r for SUA and adiponectin are 0.59 and -0.63 respectively $P < 0.05$ while for L2D:4D r = 0.54 and -0.57 respectively $P < 0.05$).

ii. The study has identified 2D:4D as a likely marker of an individual's PA behaviour and PA tendency (mean 2D:4D was 0.98, 0.97, 0.96 and 0.94 for inactive, mild, moderate and optimal PA, $P < 0.05$) .

iii. A baseline data was established for Hausa ethnic group of Kano State, Nigeria in their measures of visceral adiposity (mean VAI of 3.51 and 4.46 for males and females respectively) and body adiposity indices (mean WHR of 0.89 and 0.85 in males and females respectively), relationship with adiponectin, uric acid and MetS components (for VAI, r = 0.89 and -0.85 for SUA and adiponectin respectively $P < 0.05$. For WHR, r = 0.84 and -0.83 for SUA and adiponectin respectively $P < 0.05$). VAI was recognized to be superior to simple anthropometric measures in their

correlation with MetS components (maximum r for VAI with MetS components was 0.97, compared to 0.9 for WHR).

iv. Models were formulated for predicting each component of MetS from anthropometric indices, digit length and digit ratio. WHR was identified as the anthropometric measure that is most germane to Hausas in Kano in terms of MetS prediction. The prediction models for the MetS components are;

For male

(a) FBG= FBG= 266.07 (W/H) + 106.79(R2D:4D) +(-219.54)

(b) TC= 358.48 (W/H) + (-145.26)

(c) HDL-C =70.74(W/H) + 107.17

(d) TG= 340.56(W/H) + (0.69)(Height) + (-70.41)

(e) LDL= 361.12(W/H) + (-215.15)

(f) VAI= 19.56 (W/H) + (-13.90)

(g) DBP=104.64 (W/H)+(-10.14)

(h) SBP= 173.15(W/H) + 133.66(R2D:4D)+(-153.57)

For female

(a) FBG= FBG= 326.05 (W/H) + (-191.68)

(b) TC= 354.95 (W/H) + 405.41(L2D:4D) (-533.76)

(c) HDL-C =65.30(W/H) + 106.37

(d) TG= 299.08(W/H) + (-146.30)

(e) LDL= 366.03(W/H) + 385.1(L2D:4D)+ (-595.72)

(f) VAI= 18.06 (W/H) + (-11.74)

(g) DBP=47.18 (W/H)+ 1.46(BMI) + 59.70(R2D:4D) + (-0.54)(BAI)+ (-32.66)

(h) SBP= 226.38(W/H) + 120.64(L2D:4D) + 7.63(BMI)+ (-2.62) (Weight) + (-7.68)(BAI) + 561.75(W/Ht) + 1.26(NC) + (51.20)

v. The study established cut off values of anthropometric measures of adiposity for each parameter in the MetS.

vi. The study demonstrated the differential effects of various levels of physical activity on the various measures of body adiposity and components of MetS. In doing this, the amount of physical activity needed to impact significantly on each adiposity measure and MetS components were identified.

REFERENCES

Abba, I.S., Gabriel, O., Domnic, M., Godfery, M., Dare, S.S., Mohammed, Y.G. and Okpanachi, A.O. (2012). Assessment of the relationship between digit lengths and circumferences of the waist and hip amongst ugandans. *Asian Journal of Medical Sciences,* 4(3):113-116.

Abubakari, A.R., Lauder, W., Agyemang, W.C., Jones, M., Kirk, A. and Bhopal, R.S (2008). "Prevalence and time trends in obesity among adult West African populations: a meta-analysis." *Obesity Review,* 9(4): 297-311.

Achie, L.N., Olorunshola, K.V., Toryila, J.E. and Tende, J.A.(2012). The body mass index, waist circumference and blood pressure of postmenopausal women in Zaria, Northern Nigeria. *Current Research Journal of Biological Sciences,*4(3): 329-332.

Adediran, O., Akintunde, A.A., Edo, A.E.,Opadijo,.OG., Araoye, A.M. (2012). Impact of urbanization and gender on frequency of metabolic syndrome among native Abuja settlers in Nigeria. *Journal of Cardiovascular Diseases Research*, 3:191-6.

Adiels, M., Taskinen, M.R. and Boren, J. (2008). Fatty liver, insulin resistance, and dyslipidemia. *Current Diabetes Report,* 8: 60–64

Ahmad, M. N. and Haddad, F. H. (2015). Suitability of visceral adiposity index as a marker for cardiometabolic risks in Jordanian adults. *Nutrition Hospitals*, 32(6):2701-2709

Akuyam, S.A., Aghogho, U.B., Aliyu, I..S and Bakari, A.G. (2009). Serum total cholesterol in hypertensive Northern Nigerians. *International Journal of Medicine and Medical Science,*3: 73 – 78

Alberti, K. G. and Zimmet, P. Z. (1998). Definition, diagnosis and classificationof diabetes mellitus and its complications. Part 1: diagnosisand classification of diabetes mellitus provisional reportof a WHO consultation. *Diabetic Medine,* 15:539-553.

Al-Daghri, N.M., Al-Attas, O.S., Alokail, M.S., Alkharfy, K.M., Charalampidis, P and Livadas, S. (2013). Visceral adiposity index is highly associated with adiponectin values and glycaemic disturbances. *European Journal of Clinical Investigation,* 43(2): 183–189.

Al-Odat, A.Z., Ahmad M.N and Haddad, F.H. (2012). References of anthropometric indices of central obesity and metabolic syndrome in Jordanian men and women. *Diabetes and Metabolic Syndrome,* 6: 15–21.

Alvim, R. O. Mourao-Junior, C. A. Oliveira, C. M., Krieger, J. E. Mill, J. G.and Pereira, A. C. (2014). body mass index, waist circumference, body adiposity index, and risk for type 2 diabetes in two populationsin Brazil: General and Amerindian. *PLoS ONE* 9(6): e100223. doi:10.1371/journal.pone.0100223

Amato, M.C., Giordano C., Pitrone, M. and Galluzzo A. (2011). Cut-offpoints of the visceral adiposity index (VAI) identifying a visceral adipose dysfunction associated with cardiometabolic riskin a Caucasian Sicilian. *Lipids Health Dieases,* 10(183):1-8.DOI:10.1186/1476-511X-10-183

Amato, M.C and Giordano, C. (2014). Visceral adiposity index: an indicator of adipose tissue dysfunction. *International Journal of Endocrinology,* (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4009335/http://www.hindawi.com//ije/2014/730827/): 730827.

Amato, M.C., Giordano, C., Galia, M., Criscimanna, A., Vitabile, S. and Midiri, M. (2010).Visceral adiposity index a reliable indicator ofvisceral fat function associated with cardiometabolic risk. *Diabetes Care,* 33(4): 920-2.

Amuna, P. and Zotor, F.B. (2008). Epidemiological andnutrition transition in developing countries:impact on human health and development. *Proceeds of Nutrition Society,* 67(1):82–90.

Anazawa, S., Atsumi, Y. and Matsuoka, K. (2003). Low birth weightand development of type 2 diabetes in a Japanesepopulation. *Diabetes Care,* 26: 2210-2211.

Andersen, L. B. (2006). Physical activity and clustered cardiovascular risk in children: a cross-sectional study (The European Youth Heart Study). *Lancet,*368: 299–304

Anderson, L.A., McTernan, P.G., Barnett, A.H. and Kumar, S. (2001). The effects of androgens andestrogens on preadipocyte proliferation in human adipose tissue: influence of genderand site. *Journal of Clinical Endocrinology and Metabolism,* 86: 5045–5051.

Andreas, M., Claudia, L., Alexander, T.M.(2013). Body Adiposity Index and other indexes of body composition in SAPHIR study: Association with cardiovascular risk factors. *Obesity,* 21, 775-771

Andreasen, C.H., Mogensen, M.S. and Borch-Johnsen, K. (2009). Studies of *CTNNBL1* and *FDFT1* variants and measures of obesity: analyses of quantitative traits and case-control studies in 18,014 Danes. *Biomedical Central Medical Genetics,* 10:17.

Andreas, M., Claudia, L., Alexander, T.M. *et al.* (2013). Body Adiposity Index and other indexes of body composition in SAPHIR study: Association with cardiovascular risk factors. *Obesity,* 21, 775-771

Antoninus, O. and Elias, O. (2014) Anthropometric measures of adiposity as correlates of artherogenic index of plasma in non-obese sedentary Nigerian males. *Libyan Journal of Medicine,* 9:10.3402/ljm.v9.23798. doi: 10.3402/ijm.v9.237978

Anyanwu, G.E., Ekezie, J., Danborno, B and Ugochukwu, A.I. (2011). Body size and adiposity indicators and their relationships with blood pressure levels in Igbos of Nigeria. *Nigeria Journal of Medicine,* 20: 44 - 51

Arita, Y., Kihara, S., Ouchi, N., Takahashi, M. *et al*. (1999). Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. *Biochemical and Biophysical Research Communications,* 257: 79–83.

Arner, E., Westermark, P.O., Spalding, K.L., Britton, T., Ryden, M., Frisen, J., Bernard, S. and Arner, P. (2010). Adipocyte turnover: relevance to human adipose tissue morphology. *Diabetes,* 59: 105 – 109

Ashwell, M., Gunn, P. and Gibson, S. (2012). Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: Systematic review and meta-analysis.*Obesity Review,* 13:275-86.

Atienza, A. A., Moser, R. P., Perna, F., Dodd, K, Ballard-Barbash, R., Troiano, R. P. and Berrigan D. (2011). Self-reported and objectively measured activity related tobiomarkers using NHANES. *Medical Sciences, Sports and Exercise,*43:815–21.

Bailey, A.A. and Hurd, L (2005). Finger length ratio (2D:4D)correlates with physical aggression in men but notin women. *Biological Psychology,* 68: 215–222.

Barker, D.J.P .(1998). *Mothers, babies and health in later life*. Edinburgh: Livingstone.

Bays, H.E. (2011). Adiposopathy: is "sick fat" a cardiovascular disease? *Journal of America College of Cardiology,* 57:2461–2473.

Beaulieu, E.E. and Kelly, P.A. (1990). *Hormones: From Molecules to Disease*. Paris: Chapman and Hall, p. 697.

Beighton, P.L., Solomon, C. L., Soskolne, B., and Robint, G (1974). Serum uric acid concentrations in anurbanized South African Negro population. *Annals of rheumatoid Diseases,* 33:442

Bélanger, C., Luu-The, V., Dupont, P. and Tchernof, A. (2002). Adipose tissue intracrinology: potentialimportance of local androgen/estrogen metabolism in the regulation of adiposity. *Hormone Metabism Resource*, 34: 737–745

Belarmino, G., Horie L.M., Sala, P. C., Torrinhas, R. S., Heymsfield, S. B. and Waitzberg, D. L. (2015). Body adiposity index performance in estimating body fat in a sample of severelyobese Brazilian patients. *Nutrition Journal,*14:130

Ben Ounis, O. (2010). Exercise improves the ApoB/ApoA-I ratio, a marker of the metabolic syndrome in obese children. *Acta of Paediatrica,* 99: 1679–1685.

Benderlioglu, Z. and Nelson, R.J. (2004). Digit length ratio predict reactive aggression in women but not in men. *Hormones Behavior*, 46: 558-564

Benedict, C., Axelsson, T. and Söderberg, S. (2014). The fat mass and obesity-associated gene (*FTO*) is linked to higher plasma levels of the hunger hormone ghrelin and

lower serum levels of the satiety hormone leptin in older adults. *Diabetes*, 63(11):3955–3959.

Bergman, R. N., Stefanovski, D., Buchanan, T. A. (2011a). A better index of body adiposity.*Obesity (Silver Spring)*, 19:1083-1089.

Bergman, R.N., Kim, S.P., Catalano, K.J., Hsu, I.R., Chiu, J.D and Kabir, M. (2006). Why visceral fat is bad: mechanisms of the metabolic syndrome. *Obesity Silver SpringSupplies* 1:16S-19S, http://dx.doi.org/10.1038/oby. 2006.277.

Bergman, R.N., Van Citters, G.W., Mittelman, S.D., Dea, M.K., Hamilton-Wessler, M., Kim, S.P. and Ellmerer, M (2011b). Central role of the adipocyte in the metabolic syndrome. *Journal of Investigative Medicine*, 49: 119–126

Berthier, M.T., Houde, A., Paradis, A.M., Couture, P., Gaudet, D., Després, J.P. and Vohl, M.C. (2004). Molecular screening of the microsomal triglyceride transfer protein: association betweenpolymorphisms and both abdominal obesity and plasma apolipoprotein B concentration.*Journal of Human Genetics*,49: 684–690.

Bifulco, M., Santoro, A., Laezza, C. and Malfitano, A.M (2009). Cannabinoid receptor CB1 antagonistsstate of the art and challenges. *Vitamin and Hormones*,81: 159–189.

Billiet, L., Doaty, S., Katz, J.D.and Velasquez, M.T. (2014). Review of hyperuricemia as new marker for metabolic syndrome. *ISRN Rheumatology*, 85:29-54

Bluher, M., Engeli, S., Kloting, N., Berndt, J., Fasshauer, M., Batkai, S., Pacher, P., Schon, M.R.,Jordan, J. and Stumvoll, M (2006). Dysregulation of the peripheral and adipose tissue endocannabinoidsystem in human abdominal obesity. *Diabetes* 55: 3053–3060

Bobbert, T., Wegewitz, U. Brechtel, L. et al., (2007). Adiponectinoligomers in human serum during acute and chronic exercise:relation to lipid metabolism and insulin sensitivity," *InternationalJournal of Sports Medicine*, 28(1): 1–8.

Borel, A.L., Nazare, J.A and Smith, J. (2012). Improvement in insulin sensitivity following a 1-year lifestyle intervention program in viscerally obese men: contribution of abdominal adiposity. *Metabolism*, 61:262–272.

Borruel, S., Moltó, J.F., Alpañés, M., Fernández-Durán, E., Alvarez-Blasco, F and Luque-Ramírez, M. (2014). Surrogate markers of visceral adiposity in young adults: waist circumference and body mass index are more accurate than waist hip ratio, model of adipose distribution and visceral adiposity index. PLOS One, 9(12): e114112.

Bosco, J., Greenleaf, J., Kave,R**.** and Averkin, E. (1970). Reduction of serum uricacid in young men during physical training. *America Journal of Cardiology*, 25:46- 52

Bouchard, C., Rice, T., Lemieux, S., Després, J.P., Pérusse, L. and Rao, D.C (1996). Major gene for abdominal visceral fat area in the Quebec Family Study. *International Journal of Obesity and Related Metabolic Disorders,* 20: 420–427

Bouchard, C., Tremblay, A., Després, J.P., Nadeau, A., Lupien, P.J., Thériault. G., Dussault, J., Moorjani, S., Pinault, S. and Fournier, G. (1990). The response to long-term over feeding in identicaltwins. *New England Journal of Medicine,*322: 1477–1482.

Bouchard, L., Weisnagel, S.J, Engert, J.C., Hudson, T.J., Bouchard, C., Vohl, M.C. and Pérusse, L. (2004). Human resistin gene polymorphism is associated with visceral obesity and fasting and oral glucose stimulated C-peptide in the Quebec Family Study. *Journal of Endocrinology Investigation,* 27: 1003–1009

Bozorgmanesh, M., Hadaegh, F and Azizi, F. (2011). Predictive performance of the visceral adiposity index for a visceral adiposity-related risk: type 2 diabetes. *Lipids Health Discovery*, 10(88): 88.doi: 10.1186/1476-511x-10-88

Bradley, R. L Jeon, J. Y.. Liu F.F, and. Maratos-Flier, E. (2008). Voluntary exercise improves insulin sensitivity and adipose tissue inflammation in diet-induced obese mice, *American Journal of Physiology*, 295(3): 586–594

Braud, S., Ciufolini, M., Harosh, I. (2010). 'Energy expenditure genes' or 'energy absorption genes': a new target for the treatment of obesity and Type II diabetes. *Future Medicinal Chemistry*, 2(1 2): 1 777-1 783.

Britton, K.A., Massaro, J.M., Murabito, J.M., Kreger, B.E., Hoffmann, U and Fox, C.S. (2013). Body fat distribution, incident cardiovascular disease, cancer, and all-cause mortality. *Journal of American College of Cardiology*, 62:921–5.

Brown, L.M. and Clegg, D.J. (2010). Central effects of estradiol in the regulation of food intake, body weight, and adiposity. *Journal of Steroid Biochemistry and Molecoular Biology,* 122: 65–73

Brown, W.M., Hines, M., Fane, B.A and Breedlove, S.M. (2002). Masculinized finger length patterns in human males and females with congenital adrenal hyperplasia. *Hormone Behavior,* 42: 380-386

Browning, L.M., Hsieh, S.D and Ashwell, M. (2010). A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could bea suitable global boundary value. *Nutrition Resource Review,* 23: 247–269.

Bruunsgaard, H. (2005). Physical activity and modulation of systemic low-level inflammation, *Journal of Leukocyte Biology*, 78(4): 819–835.

Bull R and Benson P. (2006). Digit ratio (2D/4D) and the spatial representation of magnitude. *Hormones and Behavior*, 50:194–199.

Burley, N.T. and Foster, V.S. (2004). Digit ratio varies with sex, egg order, and strength of mate preference in zebra finches. *Proceedings of the Royal Society of London Series B. Biological Science,* 271: 239–244.

Butte, N. F., Puyau, M. R., Adolph, A. L., Vohra, F. A. and Zakeri, I. (2007) Physical activity in non overweight and overweight Hispanic children and adolescents. *Medical Science of Sports and Exercise,* 39: 1257–1266.

Camhi, S, M. and Bray, G. A., Bouchard, C., Greenway, F. L., Johnson, W. D., et al. (2011).The relationship of waist circumference and BMI to visceral, subcutaneous, andtotal body fat: sex and race differences. *Obesity,* 19: 402–408.

Cancello, R., Tordjman, J. and Poitou C. et al. (2006). Increased infiltration of macrophages inomental adipose tissue is associated with marked hepatic lesions in morbid humanobesity. *Diabetes,*55:1554-1561.

Canoy, D. (2008). Distribution of body fat and risk of coronary heart disease in men andwomen. *Current Opinion in Cardiology,* 23:591-598.

Carall, F.R., Vollenhoven, B.J. and Weston, G.C (2005). Anatomical evidence for in utero androgen exposure in women with polycystic ovary syndrome. *Fertility and Sterilility,* 84:1689-92.

Caraway, W.T. (1955). Determination of concentration of serum uric acid. *American Journal of Clinical Pathology,* 25: 840

Cattrall, F.R., Vollenhoven, B.J. and Weston, G.C (2005). Anatomical evidence for in utero androgen exposure in women with polycystic ovary syndrome. *Fertility and Sterility,* 84: 1689–1692.

Çelik, A., Aksu, F., Tunar, M., Daşdan, Ada, E. N., Topaçoğlu, H.(2010). The relationship between the individual performance level of master athletes and hand digit ratio. *Dokuz Eylul University Journal*, 24: 5-10.

Celis-Morales, C. A., Perez-Bravo F, Ibanez L, Salas C, Bailey, M. E and Gill, J. M. (2012). Objective self-reported physical activity and sedentary time: effects of measurement method on relationships with risk biomarkers. *PLoS One.*7:e36345.

Choi, H.K., Atkinson, K., Karlson, E.W and Curhan, G (2005). Obesity, weight change, hypertension, diuretic use,and risk of gout in men: the health professionals follow-up study. *Archieves of Internal Medicine*. 11:165:742

Choquet, H. and Meyre, D (2010). Genomic insights into earlyonsetobesity. *Genome and Medicine,* 2(6): 36

Choquet, H. and Meyre,D. (2011). Molecular basis of obesity:current status and future prospects. *Current Genomics,* 3: 1 54-68.

Ciresi, A., Amato, M.C., Guarnotta, V., Castro, F and Giordano, C. (2013). Higher doses of cabergoline further improve metabolic parameters in patients with prolactinoma regardless of the degree of reduction in prolactin levels. *Clinical Endocrinology*, 79(6): 845–852.

Ciresi, A., Amato, M.C., Pivonello, R., Nazzari, E., Grasso, L.F and Minuto, F. (2013). The metabolic profile in active acromegaly is gender-specific. *Journal of Clinical Endocrinology and Metabolism*, 98(1): E51–9.

Ciresi, A., Amato, M.C., Pizzolanti, G and Giordano, C. (2012) Visceral adiposity index is associated with insulin sensitivity and adipocytokine levels in newly diagnosed acromegalic patients. *Journal of Clinical Endocrinology and Metabolis*m, 97(8): 2907–2915.

Ciumas, C., Lindén Hirschberg, A. and Savic, I (2009). High fetal testosteroneand sexually dimorphic cerebral networks in females. *Cerebral Cortex,*19:1167-74.

Clee, S.M (2009). Genetic gains on the obesity and metabolicdisease fronts. *Clinical Genetics*, 76 (3): 236-241

Cooper, K**.,**Pollock, M., Martin ,R., White,**S**.,Linnerud, A. and Jackson, A (1976). Physical fitness levels vs selected coronary risk factors. *JAMA*, 236:166-169

Cooper,K:(1982). Physical training programs for mass scale use: Effectson cardiovascular disease. *Annal of Clinical Resource*, 34:25-32

Côté, M., Matias, I., Lemieux, I., Petrosino, S., Alméras, N., Després, J.P. and Di Marzo V (2007).Circulating endocannabinoid levels, abdominal adiposity and related cardiometabolicrisk factors in obese men. *International Journal of Obesity*, 31: 692–699

Côté, M., Mauriège, P., Bergeron, J., Alméras, N., Tremblay, A., Lemieux, I. and Després, J.P (2005).Adiponectinemia in visceral obesity: impact on glucose tolerance and plasma lipoproteinand lipid levels in men. *Journal of Clinical Endocrinology and Metabolism*, 90: 1434–1439.

Couillard, C., Gagnon, J., Bergeron, J., Leon, A.S., Rao, D.C., Skinner, J.S., Wilmore, J.H., Després, J.P. and Bouchard, C (2010). Contribution of body fatness and adipose tissue distribution to the agevariation in plasma steroid hormone concentrations in men: the HERITAGE FamilyStudy. *Journal of ClinicalEndocrinology and Metabolism*, 85: 1026– 103.

Couillard, C., Vohl, M.C., Engert, J.C., Lemieux, I., Houde, A., Alméras, N., Prud'homme, D.,Nadeau, A., Després, J.P. and Bergeron, J (2003). Effect of apoC-III gene polymorphisms on thelipoprotein-lipid profile of viscerally obese men. *Journal of Lipid Resources*, 44: 986–993.

D'Eon, T.M., Souza, S.C., Aronovitz, M., Obin, M.S., Fried, S.K. and Greenberg, A.S (2005). Estrogenregulation of adiposity and fuel partitioning. Evidence of genomic and non-genomicregulation of lipogenic and oxidative pathways. *Journal Biological Chemistry,*280: 35983–35991

Dagenais G.R., Yi, Q. and Mann, J.F.(2005). Prognostic impact of body weight and abdominal obesity in women and men with cardiovascular disease. *America Heart Journal* 149:54–60.

Dan-Asabe, A.U., (2000). "Biography of selected Kano merchants, 1853-1955". *FAIS Journal of Humanities,* 1 (2). Archived from the original on September 3, 2007.

Danborno B. and Afegbua, A (2006). Ethnic differences in birthweight and cesarean deliveries in Zaria, Nigeria. *Journal of Experimental and Clinical Anatomy,* 5: 21-24.

Danborno, B and Danborno, A. M. (2015). The effect of the season of birth and fluctuating asymmetry on second and fourth digit lengths and digit ratio (2D:4D) in Nigerians. *European Journal of Zoological Research*, 4 (1) :7-11

Danborno, B., Adebisi, S.S., Adelaiye, A.B. and Ojo, S.A (2010). Relationship between Digit Ratio (2D:4D) and Birth Weight in Nigerians. *Anthropologist*, 12(2): 127-130

Danborno, B., Adebisi, S., Adelaiye, A.B. and Ojo, S. (2008) Sexual dimorphism and relationship between chest, hip and waist circumference with 2D, 4D and 2D:4D in Nigerians. *Internet Journal of Biological Anthropology*, 1: 2

De Pergola, G., Zamboni, M., Pannacciulli, N., Turcato, E., Giorgino, F., Armellini, F.,Logoluso, F., Sciaraffia, M., Bosello, O. and Giorgino, R. (1998). Divergent effects of short-term,very-low-caloriediet on insulin-like growth factor-I and insulin-like growth factorbinding protein-3 serum concentrations in premenopausal women with obesity. *ObesityResources*, 6: 408–415.

De Vriendt, T., Moreno, LA. and De Henauw, S. (2009). Chronic stress and obesity in adolescents:scientific evidence and methodological issues for epidemiological research. *Nutrition Metabolism and Cardiovascular Disease,*19: 511–519

DeNino, W.F., Tchernof, A., Dionne, I.J., Toth, M.J., Ades, P.A., Sites, C.K and Poehlman, E.T. (2001).Contribution of abdominal adiposity to age-related differences in insulin sensitivityand plasma lipids in healthy nonobese women. *Diabetes Care* ,24: 925–932.

Després, J.P. and Lemieux, I (2006). Abdominal obesity and metabolic syndrome. *Nature* 444: 881–887

Després, J.P., Arsenault, B.J., Côté, M., Cartier, A. and Lemieux, I (2008). Abdominal obesity: thecholesterol of the 21st century? *Canadian Journal of Cardiolology,* 24: 7-12

Després, J.P., Couillard, C., Gagnon, J., Bergeron, J., Leon, A.S., Rao, D.C., Skinner, J.S., Wilmore, J.H. and Bouchard, C (2000). Race, visceral adipose tissue, plasma lipids, and lipoprotein lipaseactivity in men and women: the Health, Risk Factors, Exercise Training, Genetics(HERITAGE) family study. *Arteriosclerosis, Thrombosis, Vascular Biology,*20: 1932–1938

Després, J.P., Lemieux, I., Bergeron, J., Pibarot, P., Mathieu, P., Larose, E., Rodés-Cabau, J.,Bertrand, O.F and Poirier, P (2008). Abdominal obesity and the metabolic syndrome: contributionto global cardiometabolic risk. *Arterioscler Thromb Vasc Biol* 28: 1039–1049.

Deurenberg, P., Deurenberg-Yap, M. and Guricci, S (2002). Asians are different from Caucasiansand from each other in their body mass index/body fat per cent relationship. *Obesity Review*, 3: 141–146.

Deurenberg, P., Yap, M. and van Staveren, W.A. (1998). Body mass index and percent body fat: ameta analysis among different ethnic groups. *International Journal of Obesity and Related Metabolic Disorders*, 22: 1164– 1171

Di Marzo, V (2008). The endocannabinoid system in obesity and type 2 diabetes. *Diabetologia*, 51: 1356–1367.

Di Marzo, V. and Després, J.P (2009). Endocannabinoid overactivity and abdominal obesity. *Abdominal Obesity and the Endocannabinboid System*, edited by Després JP and DiMarzo V. New York: Informa Healthcare, p. 203–208.

Dietz, W. H. (1997). Periods of risk in childhood for the development of adult obesity--what do we need to learn? *Journal of Nutrition*, 127: 1884S–1886S

Dieudonne, M.N., Leneveu, M.C., Giudicelli, Y. and Pecquery, R. (2004). Evidence for functional estrogenreceptors alpha and beta in human adipose cells: regional specificities andregulation by estrogens. *American Journal of Physiology - Cell Physiology*, 286: 655 – 661.

Dieudonne, M.N., Pecquery, R., Leneveu, M.C. and Giudicelli, Y. (2000). Opposite effects of androgensand estrogens on adipogenesis in rat preadipocytes: evidence for sex and siterelatedspecificities and possible involvement of insulin-like growth factor 1 receptorand peroxisome proliferator-activated receptor gamma2. *Endocrinology* 141: 649– 656.

Doche, M.E., Bochukova, E.G. and Su, H.W. (2012). Human SH2B1 mutations are associated with maladaptive behaviors and obesity. *J ournal of Clinical Invest*igation, 122(12):4732–4736.

Donoho, C.J., Weigensberg, M.J., Emken, B.A., Hsu, J.W. and Spruijt-Metz, D. (2011). Stress and abdominalfat: Preliminary evidence of moderation by the cortisol awakening response inHispanic peripubertal girls. *Obesity* 19: 946–952.

Duclos, M., Gatta, B., Corcuff, J.B., Rashedi, M., Pehourcq, F. and Roger, P. (2001). Fat distribution inobese women is associated with subtle alterations of the hypothalamic-pituitary-adrenalaxis activity and sensitivity to glucocorticoids. *Clinical Endocrinology*,55: 447–454

Duez, H., Lamarche, B., Uffelman, K.D., Valero, R., Cohn, J.S. and Lewis, G.F. (2006). Hyperinsulinemia isassociated with increased production rate of intestinal apolipoprotein B-48-containinglipoproteins in humans. *Arteriosclerosis, Thrombosis and Vascular Biology*,26: 1357–1363

Dunaif, A (1997). Insulin resistance and the polycystic ovary syndrome: mechanism and implicationsfor pathogenesis. *Endocrinology Review,* 18: 774–800.

Dusserre, E. and Moulin, P, and Vidal, H.(2000). Differences in mRNA expression of the proteinssecreted by the adipocytes in human subcutaneous and visceral adipose tissues. *Biochim Biophysics Acta*, 1500:88-96.

Eckel, R. H., Alberti, K. G., Grundy, S. M. and Zimmet, P. Z. (2010). The metabolic syndrome. *Lancet*,375:181-183.

Edwardson, C. L., Gorely, T., Davies, M. J., Gray, L. J., Khunti, K., Wilmot, E. G, Yates, T. and Biddle, S. J. (2012). Association of sedentary behaviour with metabolic syndrome: a meta-analysis. *PLoS ONE.*,7, e34916.

Einhorn, D., Reaven, G. M., Cobin, R. H., Ford, E., Ganda, O. P.,Handelsman, Y, et al. (2003). American College of Endocrinologyposition statement on the insulin resistance syndrome. *Endocrine Practice,* 9:237-252.

Eisenmann, J. C., DuBose, K. D. and Donnelly, J. E. (2007). Fatness, fitness, and insulin sensitivity among 7- to 9-year-old children. *Obesity*,15: 2135–2144

Ekelund, U., Franks, P. W., Sharp, S., Brage, S. and Wareham N. J. (2007). Increase in physical activityenergy expenditure is associated withreduced metabolic risk independent ofchange in fatness and fitness. *Diabetes Care*, 30:2101–2106

Ekezie, J., Anyanwu, E.G., Danborno, B and Anthony, U. (2011). Impact of urbanization on obesity, anthropometric profile and blood pressure in the Igbos of Nigeria. *North America Journal of Medical Science,* 3: 242-246.

Elbers, J.M., Giltay, E.J., Teerlink, T., Scheffer, P.G., Asscheman, H., Seidell, J.C. and Gooren, L.J (2003).Effects of sex steroids on components of the insulin resistance syndrome in transsexualsubjects. *Clinical Endocrinology*,58: 562–571

El-Sayed, J.S and Froguel, P. (2013). From obesity genetics to the future of personalized obesity therapy. *National Review of Endocrinology*, 9(7):402–413.

Engeli, S., Feldpausch, M., Gorzelniak, K., Hartwig, G., Heintze, U., Janke, J., Mohlig, M., Pfeiffer, A.F., Luft, F.C and Sharma, A.M. (2003). Association between adiponectin and mediators of inflammation in obese women. *Diabetes*, 52: 942–947.

English, K. M., Mandour, O., Steeds, R. P., Diver, M. J., Jones, T. H. and Channer, K. S. (2000). Men with coronary artery disease have lower levels of androgens than men with normal coronary angiograms. *European Heart Journal*, 21:890-4.

Esmaillzadeh, A,, Mirmiran, P, and Azizi F. (2004). Waist-to-hip ratio is abetter screening measure for cardiovascular risk factors thanother anthropometric indicators in Tehranian adult men. *Internation Journal Obesity Relative Metabolic Disorders,*28:1325-32.

Falchi, M., El-Sayed, J.S. and Takousis, P (2014). Low copy number of the salivary amylase gene predisposes to obesity. *Nature Genetics*, 46(5): 492–497.

Fang. J. and Alderman, M.H. (2000). Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study, 1971-1992. National Health and Nutrition Examination Survey, *Journal of American Medical Association*, 283:2404-2410

Farb, M.G., Bigornia, S and Mott, M. (2011). Reduced adipose tissue inflammation represents an intermediate cardiometabolic phenotype in obesity. *Journal of American College ofCardiology*, 58:232–237.

Farnier, C., Krief, S., Blache, M., Diot-Dupuy, F., Mory, G., Ferre, P. and Bazin, R (2003). Adipocytefunctions are modulated by cell size change: potential involvement of an integrin/ERKsignalling pathway. *International Journal of Obesity Related Metabolic Disorders*, 27: 1178–1186.

Farooqi, I.S., Drop, S. and Clements A. (2006). Heterozygosity for a POMC-null mutation and increased obesity risk in humans. *Diabetes*, 55(9): 2549–2553.

Farooqi, I.S., Keogh, J..M. and Kamath, S. (2001). Partial leptin deficiency and human adiposity. *Nature*, 414(6859):34–35.

Farooqi, I.S. (2008). Monogenic human obesity. *Frontiers Hormone Research*, 36: 1 - 1 1

Farooqi, I.S., Wangensteen, T. and Collins, S (2007). Clinical and molecular genetic spectrum of congenital deficiency of the leptin receptor. *National England Journal of Med*icine, 356(3):237–247.

Farooqi, S and O'Rahilly, S. (2006). Genetics of obesity inhumans. *Endocrinology Review*, 27(7): 710-71 8.

Felix, K.., Ulf., E, Soren B. (2011). Urbanization, physical activity, and metabolic health in Sub-Saharan Africa.*Diabetes Care*, 34:491–496, 2011

Feng, R.N., Zhao, .C, Wang, C., Niu, Y.C and Li, K. (2012). BMI is strongly associated with hypertension, and waist circumference is strongly associated with type 2 diabetes and dyslipidemia, in northern Chinese adults. *Journal of Epidemiology*, 22: 317–323.

Ferguson, M. A.., L. J. White, S. McCoy, H.-W. Kim, T. Petty,and J. Wilsey, (2004). Plasma adiponectin response to acute exercisein healthy subjects,*European Journal of Applied Physiology*, 91(2-3): 324–329

Ferre, P. and Foufelle, F. (2007). SREBP-1c transcription factor and lipid homeostasis: clinical perspective.*Hormone Resource*, 68: 72–82

Fezeu, L. K, Assah, F. K, Balkau, B., et al.(2008). Tenyearchanges in central obesity and BMI inrural and urban Cameroon. *Obesity*, 16:1144–1147

Fink, B., Manning, J.T. and Neave, N (2006). The 2nd–4th digit ratio (2D:4D) and neck circumference: implications for risk factors in coronary heart disease. *International Journal of Obesity*, 30: 711-4.

Fink, B., Manning, J.T., Williams, J.H.G. and Podmore-Nappin, C (2007). The 2nd to 4th digit ratio developmental psychopathology in school-aged children. *Personality and Individual Difference*, 42: 369–379.

Fink, B., Neave, N., Manning, J.T (2003). Second to fourth digit ratio,body mass index, waist-to-hip ratio, and waist-to-chest ratio: theirrelationships in heterosexual men and women. *Annals of Human Biology*, 30(6):728-738.

Fontana, L., Eagon, J. C., Trujillo, M. E., Scherer, P. E. and Klein S. (2007). Visceral fat adipokinesecretion is associated with systemic inflammation in obese humans. *Diabetes*,56:1010-1013.

Ford, D. K., and De Mos, A. M. (1964). Serum uric acid levels of healthy Caucasian,Chinese, and Haida Indian males in British Columbia. *Canada medical Association Journal*, 90: 1295

Ford, E.S., Mokdad, A.H., Giles, W.H.(2003) Trends in waist circumference among U.S. adults. *Obesity Research* **11**:1223–1231.

Forshee, R.A., Anderson, P.A. and Storey, M.L (2008). Sugar-sweetened beverages and body mass index in children and adolescents: a meta-analysis. *American Journal of Clinical Nutrition*,87: 1662–1671

Fox, C.S., Massaro, J.M., Hoffmann, U., Pou, K.M., Maurovich-Horvat, P. and Liu, C.Y (2007). Abdominal visceral and subcutaneous adipose tissuecompartments: association with metabolic risk factors in theFramingham Heart Study. *Circulation*, 116(1): 39-48,

Franks, P. W., Ekelund, U., Brage, S., Wong, M. Y. and Wareham N.J. (2004).Does the association ofhabitual physical activity with the metabolicsyndrome differ by level of cardiorespiratory fitness? *Diabetes Care,* 27:1187–1193

Frayn, K.N (2002). Adipose tissue as a buffer for daily lipid flux. *Diabetologia* 45: 1201–1210

Freedman, D.S., Thornton, J., Pi-Sunyer, F.X., Heymsfield, S.B., Wang, J. (2012). The body adiposity index (hip circumference/height(1.5) is not a more accurate measure of adiposity than is BMI, waist circumference, or hip circumference.*Obesity*, 20(12):2438-44.

Fried, S.K. and Kral, J.G. (1987) Sex differences in regional distribution of fat cell size and lipoproteinlipase activity in morbidly obese patients. *International Journal of Obesity*,11: 129–140

Friedewald, W.T., Levy, R.I. and Fredrickson, D.S. (1972). Estimation of concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clinical Chemistry,* 18:499-500

Fujioka, S., Matsuzawa, Y., Tokunaga, K and Tarui, S. (1987). Contribution of intra-abdominal fat accumulation to the impairment of glucose and lipid metabolism in human obesity. *Metabolism,* 36:54 –59.

Galis, F., Ten Broek, C.M., Van Dongen, S. and Wij-naendts, L.C (2010). Sexualdimorphism in the prenatal digit ratio (2D:4D). *Archieves of Sexual Behavior,* 39:57-62.

Gallagher, D., Heymsfield, S.B., Heo, M., Jebb, S.A., Murgatroyd, P.R. and Sakamoto, Y (2000). Healthypercentage body fat ranges: an approach for developing guidelines based on bodymass index. *American Journal of Clinical Nutrition*,72: 694–701

Gapstur, S.M., Gann, P.H., Kopp, P., Colangelo, L., Longcope, C. and Liu, K (2002). Serum androgenconcentrations in young men: a longitudinal analysis of associations with age, obesity,and race. The CARDIA male hormone study. *Cancer Epidemiol Biomarkers and Prevention*, 11:1041–1047

Garaulet, M., Hernandez-Morante, J.J., Lujan, J., Tebar, F.J. and Zamora, S (2006). Relationship betweenfat cell size and number and fatty acid composition in adipose tissue fromdifferent fat depots in overweight/obese humans. *International Journal of Obesity*,30: 899–905

Gennuso, K. P., Matthews, C. E. and Colbert, L. H. (2015). Reliability and validity of 2 self-report measures to assess sedentary behavior in older adults. *Journal of Physical Acta Health*, 12:727–32.

Ghantous, C.M, Azrak, Z., Hanache, S., Abou-Kheir, W. and Zeidan, A. (2015). Differential role of leptin and adiponectin in cardiovascular system. *International Journal of Endocrinology,* 5:(34)3-20.

Giliane, B., Lilian, M.H., Priscila, C.S., Raquel, S. and Dan, L.W. (2015). Body adiposity index performance in estimating body fat in a sample of severely obese Brazilian patients. *Nutrition Journal*, 14:130

Goh, L.G.H., Dhaliwal, S.S. and Welborn, T.A (2014). Anthropometric measurements of central and general obesity and the prediction of cardiovascular disease in women: a cross sectional study.*British Medical Journal*, 4:e004138. doi:10.1136/bmjopen-004138

Goodpaster, B.H., Krishnaswami, S., Resnick, H., Kelley, D.E., Haggerty, C., Harris, T.B. (2003) Association between regional adipose tissue distribution and both type 2 diabetes and impaired glucose tolerance in elderly men and women. *Diabetes Care,* 26(2):372-9.

Gorely, T., Henson, J., Charlotte, L., Morgan, B. (2015). Association of sedentary time with fat distribution in high risk population. *Medicine and Science in Sports and Exercise,* 47(8):1727-1734

Goulart, A.C., Zee, R.Y. and Rexrode, K.M (2009). Estrogen receptor 1 gene polymorphisms anddecreased risk of obesity in women. *Metabolism,*58: 759–764.

Gray, S.L. and Vidal-Puig, A.J (2007). Adipose tissue expandability in the maintenance of metabolichomeostasis. *Nutrition Review,*65: 7–12..

Grundy, S.M. (1999). Hypertriglyceridemia, insulin resistance, and the metabolic syndrome. *American Journal of Cardiology*, 83: 25F– 29F.

Grundy, S.M., Cleeman, J.I., Daniels, S.R., Donato, K.A., Eckel, R.H and Franklin, B.A. (2005). Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*, 112(17):2735-52, http://dx.doi..

Guinhouya, B. C., Samouda, H., Zitouni, D., Vilhelm, C. and Hubert, H. (2011). Evidence of the influence of physical activity on metabolic syndrome and insulin resistance: A systematic review. *International Journal of Pediatric Obesity*, 6: 361-388

Guthrie, J.R., Dennerstein, L., Taffe, J.R., Lehert, P., Burger, H.G (2004). The menopausal transition:a 9-year prospective population-based study. The Melbourne Women's MidlifeHealth Project. *Climacteric,*7: 375–389

Haffner, S.M., Ferrannini, E., Hazuda, H.P. and Stern, M.P. (1992) Clustering of cardiovascularrisk factors in confirmed prehypertensive individuals. *Hypertension,* 20: 38-45.

Hamer, M. and Chida, Y (2008). Walking and primary prevention: ameta-analysis of prospective cohort studies. *British Journal of Sports Medicine,* 42:238–43.

Hara, M., Saitou, E., Iwata, F., Okada, T. and Harada, K. (2002). Waist-to-heightratio is the best predictor of cardiovascular diseaserisk factors in Japanese schoolchildren. *Journal Atherosclerosis and Thrombosis,* 9:127-32.

Hassinen, M., Lakka, T.A., Hakola, L. (2010) Cardiorespiratory fitness andmetabolic syndrome in older men and women: the Dose Responsesto Exercise Training (DR's EXTRA) study. *Diabetes Care,* 33:1610–17.

Healy, G. N. Wijndaele, K and Dunstan, DW, et al. (2008). Objectively measured sedentarytime, physical activity, and metabolic risk:the Australian Diabetes, Obesity and LifestyleStudy (AusDiab).*Diabetes Care,* 31:369–371

Heloisa, G., Fernanda, S.A., Antunes, M.T et al. (2015). Applicability of visceral adiposity index in prediction of components of metabolic syndrome in elderly. *Nutrition Hospital,* 32(4):1609-1615

Heine, P.A., Taylor, J.A., Iwamoto, G.A., Lubahn, D.B. and Cooke, P.S (2000). Increased adipose tissue inmale and female estrogen receptor-alpha knockout mice. *Proceedings of National Academy of Science USA,* 97: 12729–12734

Henkin, L., Bergman, R.N., Bowden, D.W., Ellsworth, D.L., Haffner, S.M., Langefeld, C.D.,Mitchell, B.D., Norris, J.M., Rewers, M., Saad, M.F., Stamm, E., Wagenknecht, L.E., Rich, S.S (2003).Genetic epidemiology of insulin resistance and visceral adiposity. The IRAS FamilyStudy design and methods. *Annals of Epidemiology,*13: 211–217.

Henriksen, E. J. (2002). Effects of acute exercise and exercise training on insulin resistance. *Journal of Applied Physiology,*93: 788–796

Henson, J., Edwardson, C. L., Morgan, B., Horsfield, M.A., Bodicoat, D. H., Biddle, S. J., Gorely, T., Nimmo, M. A., McCann, G. P., Khunti, K., et al. (2014). Associations of sedentary time with fat distribution in a high-risk population. *Medical Sciences and Sports Exercise,*247:1727–34.

Henson, J., Edwardson, C.L., Morgan, B., Horsfield, M.A., Bodicoat, D.H., Biddle, S.J,Gorely, T., Nimmo, M.A., McCann, G.P., Khunti, K. (2014). Associations of sedentarytime with fat distribution in a high-risk population. *Medical Science of Sports and Exercise,* 247:1727–34.

Hernandez-Morante, J.J, Milagro, F.I., Larque, E., Lujan, J., Martinez, J.A., Zamora, S., Garaulet, M (2007). Relationship among adiponectin, adiponectin gene expression and fatty acids compositionin morbidly obese patients. *Obesity Surgery,*17: 516–524

Ho, S.C., Chen, Y.M., Woo, J.L., Leung, S.S and Lam, T.H. (2001). Association between simple anthropometric indices and cardiovascular risk factors. *International Journal of Obesity Related Metabolic Disorders,* 25: 1689–1697.

Ho, S.Y., Lam, T.H and Janus, E.D. (2003). Waist to stature ratio is more strongly associated with cardiovascular risk factors than other simple anthropometric indices. *Annals of Epidemiology,* 13: 683–691.

Hoffstedt, J., Arner, E., Wahrenberg, H., Andersson, D.P., Qvisth, V., Lofgren, P., Ryden, M.,Thorne, A., Wiren, M., Palmer, M., Thorell, A., Toft, E. and Arner, P. (2010). Regional impact of adiposetissue morphology on the metabolic profile in morbid obesity. *Diabetologia*,53: 2496– 2503

Holloszy, J. O. (2005). Exercise-induced increase in muscle insulin sensitivity. *Journal of Applied Physiology,* 99: 338–343.

Hone, L.S.E. and McCullough M.E. (2012). 2D:4D ratio predict hand grip strength in (but not hand grip endurance) in men (but not in women). *Evolution and Human Behavior*, 33:780-789.

Hotta, K., Funahashi, T and Arita,Y. (2000) Plasma concentrations of a novel, adipose-specific protein, adiponectin, in type 2 diabetic patients. *Arteriosclerosis, Thrombosis and Vascular Biology,* 20:1595-1599.

Hotta, K., Funahashi, T and Bodkin, N.L. (2001). Circulating concentrations of the adipocyte protein adiponectin are decreased in parallel with reduced insulin sensitivity during the progression to type 2 diabetes in rhesus monkeys. *Diabete*s, 50:1126-1133.

Hsieh, S.D. and Muto T.(2006). Metabolic syndrome in Japanese men andwomen with special reference to the anthropometric criteriafor the assessment of obesity: Proposal to use the waist-toheight ratio. *Preventive Medcine*,42:135-9.

Hsieh, S.D. and Muto, T. (2005). The superiority of waist-to-height ratio asan anthropometric index to evaluate clustering of coronaryrisk factors among non-obese men and women. *Preventive Medcine*, 40:216-220.

Hsieh, S.D., Yoshinaga, H and Muto, T. (2003). Waist-to-height ratio, a simple and practical index for assessing central fat distribution and metabolic risk in Japanese men and women. *International Journal of Obesity Related Metabolic Disorders,* 27: 610–616.

Hu, E., Liang, P and Spiegelman, B.M (1996).AdipoQ is a novel adipose-specific gene dysregulated in obesity. *Journal of Biological Chemistry,* 271: 10697–10703.

Hu, F. B., Li, T. Y., Colditz, G. A,, Willett, W. C. and Manson, J. E. (2003). Television watching andother sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *JAMA*, 289:1785–91.

Huxley, R.R., Shiell, A.W. and Law, C.M (2000). The role of size atbirth and postnatal catch-up growth in determiningsystolic blood pressure: a systemic review of literature.*Journal of Hypertension,*18: 815-831.

Ibrahim, M.M (2010). Subcutaneous and visceral adipose tissue: structural and functional differences. *Obesity Review,*11: 11–18

Ike, O.,Youlian, L., Charles, N. R., Elaine, P., and Richard, S. (2000). Abdominal adiposity and clustering of multiple metabolic syndrome in White, Black and Hispanic Americans. *Annal of Epidemiology,* 10:263-270

Ilanne-Parikka, P., Laaksonen, D.E., Eriksson, J.G (2010). Leisure-time physical activity and the metabolic syndrome in the Finnish diabetesprevention study. *Diabetes Care,* 33:1610–17.

Iloh, G.U.P., Amadi, A.N., Njoku, P.U., Ofoedu, J.N. and Awa-Madu, J. (2012). The magnitude of abdominaladiposity and atherogenic dyslipidemiaamong geriatric Nigerians with arterial hypertensionin a rural hospital in South-easternNigeria. *Nigeria Journal of Clinical Practice.*,15(4): 462–468.

International Diabetes Federation. (2006). The IDF consensusworldwide definition of the metabolic syndrome. Available from: http://www.idf.org/webdata/docs/IDF_Meta_def_final.pdf

Jacob, M., Avadhani, R., Nair, B., Nallathamby, R. and Soman, M.A (2015). Cross sectional study of second and fourth digit ratio with physical attributes in South Indian population. *International Journal of Anatomical Researches*, 3(2):1133-37.

Jamurtas, A.Z., Theocharis,V. Koukoulis, G. et al., (2006). The effects of acute exercise on serum adiponectin and resistin levels and their relation to insulin sensitivity in overweight males. *EuropeanJournal of Applied Physiology*, 97 (1) 122–126.

Jensen, M.D., Martin, M.L., Cryer, P.E. and Roust, L.R (1994). Effects of estrogen on free fatty acid metabolism in humans. *American Journal of Physiology, Endocrinology and Metabolism,* 266: 914 – 920.

Jensen, M.D. (2008). Role of body fat distribution and the metabolic complications of obesity. *Journal of Clinical Endocrinology and Metabolism,* 93: 57–63.

Johnson, R.J., Gaucher, E.A., Sautin, Y.Y., Henderson, G.N., Angerhofer, A.J and Benner, S.A. (2008). The planetary biology of ascorbate and uric acid and their relationship with the epidemic of obesity and cardiovascular disease. *Medical Hypotheses,*71*:22-31*.

Johnson, R.J., Rodriguez-Iturbe, B., Kang, D.H., Feig, D.I. and Herrera-Acosta, J. (2005). A unifying pathway for essential hypertension. *American Journal of Hypertension,*18: 431-440.

Johnson, R.J.and Rideout, B.A. (2004): Uric acid and diet--insights into the epidemic of cardiovascular disease. *National England Journal of Medicine,*350:1071-3.

Kabir, M., Stefanovski, D. and Hsu, I.R. (2011). Large size cells in the visceral adipose depot predict insulin resistance in the canine model. *Obesity*, 19:2121– 2129.

Kadiri, S. and Salako, B.L. (1997) Cardiovascular risk factors in middle aged Nigerians. *East African Medical Journal*, 74(5):303–6.

Kadowaki, T., Sekikawa, A., Murata, K., Maegawa, H., Takamiya, T., Okamura, T.*et al.* (2006a).Japanese men have larger areas of visceral adipose tissue than Caucasian men in thesame levels of waist circumference in a population-based study. *International Journal of Obesity,*30: 1163– 1165.

Kadowaki, T., Yamauchi, T., Kubota, N., Hara, K., Ueki, K. and Tobe, K.(2006b) Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome. *The Journal of Clinical Investigation*, 116: 1784-1792.

Kahn, B.B and Flier, J.S. (2000) Obesity and insulin resistance. *Journal of Clinical Investigations*, 106: 473 – 481.

Kanai, H., Tokunaga, K., Fujioka, S., Yamashita, S., Kameda-Takemura, K.K and Matsuzawa, Y. (1996). Decrease in intra-abdominal visceral fat may reduce blood pressure in obese hypertensive women. *Hypertension*, 27:125–129.

Kangassalo, K., Pölkki, M. and Rantala, M.J. (2011). Prenatal influences on sexual orientation: (2D:4D) and number of older siblings.*Evolutionary Psychology*, 9: 496-508.

Karra, E., O'Daly, O.G. and Choudhury, A.I (2013). A link between FTO, ghrelin, and impaired brain food-cue responsivity. *Journal of ClinicalInvestigation*, 123(8): 3539–3551.

Kasapis, C and.Thompson, P. D. (2005). The effects of physical activityon serum C-reactive protein and inflammatory markers: a systematicreview, *Journal of the American College of Cardiology*, 45(10): 1563–1569

Katzmarzyk, P.T., Bray, G.A., Greenway, F.L., Johnson, W.D., Newton, R.L, Ravussin, E.,Ryan, D.H. and Bouchard, C (2011). Ethnic-specific BMI and waist circumference thresholds. *Obesity*, 19: 1272–1278

Katzmarzyk, P.T., Bray, G.A., Greenway, F.L., Johnson, W.D., Newton, R.L., Ravussin, E.,Ryan, D.H., Smith, S.R. and Bouchard, C. (2010). Racial differences in

abdominal depot-specific adiposityin white and African American adults. *American Journal ofClinical Nutrition,*91: 7–15

Katzmarzyk, P.T., Malina, R.M., Pérusse, L., Rice, T., Province, M.A., Rao, D.C. and Bouchard, C. (2011). Familial resemblance in fatness and fat distribution. *American Journal of Human Biology*, 12: 395–404

Kavanagh, K., Jones,K..L, Sawyer, J., Kelley, K., Carr, J.J., Wagner, J.D. and Rudel, L.L (2007). Trans fat dietinduces abdominal obesity and changes in insulin sensitivity in monkeys. *Obesity,*15: 1675–1684

Keller, C., Larkey, L., Distefano, J.K., Boehm-Smith, E., Records, K., Robillard, A., Veres, S.,Al-Zadjali, M. and O'Brian, A.M (2010). Perimenopausal obesity. *Journal of Womens Health,*19: 987–996

Kelly, A. S. (2004). Inflammation, insulin, and endothelial function in overweight children and adolescents: the role of exercise. *Journal of Pediatrics,* 145: 731–736.

Kim, S.H., Lee, S.H., Ahn, K.Y. et al. (2013). Effect of lifestyle modification on serum chemerin concentration and its association with insulin sensitivity in overweight and obese adults with type2 diabetes. *Clinical Endocrinology*, 80(6):825-33

Kim, S.P., Catalano,K..J., Hsu, I.R., Chiu, J.D., Richey, J.M. and Bergman, R.N (2007). Nocturnal free fattyacids are uniquely elevated in the longitudinal development of diet-induced insulinresistance and hyperinsulinemia. *American Journal of Physiology, Endocrinology and Metabolism*, 292: 1590–1598

Kimura, D. (1996) Sex, sexual orientation and sex hormones influence human cognitive function. *Current Opinion in Neurobiology*, 6:259-263

Kishino, T., Watanabe, K., Urata, T., Takano, M., Uemura, T., Nishikawa, K., Mine, Y., Matsumoto, M., Ohtsuka, K., Ohnishi, H., Mori, H., Takahashi, S., Ishida, H. and Watanabe, T. (2008). Visceralfat thickness in overweight men correlates with alterations in serum fatty acid composition.*Clinica Chimica Acta*, 398: 57–62

Kissebah, A.H. and Peiris, A.N. (1989)Biology of regional body fat distribution: relationship to non-insulin-dependent diabetes mellitus. *Diabetes and Metabolism Review,* 5: 83–109.

Kissebah, A.H., Vydelingum, N., Murray, R., Evans, D.J., Hartz, A.J. and Kalkhoff, R.K.(1982). Relation of body fat distribution to metabolic complications of obesity. *Journal of Clinical Endocrinology and Metabolism*, 54: 254– 260.

Ki-Zerbo, J. (1998) UNESCO General history of Africa, vol.IV, Abridged edition; Africa from twelfth to sixteenth century. P. 107

Knowles, K.M., Paiva, L.L., Sanchez, S.E., Revilla, L., Lopez, T. and Yasuda, M.B (2011). Waist Circumference, Body Mass Index, andOther Measures of Adiposity in

Predicting Cardiovascular DiseaseRisk Factors among Peruvian Adults. *International Journal Hypertension.*, 11:1-10.

Konarzewski, M. (2006).Epidemics of obesity, *Nauka*, 4:85-96.

Kondo, T., Zakany, J. and Innis, J.(1997) . Of fingers, toes and penises. *Nature*, 390 (6655): 29.

Korenblat, K.M, Fabbrini, E., Mohammed, B.S. and Klein, S (2008). Liver, muscle, and adipose tissueinsulin action is directly related to intrahepatic triglyceride content in obese subjects.*Gastroenterology*, 134: 1369–1375

Kotani, K., Tokunaga, K., Fujioka, S., Kobatake, T., Keno, Y., Yoshida, S., Shimomura, I., Tarui, S. and Matsuzawa, Y. (1994). Sexual dimorphism of age-related changes in whole-body fat distributionin the obese. *International Journal Obesity and Related Metabolic Disorder,*18: 207–212.

Kraegen, E.W., Clark, P.W., Jenkins, A.B., Daley, E.A., Chisholm, D.J and Storlien, L.H. (1991). Development of muscle insulin resistance after liver insulin resistance in high-fat-fed rats. *Diabetes*, 40:1397– 403.

Kraemer, R. R., and V. D. Castracane (2007). Exercise and humoralmediators of peripheral energy balance: ghrelin andadiponectin," *Experimental Biology and Medicine*, 232(2): 184–194.

Kramer, C.K., Zinman, B and Retnakaran, R. (2013). Are metabolically healthy overweight and obesity benign conditions? A systematic review and metaanalysis. *Annals of Internal Medicine*, 159:758–769.

Kreier, F., Fliers, E., Voshol, P.J., Van Eden, C.G., Havekes, L.M., Kalsbeek, A., Van Heijningen, C.L., Sluiter, A.A., Mettenleiter, T.C., Romijn, J.A, Sauerwein, H.P and Buijs, R.M (2002). Selective parasympatheticinnervation of subcutaneous and intra-abdominal fat: functional implications.*Journal of Clinical Investigation*, 110: 1243–1250

Kuke, J.L., Lee, S., Heymsfield, S.B. and Ross, R. (2005). Waist circumference and abdominal adipose tissue distribution: influence of age and sex. *American Journal of Clinical Nutrition,*81: 1330–1334

Kyriakidis, I., Papaioannidou, P., Pantelidou, V., Kalles, V and Gemitzis, K. (2010). Digit ratios and relation to myocardial infarction in Greekmen and women. *Gender Medicine*, 7:628-636.

Kyrou, I. and Tsigos, C. (2007). Stress mechanisms and metabolic complications. *Hormone and Metabolic Research*, 39: 430–438.

Kyrou, I. and Tsigos, C. (2008). Chronic stress, visceral obesity and gonadal dysfunction. *Hormones*, 7: 287–293.

Kyrou, I. and Tsigos, C. (2009). Stress hormones: physiological stress and regulation of metabolism.*Current Opinion in Pharmacology*,9: 787–793.

Laaksonen, D.E., Niskanen, L., Punnonen, K., Nyyssonen, K., Tuomainen, T.P., Salonen, R.,Rauramaa, R. and Salonen, J.T. (2003). Sex hormones, inflammation and the metabolic syndrome: apopulation-based study. *European Journal of Endocrinology,* 149: 601–608.

Labbe, S.M., Grenier-Larouche, T., Croteau, E., Normand-Lauziere, F., Frisch, F., Ouellet, R.,Guerin, B., Turcotte, E.E. and Carpentier, A.C. (2011). Organ-specific dietary fatty acid uptake inhumans using positron emission tomography coupled to computed tomography. *America Journal of Physiology, Endocrinology and Metabolism,* 300: 445 – 453

Lanska, D.J., Lanska, M.J., Hartz, A.J. and Rimm,A.A. (1985). Factors influencing anatomic location of fattissue in 52,953 women. *International Journal of Obesity*, 9: 29–38

Lara-Castro, C., Fu, Y., Chung, B.H.and Garvey, W.T. (2007) Adiponectin and the metabolic syndrome: mechanisms mediating risk for metabolic and cardiovascular disease. *Current Opinion in Lipidology*, 18: 263-70.

Lara-Castro, C., Weinsier, R.L., Hunter, G.R. and Desmond R (2002). Visceral adipose tissue inwomen: longitudinal study of the effects of fat gain, time, and race. *Obesity Resource,* 10: 868–874

Lean, M.E., Han, T.S. and Morrison, C.E. (1995) Waist circumference as a measure for indicating need for weight management. *British Medical Journal*, 311(6998): 158e61.

Lear, S.A, Humphries, K.H., Kohli, S., Chockalingam, A., Frohlich, J.J. and Birmingham, C.L. (2007a). Visceraladipose tissue accumulation differs according to ethnic background: results ofthe Multicultural Community Health Assessment Trial (M-CHAT). *American Journal of Clinical Nutrition,*86: 353–359.

Lear, S.A, James, P.T., Ko, G.T. and Kumanyika, S. (2010). Appropriateness of waist circumference andwaist-to-hip ratio cutoffs for different ethnic groups. *European Journal of Clinical Nutrition,*64: 42–61.

Lear, S.A., Humphries, K.H., Frohlich, J.J. and Birmingham,. CL. (2007c). Appropriateness of current thresholds for obesity-related measures among Aboriginal people. *Canadian Medical Association Journal,*177: 1499–1505.

Lear, S.A., Humphries, K.H., Kohli, S., Frohlich, J.J., Birmingham, C.L. and Mancini, G.B. (2007b). Visceraladipose tissue, a potential risk factor for carotid atherosclerosis: results of the Multicultural Community Health Assessment Trial (M-CHAT). *Stroke* 38: 2422–2429.

Lear, S.A., Kohli, S., Bondy, G.P., Tchernof, A. and Sniderman, A.D. (2009). Ethnic variation in fat andlean body mass and the association with insulin resistance. *Journal of Clinical Endocrinology and Metabolism,* 94: 4696–4702

Ledoux, S., Coupaye, M., Essig, M., Msika, S., Roy, C., Queguiner, I., Clerici, C. and Larger, E (2010).Traditional anthropometric parameters still predict metabolic disorders in womenwith severe obesity. *Obesity,*18: 1026–1032.

Lee, K.J., Shin, Y.A., Lee, K.Y., Jun, T.W. and Song, W. (2010). Aerobic exercise training-induced decrease in plasma visfatin and insulin resistance in obese female adolescents. *International. Journal of Sports, Nutrition Exercise and Metabolism,*20: 275–281.

Lee, S. (2012). Effects of aerobic versus resistance exercise without caloric restriction on abdominal fat, intrahepatic lipid, and insulin sensitivity in obese adolescent boys: a randomized, controlled trial. *Diabetes,*61: 2787–2795.

Lemieux, I., Pascot, A., Tchernof, A., Bergeron, J., Prud'homme, D., Bouchard, C. and Després, J.P (1999). Visceral adipose tissue and low-density lipoprotein particle size in middle-agedversus young men. *Metabolism* 48: 1322–1327

Lemieux, S., Prudhomme, D., Bouchard, C., Tremblay, A. and Despres, J.P (1993). Sex differences in the relation of visceral adipose tissue to total body fatness. *American Journal of Clinical Nutrition,*58: 463–467.

Leopold, F., Beverley B., Andre, P., Eug`ene, S., Mbanya, J (2007). Metabolic syndrome in a sub-Saharan African setting: Central obesity may be the key determinant. *Atherosclerosis,*193(2007) 70–76

Li, Y., Liu, L., Wang, B and Chen, D. (2013). Letter: Is visceral adiposity index a predictor of liver histology in patients with non-alcoholic fatty liver disease? *Alimentary Pharmacology and Therapeutics*, 37(5): 583.

Lichtman, S.W., Pisarska, K., Berman,. ER. (1992). Discrepancy betweenself-reported and actual caloric intake and exercise in obesesubjects. *New England Journal of Medicine,*327:1893–1898.

Lin, W. Y., Lee, L. T., Chen, C. Y., Lo, H., Hsia,, H. H., Liu, I. L., Lin, R.S., Shau, W. Y. and Huang, K.C. (2002).Optimal cut-off values for obesity:using simple anthropometric indices to predict cardiovascularrisk factors in Taiwan. *International Journal of Obesity and Relative Metabolic Disorder*, 26:1232-1238.

Liu, J., Fox, C.S and Hickson, D.A. (2010). Impact of abdominal visceral and subcutaneous adipose tissue on cardiometabolic risk factors: the Jackson Heart Study. *Journal of Clinical Endocrinology and Metabolism*, 95: 5419–5426.

Liu, M., He, Y. Jiang, B., Wu, L. Yang, S., Wang, Y., and Li, X. (2014). Association between Serum Uric Acid Level and Metabolic Syndrome and Its Sex Difference in

a Chinese Community Elderly Population, *International Journal of Endocrinology*, Article ID 754678, 11 pageshttp://dx.doi.org/10.1155/2014/754678

Liu, Y.J, Liu, X.G andWang , L (2008). Genome-wide association scans identified *CTNNBL1* as a novel gene for obesity. *Human Molecoular Genetics*, 17(12):1803–1813.

Loehlin, J.C., Medland, S.E. and Martin, N.G. (2012). Is CAG sequence length in the androgen receptor gene correlated with finger-length ratio? *Personality and Individual Differences*, 52(2):224-27

Loehlin. J.C., McFadden, D., Medland, S.E. and Martin, N.G. (2006).Population differences in finger-length ratios: Ethnicity or latitude?*Archives of Sexual Behavior*, 35(6):739-742.

Lopez, A.D., Mathers, C.D, Ezzati M, JamisonDT, Murray C.J. (2001). Global and regional burdenof disease and risk factors:systematic analysis of population health data. *Lancet*, 367:1747–1757

Lopez, A. D., Mathers, C. D., Eszati, M., Jamison, D. T. and Murray, C. J. L. (2006). Global burden of disease and risk factors. Washington, DC: World Bank.

Lovejoy, J.C., Champagne, C.M., de Jonge, L., Xie, H. and Smith, S.R (2008). Increased visceral fat anddecreased energy expenditure during the menopausal transition. *International Journal of Obesity*,32: 949– 958.

Lutchmaya, S., Baron-Cohen, S., Raggatt, P., Knicmeyer, R. and Manning, J.T (2004). 2nd to 4th digit ratios, fetaltestosterone and estradiol. *Early Human Development*, 77: 23-28.

Lutz, T.A. and Woods, S.C (2012). Overview of animal models ofobesity. *Current Protocols of Pharmacology*, 5: 61

Lwanga, S.K. and Lemeshow, S. (1991). *Sample size determination in health studies; a practical manual*, World Health Organization, Geneva, p. 10.

MacKay, M. F., Haffner, S. M., Wagenknecht, L. E., D'Agostino, R. B. and Jr, Hanley, A. J. (2009). Prediction of type 2 diabetes using alternate anthropometric measures in a multi-ethnic cohort: the insulin resistance atherosclerosis study. *Diabetes Care*, 32(5):956-8

Maeda, N., Shimomura, I., Kishida, K., Nishizawa, H., Matsuda, M., Nagaretani, H., Furuyama, N., Kondo, H., Takahashi, M., Arita, Y., Komuro, R., Ouchi, N., Kihara, S., Tochino, Y., Okutomi, K., Horie, M., Takeda, S., Aoyama, T., Funahashi, T and Matsuzawa,Y.(2002).Diet-induced insulin resistance in mice lacking adiponectin/ACRP30. *Nature Medicine*, 8: 731–737.

Mahmoud, U.S., Kolawole, W.W, Bashir, O.Y.,Maruf, G., Omolara, V.J, Akeem, G. (2010) Modifiablecardiovascular risk factors among apparentlyhealthy adult Nigerian population - a crosssectional study. *BMC Research Notes*, 3:11.

Makimura, H., Stanley, T., Mun, D., You, S.M. and Grinspoon, S (2008). The effects of central adiposityon growth hormone (GH) response to GH-releasing hormone-arginine stimulationtesting in men. *Journal of Clinical Endocrinology and Metabolism*,93: 4254–4260

Malas, M.A., Dogan, S., Evcil, E.H, Desdicioglu K.(2006) Fetal developmentof the hand, digits and digit ratio (2D:4D). *Early Human Development*,82:469-75.

Malik, V.S., Popkin, B.M., Bray, G.A., Després, J.P., Willett, W.C and Hu, F.B (2010). Sugar-sweetenedbeverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis.*Diabetes Care* 33: 2477–2483.

Manning, J.T., Bundredb, P.E., Newtonc, D.J., Flanagan, B.F. (2003). The second to fourth digit ratio and variation in the androgen receptor gene. *Evolution Human Behavior* 24:399–405

Manning , J.T.and Bundred, P.E. (2001). The ratio of 2nd to 4th digit lengthand age at first myocardial infarction in men: a link withtestosterone? *British Journal of Cardiology,* 8:720-723.

Manning, J., Barley, L., Walton, J., Lewis-Jones, D., Trivers, R. and Singh, D. et al. (2000a) The 2nd and 4th digit ratio, sexual dimorphism, population differences, and reproductive success: Evidence for sexually antagonistic genes? *Evolution & Human Behavior*, 21:163–183

Manning, J., Trivers, R., Thornhill, R., Singh, D. (2000). The 2nd:4th digit ratio and asymmetry of hand performance in Jamaican children. *Laterality*, 5:121–132.

Manning, J.T .(2011). Resolving the role of prenatal sex steroids in the development of digit ratio. *Proceedings of National Academy of Science, U S A*, 108:16143-4.

Manning, J.T and Taylor, R.P. (2002). Second to fourth digit ratio and male ability in sport: implications for sexual selection in humans. *Evolution of Human Behaviours*, 22:61–9.

Manning, J.T, Baron-Cohen, S., Wheelwright, S and Sanders, G. (2001). The 2nd to 4th digit ratio and autism. *Developmental Medicine, Child Neurology*, 43: 160–164.

Manning, J.T. (2010) Digit ratio (2D:4D), sex differences, allometry,and finger length of 12-30-year olds: Evidence from the BritishBroadcasting Corporation (BBC) Internet study. *American Journal of Human Biology*, 22:604-8.

Manning, J.T., Scutt, D., Wilson, J and Lewis-Jones, D.I. (1998). The ratio of 2nd to 4th digit length: a predictor of sperm numbers and concentrations of testosterone, leutinizing hormone and estrogen. *Human Reproduction,*, 13:3000-3004.

Manning, J.T. (2002b). The ratio of 2nd to 4th digit length and performance in skiing. *Journal of Sports Medicine and Physical Fitness*, 42, 446–450.

Manning, J.T., Barley, L., Walton, J., Lewis-Jones, D., Trivers, R.L. and Singh, D. et al. (2000). The 2nd:4th digit ratio, sexual dimorphism, population differences, and reproductive success: evidence for sexually antagonistic genes. *Evolution and Human Behavior*, 21: 163–183

Manning, J.T., Churchill, A.J.G. and Peters, M. (2007). The effects of sex, ethnicity and sexual orientation on self-measured digit ratio(2D:4D). *Archives of Sexual Behavior,* 36:223-233.

Manning, J.T. (2002a). Digit ratio: a pointer to fertility, behavior and health. New Brunswick, NJ: Rutgers University Press

Manning, J.T., Stewart, A., Bundred, P.E. and Trivers, R.L. (2004). Sex andethnic differences in 2nd to 4th digit ratio of children. *Early Human Development* 80(2):161-168.

Manning, T., Fink, J and Trivers, T. (2014). Digit ratio (2D:4D) and gender inequalities across nations. *Evolutionary Psychology*,124: 757-768.

Markman, B. and Barton, F.E (1987). Anatomy of the subcutaneous tissue of the trunk and lower extremity. *Plastic Reconstruction Surgery*,80: 248–254.

Marno, C.R., Helke, M.F. and Fahim, A. (2008). Comparism of waist circumference versus body mass index in diagnosing metabolic syndrome. *American Journal of Cardiology,* 102: 40-46

Maslowska, M.H., Sniderman, A.D., MacLean, L.D. and Cianflone, K (1993). Regional differences intriacylglycerol synthesis in adipose tissue and in cultured preadipocytes. *Journal of Lipid Resources*,34: 219–228

Masuzaki, H. and Flier, J.S (2003). Tissue-specific glucocorticoid reactivating enzyme, 11 betahydroxysteroiddehydrogenase type 1 (11 beta-HSD1)–a promising drug target forthe treatment of metabolic syndrome. *Current Drug Targets in Immune Endocrine MetabolicDisorders*,3: 255–262

Masuzaki, H., Paterson, J., Shinyama, H., Morton, N.M., Mullins, J.J., Seckl, J.R. and Flier, J.S (2001). Atransgenic model of visceral obesity and the metabolic syndrome. *Science*,294: 2166– 2170

Mathieu, P., Poirier, P., Pibarot, P., Lemieux, I and Després, J.P (2009). Visceral obesity: the link among inflammation, hypertension, and cardiovascular disease. *Hypertension,*53: 577–584.

Matias, I., Gonthier, M.P., Orlando, P., Martiadis, V., De Petrocellis, L., Cervino, C., Petrosino, S., Hoareau, L., Festy, F., Pasquali, R., Roche, R., Maj, M., Pagotto, U., Monteleone, P. and Di Marzo,V (2006). Regulation, function, and dysregulation of endocannabinoids in models of adiposeand beta-pancreatic cells and in obesity and hyperglycemia. *Journal of Clinical Endocrinology and Metabolism,*91: 3171–3180

Matsuzawa, Y (2008). The role of fat topology in the risk of disease. *International Journal of Obesity,*7: 83–92.

Matsuzawa, Y(2005). Adiponectin: Identification, physiology and clinical relevance in metabolic and vascular disease. *Atherosclerosis. Supplements*, 6: 7–14.

Mattsson, C. and Olsson, T. (2007). Estrogens and glucocorticoid hormones in adipose tissuemetabolism. *Current Medicinal Chemistry,*14: 2918–2924

Mbanya ,V.N., Kengne , A.P., Mbanya., J.C. and Akhtar, H.(2015) Body mass index, waist circumference, hip circumference, waist–hip-ratio and waist–height-ratio: Which is the better discriminator of prevalent screen-detected diabetes in a Cameroonian population? *Diabetes Research and Clinical Practice,* 62: 91-98

Mbanya, J.C., Assah, F.K., Saji, J. andAtanga, E.N (2014). "Obesity and type 2 diabetes in Sub-Sahara Africa.*Current Diabetes Report*, 14(7):501.

McFadden, D., and Champlin, C. A. (2000). Comparison of auditory evoked potentials in heterosexual, homosexual, and bisexual males and females. *Journal Association Research. Otolaryngology*, 1, 89–99.

McIntyre, M.H., Cohn, B.A., Ellison, P.T. (2006). Sexdimorphism in digital formulae of children. *American Journal ofPhysical Anthropology,* 129: 143–150.

McNamara, J.R., Campos, H., Ordovas, J.M., Peterson, J., Wilson, P.W. and Schaefer, E.J. (1987). Effect ofgender, age, lipid status on low density lipoprotein subfraction distribution. Resultsfrom the Framingham Offspring Study. *Arteriosclerosis* 7: 483–490.

McQuaid, S.E, Hodson, L., Neville, M.J., Dennis, A.L., Cheeseman, J., Humphreys, S.M., Ruge, T., Gilbert, M., Fielding, B.A., Frayn, K.N. and Karpe, F. (2011). Downregulation of adipose tissue fatty acid trafficking in obesity: a driver for ectopic fat deposition? *Diabetes* 60: 47–55.

McQuaid, S.E., Humphreys, S.M., Hodson, L., Fielding, B.A., Karpe, F., Frayn, K.N (2010). Femoral adipose tissue may accumulate the fat that has been recycled as VLDL and nonesterifiedfatty acids. *Diabetes,*59: 2465–2473

McTigue, K.M., Garrett, J.M. and Popkin, B.M. (2002). The natural history of the development ofobesity in a cohort of young U.S. adults between 1981 and 1998. *Annals of Internal Medicine,*136: 857–864.

Meczekalski, B., Czyyk, A. and Warenik-Szymankiewicz, A (2008). Rola genów w powstawaniu otyłosci. Współczesne poglady, patogeneza, aspekty kliniczne. Endokrynol Otyłosc Zaburz Przemiany Materii, 5(1): 27 - 37.

Medland, S. E., Zayats, T., Glaser, B., Nyholt, D. R., Gordon, S. D., Wright, M. J. (2010). A variant in LIN28B is associated with 2D:4D fi nger-lengthratio, a putative retrospective biomarker of prenatal testosterone exposure. *American Journal of Human Genetics,*86:519-25.

Melmer, A., Lamina, C., Tschoner, A., Ress, C., Kaser, S., Laimer, M., Sandhofer A., Paulweber, B. and Christoph F. (2013). Ebenbichler Body Adiposity Index and Other Indexes of Body Composition in the SAPHIR Study: Association with Cardiovascular Risk Factors. *Obesity*, 21: 775-781. doi:10.1038/oby.2012.160

Melmer, A., Lamina, C., Tschoner, A., Ress C., Kaser S. Laimer M., Sandhofer A., Paulweber, B. and Ebenbichler, C. F. (2013) Body Adiposity Index and Other Indexe of Body Composition in the SAPHIR Study: Association with Cardiovascular Risk Factors. *Obesity*, 21, 775-781.

Meyer, A.A., Kundt, G., Lenschow, U., Schuff-Werner, P. and Kienast, W. (2006). Improvement of early vascular changes and cardiovascular risk factors in obese children after a six-month exercise program. *Journal of American College of Cardiology,*48: 1865–1870

Miller, K.K., Biller, B.M., Lipman, J.G., Bradwin, G., Rifai, N. and Klibanski,A (2005). Truncal adiposity,relative growth hormone deficiency, and cardiovascular risk. *J ournal of Clinical Endocrinology and Metabolism,* 90: 768–774

Millet, K. and Dewitte, S. (2007). Digit ratio (2D:4D) moderates the impact of an aggressive music video on aggression. *Personality and Individual Difference,* doi:10.1016/j.paid. 2006.11.024

Misra, A. and Khurana, L. (2009). The metabolic syndrome in South Asians: epidemiology, determinants,and prevention. *Metabolic Syndrome and Related Disorders,*7: 497–514

Misra, M., Bredella, M.A, Tsai, P., Mendes, N., Miller, K.K. and Klibanski, A (2008). Lower growthhormone and higher cortisol are associated with greater visceral adiposity, intramyocellularlipids, and insulin resistance in overweight girls. *American Journal of Physiology, Endocrinology and Metabolism,* 295: 385 – 392

Mlinar, B., Marc, J., Janez, A. and Pfeifer, M (2007). Molecular mechanisms of insulin resistance andassociated diseases. *Clinica Chimica Acta,* 375: 20–35.

Molarius, A., Seidell, J.C., Sans, S., Tuomilehto, J., Kuulasmaa, K (1999). Waist and hip circumferences, and waist-hip ratio in 19 populations of the 32 National Center for Health Statistics. National Health and Nutrition WHO MONICA project. *International Journal of Obesity Related Metabolic Disorders,* 23:116–125

Moldoveanu, A. I . Shephard, R. J and. Shek, P. N. (2001). The cytokine response to physical activity and training,*SportsMedicine,* 31(2): 115–144.

Moller, D.M and Kaufman, K.D. (2005). Metabolic syndrome: a clinical and molecular perspective. *Annual Review of Medicine,* 56: 45–62.

Mortlock,D.P. and Innis, J.W. (1997). Mutation of *HoxA* 13 in hand-foot-genital syndrome. *Nature Genetics,* 15(2): 179-80.

Mueller, W.H., Wear, M.L., Hanis, C.L., Emerson, J.B., Barton, S.A. and Hewett-Emmett, D. (1991). Which measure of body fat distribution is best for epidemiologic research? *American Journal of Epidemiology,* 133: 858–869.

Muller, D.C., Baglietto, L., Manning, J.T., McLean, C., Hopper, J.L., English, D.R., Giles, G.G., Severi, G (2012). Second to fourth digit ratio(2D:4D), breast cancer risk factors, and breast cancer risk: aprospective cohort study. *British Journal of Cancer,* 107:1631-636.

Muller, D.C., Giles, G.G., Bassett, J., Morris, H.A., Manning, J.T., Hopper, J.L., English, D.R and Severi, G. (2011). Second to fourth digit ratio and concentration of circulating sex hormones in adulthood. *Reproductive Biology and Endocrinology,* 9: 57

Muller, M.J., Lagerpusch, M., Enderle, J., Schautz, B and Heller, M (2012). Beyond the body mass index: tracking body composition in the pathogenesis of obesity and the metabolic syndrome. *Obesity Review,* 13 Supplies. 2: 6–13.

Mussig, K., Staiger, H., Machicao, F., Thamer, C., Machann, J., Schick, F., Claussen, C.D., Stefan, N., Fritsche, A. and Haring, H.U (2009). RARRES2, encoding the novel adipokine chemerin, is agenetic determinant of disproportionate regional body fat distribution: a comparativemagnetic resonance imaging study. *Metabolism,*58: 519–524.

Naika, N. and Zasshi, G. (2005). Definition and the diagnostic standard for metabolic syndrome-- Committee to Evaluate Diagnostic Standards for Metabolic Syndrome. 94:794-809.

Naylor, L. H. (2008). Resistance training and diastolic myocardial tissue velocities in the obese. *Medical Science of Sports and Exercise,* 40: 2027–2032 .

Neelambikai, N.and Sowmya, M. (2015). Relationship between digit ratio (2D:4D) and neck circumference *Indian Journal of Clinical Anatomy and Physiology, 2(3):126-130*

Neeland, I.J., Gupta, S. and Ayers, C.R (2013). Relation of regional fat distribution to left ventricular structure and function. *Cardiovascular Imaging*, 6:800–807.

Nicholls, A., and Scott, J. T (1972). Effect of weight-loss on plasma and urinary levels of uric acid. Lancet, 2: 1223

Nicholls, A., Snaith, M. and Scott, J. (1973). Effect of estrogen therapy on plasma and urinary levels of uric acid. *Biomedical Journal*,1:449-451.

Nielsen, S., Guo, Z., Johnson, C.M., Hensrud, D.D. and Jensen, M.D (2004). Splanchnic lipolysis inhuman obesity. *Journal of ClinicalInvestigation*,113: 1582–1588

Nilsson, M., Dahlman, I., Jiao, H., Gustafsson, J.A., Arner, P. and Dahlman-Wright, K (2007). Impact ofestrogen receptor gene polymorphisms and mRNA levels on obesity and lipolysis–acohort study. *BMC Medical Genetics*,8: 73.

NPC(National population commission) (2006).National Census 21-03-06. www.citypopulation.de/php/nigeria.metrokano.php?cid

Nutrition Examination Survey. *Journal of America Medical Association*,283:2404-10..

Nyenwe, E.A., Osaretin, J.O., Anele, E.I. (2003). Type 2diabetes in adult Nigerians: a study of itsprevalence and risk factors in Port Harcourt,Nigeria. *Diabetes Research and Clinical Practice*, 62:177–185.

O'Rahilly, S (2009). Human genetics illuminates the paths to metabolic disease. *Nature*, 462(7271):307–314.

O'Rahilly, S. and Farooqi, I.S. (2008) Human obesity: a heritable neurobehavioral disorder that is highly sensitive to environmental conditions. *Diabetes*, 57(11):2905–2910.

O'Rahilly, S., Farooqi, I.S., Yeo, G.S.H., Challis, B.G (2003) Minireview: human obesity - lessons from monogenicdisorders. *Endocrinology*, 9: 3757-3764.

Obeidat, A.A., Ahmad, M.N., Haddad, F.H. and Azzeh, F.S. (2015). Evaluation of several anthropometric indices of obesity as predictors of metabolic syndrome in Jordanian adults. Nutrition and Hospitals, 2015;32(2):667-677.

Obirikorang, C., Osakunor, D.N.M., Anto, E.O., Amponsah, S.O., Adarkwa, O.K.. (2015). Obesity and cadiometabolic risk factors in urban and rural population in the Ashanti region-Ghana: A comparative cross sectional study. *PLoS ONE*, 10(6)e0129494 doi:10.1371/journal.pone.0129494

Okamoto, Y., Kihara, S., Ouchi, N., Nishida, M., Arita, Y., Kumada, M., Ohashi, K., Sakai, N., Shimomura, I., Kobayashi, H., Terasaka, N., Inaba, T., Funahashi, T and Matsuzawa, Y. (2002). Adiponectin reduces atherosclerosis in apolipoprotein E-deficient mice. *Circulation*, 106: 2767–2770.

Okamkpa, C.J., Nwankwo, M. and Danborno, B. (2016). Predicting high blood pressure among adults in Southeastern Nigeria using anthropometric variables. *Journal of Experimental and Clinical Anatomy*, 15: 111-7

Okten, A., Kalyoncu, M. and Yaris, N. (2002). The ratio of second and fourth-digit lengths and congenital adrenalhyperplasia due to 21-hydroxylase deficiency. *EarlyHuman Development*, 70: 47-54.

Okura, T., Koda, M., Ando, F., Niino, N., Ohta, S. and Shimokata, H. (2003). Association of polymorphismsin the estrogen receptor alpha gene with body fat distribution. *International Journal of Obesity and RelatedMetabolic Disorders*, 27: 1020–1027.

Olsen, N.J., Heitmann, B.L. (2009). Intake of calorically sweetened beverages and obesity. *Obesity Review,*10: 68–75.

Onat, A., Hergenç, G., Yüksel, H., Can, G., Ayhan, E., Kaya, Z., *et al*. (2009). Neck circumference as a measure of central obesity: Associationswith metabolic syndrome and obstructive sleep apnea syndromebeyond waist circumference. *Clinical Nutrition*, 28:46-51.

Ouchi, N. (2010). Sfrp5 is an anti-inflammatory adipokine that modulates metabolic dysfunction in obesity. *Science*,329: 454–457.

Ouchi, N., Kihara, S., Arita, Y., Nishida, M., Matsuyama, A., Okamoto, Y., Ishigami, M., Kuriyama, H., Kishida, K., Nishizawa, H., Hotta, K., Muraguchi, M., Ohmoto, Y., Yamashita, S., Funahashi, T and Matsuzawa, Y. (2001). Adipocyte-derived plasma protein, adiponectin, suppresses lipid accumulation and class A scavenger receptor expression in human monocyte-derived macrophages. *Circulation*, 103: 1057–1063.

Owolabi, L.F., Danborno, B., Adebisi, S.S and Buraimoh, A.A.(2016). A comparative evaluation of body composition analysis in type – 2 diabetes mellitus patients and healthy Nigerians using bioelectric impendance analysis technique. *Nigerian Journal of Basic and Clinical Sciences*,13: 3-8.

Oyeyemi, B.F., Adebayo, J.O., Anifowoshe, A.T., Iyiola, O.A (2016). Relationship between ratio of second and fourth digit and obesitytraits among different ethnic groups in Ilorin, North Central Nigeria. *Notulae Scientia Biologicae*, 8(4):396-400. DOI: 10.15835/nsb.8.4.9888

Oyeyemi, B.F., Iyiola, O.A., Oyeyemi, A.W., Oricha, K.A, Anifowoshe, A.T,Alamukii, N.A (2014). Sexual dimorphism in ratio of second andfourth digits and its relationship with metabolic syndrome indicesand cardiovascular risk factors. *Journal of Research in Medical Sciences,* 19(3): 234-239.

Oyeyemi, B.F., Iyiola, O.A., Oyeyemi, A.W., Oricha, K.A., Anifowoshe, A.T.,Alamukii, N.A (2014). Sexual dimorphism in ratio of second andfourth digits and its relationship with metabolic syndrome indicesand cardiovascular risk factors. *Journal of Research in Medical Sciences* 19(3):234-239.

Pajvani, U.B., Du, X. and Combs, T.P. (2003). Structure-function studies of the adipocyte-secreted hormone Acrp30/adiponectin. Implications for metabolic regulation and bioactivity. *Journal of biological Chemistry*, 278: 9073–9085

Palin,.SL., McTernan, P.G., Anderson, L.A., Sturdee, D.W., Barnett, A.H. and Kumar, S (2003). 17Betaestradioland anti-estrogen ICI:compound 182,780 regulate expression of lipoproteinlipase and hormone-sensitive lipase in isolated subcutaneous abdominal adipocytes.*Metabolism* ,52: 383–388.

Paniagua, J.A., Sacristana, A., Romero, I., Vidal-Puig, A., Latre, J.M., Sanchez, E.,Perez-Martinez, P., Lopez-Miranda, J. and Perez-Jimenez, F. (2007). Monounsaturated fat-rich dietprevents central body fat distribution and decreases postprandial adiponectin expressioninduced by a carbohydrate-rich diet in insulin-resistant subjects. *Diabetes Care*,30: 1717–1723

Pasquali, R. and Vicennati, V. (2000). Activity of the hypothalamic-pituitary-adrenal axis in differentobesity phenotypes. *International Journal of Obesity Related Metabolic Disorders*,2: 47–49

Pattyn, N., Cornelissen,V.A., Eshghi,S. R. and Vanhees,L. (2013). "Theeffect of exercise on the cardiovascular risk factors constitutingthe metabolic syndrome: a meta-analysis of controlled trials,"*Sports Medicine*, 43(2), 121–133.

Paul, T.W. (2008). Effects of diet, physical activity and performance, and body weight on incident gout in ostensibly healthy, vigorously active men. *America Journal of Clinical Nutrition*, 87(5): 1480–1487.

Pausova, Z., Abrahamowicz, M., Mahboubi, A., Syme, C., Leonard, G.T., Perron, M., Richer, L., Veillett, S., Gaudet, D. and Paus, T. (2010). Functional variation in the androgen-receptor gene is associated with visceral adiposity and blood pressure in male adolescents. *Hypertension*, 55: 706–714.

Pedersen, S. B., Kristensen, K., Hermann, P. A.et al. (2004). Estrogen controls lipolysis by upregulatingalpha2A-adrenergic receptors directly in human adipose tissue through theestrogem receptor alpha. Implications for female fat distribution. *Journal of Clinical Endocrinology and Metabolism*, 89: 1869-78.

Peeke, P.M. and Chrousos, G.P. (1995). Hypercortisolism and obesity. *Annals of NewYork Academy of Science*,771: 665– 676

Peeters, A., Beckers, S., Mertens, I., Van Hul, W. and Van Gaal, L. (2007). The G1422A variant of thecannabinoid receptor gene (CNR1) is associated with abdominal adiposity in obesemen. *Endocrine* 31: 138–141.

Peeters, A.V., Beckers, S., Verrijken, A., Mertens, I., Roevens, P., Peeters, P.J, Van Hul, W. and VanGaal, L.F. (2008) Association of SIRT1 gene variation with visceral obesity. *Human Genetics*,124: 431–436.

Perry, G.H., Dominy, N.J. and Claw, K.G. (2007). Diet and the evolution of human amylase gene copy number variation. *Nature Genetics*, 39(10):1256–1260.

Pérusse, L., Després, J.P., Lemieux, S., Rice, T., Rao, D.C. and Bouchard, C. (1996). Familial aggregationof abdominal visceral fat level: results from the Quebec family study. *Metabolism,*45: 378–382

Pérusse, L., Rankinen, T., Zuberi. A., Chagnon, Y.C., Weisnagel, S.J., Argyropoulos, G., Walts, B., Snyder, E.E. and Bouchard, C. (2005). The human obesity gene map: the 2004 update. *Obesity Resource,* 13: 381–490

Petersen, A.M.W. and. Pedersen, B.K. (2005). The anti-inflammatory effect of exercise.*Journal of Applied Physiology*, 98(4) : 1154–1162.

Petta, S., Amato, M., Cabibi, D., Cammà, C., Di Marco, V and Giordano, V. (2010). Visceral adiposity index is associated with histological findings and high viral load in patients with chronic hepatitis C due to genotype 1. *Hepatology Medicine*, 52(5): 1543–52.

Phillips, G.B., Jing, T. and Heymsfield, S.B. (2003). Relationships in men of sex hormones, insulin,adiposity, and risk factors for myocardial infarction. *Metabolism,*52: 784–790

Piazza, P.V., Lafontan, M. and Girard, J. (2007). Integrated physiology and pathophysiology of CB1-mediated effects of the endocannabinoid system. *Diabetes and Metabolism*,33: 97–107

Pijl, H., Langendonk, J.G., Burggraaf, J., Frolich, M., Cohen, A.F., Veldhuis, J.D. and Meinders, A.E. (2001).Altered neuroregulation of GH secretion in viscerally obese premenopausal women.*Journal of Clinical Endocrinology and Metabolism,*86: 5509–5515

Pillot, B., Duraffourd, C., Begeot, M., Joly, A., Luquet, S., Houberdon, I. (2011). Role of hypothalamic melanocortin system in adaptation of food intake to food protein increase in mice. *Public Library of Science*, 6(4): e1 91 07.

Pınar, Y., Mustafa, Y., Ali, C. and Yıldırım, S. (2015). The 2nd to 4th digit length difference and ratio as predictors of hyperandrogenism and metabolic syndrome in females. *Konuralp Tıp Dergisi*, 7(1):45-49

Pischon, T., Boeing, H., Hoffmann, K., Bergmann, M., Schulze, M. B., OvervadK, et al. (2008). General and abdominal adiposity and risk of death in Europe.*North England Journal Medicine*, 359(20): 2105- 2121.

Pischon, T., Hotamisligil, G.S. and Rimm, E.B. (2003). Adiponectin Stability in plasma over 36 hours and within person variation over 1 year. *Clinical Chemistry*, 49:650-652.

Pokrywka, L., Rachoń, D., Suchecka-Rachoń, K., and Bitel, L. (2005). The second to fourth digit ratio in elite and non-elite female athletes. *American Journal Human Biology*, 17:796-800.

Pond, C.M. (1992). An evolutionary and functional view of mammalian adipose tissue. *Proceedings of Nutritional Society,* 51: 367–377

Pou, K.M., Massaro, J.M., Hoffmann, U., Vasan, R.S., Maurovich-Horvat, P., Larson, M.G. (2007) Visceral and subcutaneous adipose tissue volumes are cross-sectionally related to markers of inflammation and oxidative stress: *Framingham Heart Study Circulation*, 116(11):1234-41

Price, G.M., Uauy, R., Breeze, E., Bulpitt, C.J. and Fletcher, A.E. (2006). Weight, shape, and mortality risk in older persons: elevated waist-hipratio, not high body mass index, is associated with a greater risk of death. *American Journal of Clinical Nutrition,* 84(2): 449e60.

Price, T.M., O'Brien, S.N., Welter, B.H., George, R., Anandjiwala, J. and Kilgore, M. (1998). Estrogenregulation of adipose tissue lipoprotein lipase–possible mechanism of body fat distribution. .*American Journal Obstetetric and Gynecology,*178: 101–107

Prisant, L.M., Alpert, B.S., Robbins, C.B., Berson, A.S., Hayes, M., Cohen, M.L. and Sheps, S.G.(1995). American National Standard for non automated sphygmomanometers: summary report. *American Journal of Hypertension*, 8: 210 –213.

Privette, RC., Bower, J., Hao, J., Udupi, E., Green, v., Pories, A. and MacDonald, K. (2002) Differences in the lipolytic function of adipose tissue preparations fromBlack American and Caucasian women. *Metabolism,* 51: 1514–1518

Puepet, F.H., Zoakah, A.I. and Chuhwak, E.K. (2002). Prevalence of overweight and obesity among urban Nigeria adults in Jos. *Highland Medical Research Journal*, 1:13 – 16.

Punyadeera, C., Zorenc, A. H. G. Koopman R. et al., "The effects of exercise and adipose tissue lipolysis on plasma adiponectin concentration and adiponectin receptor expression in human skeletalmuscle," *European Journal of Endocrinology*, 152(3) 427–436.

Putz, D.A., Gaulin, S.J.C, Sporter, R.J. and McBurney, D. H. (2004). Sex hormones and finger length: What does 2D:4D indicate? *Evolution of Human Behavior,* 25: 182–199.

Ramachandran, A.., Mary, S., Yamuna, A., Murugesan, N. and Snehalatha, C. (2008). High prevalence ofdiabetes and cardiovascular risk factors associated with urbanization in India.*Diabetes Care,*31(5):893-898.

Ravinder, K.Y. and Manju, B. (2016). A study of 2nd to 4th digit ratio (2D:4D) in relation to hypertension in north Indian males and its implications for risk factors in coronary heart disease *Indian Journal of Clinical Anatomy and Physiology,* 3(1):24-26

Razak, F., Anand, S.S., Shannon, H., Vuksan, V., Davis, B., Jacobs, R., Teo, K.K., McQueen, M. and Yusuf, S. (2007). Defining obesity cut points in a multiethnic population. *Circulation* 115: 2111– 2118.

Ren, J. M., Semenkovich, C. F., Gulve, E. A., Gao, J. and Holloszy, J. O.(1994). Exercise induces rapid increases in GLUT4 expression, glucose transport capacity, and insulin-stimulated glycogen storage in muscle. *Journal of Biological Chemistry,*269: 14396–14401

Rice, T., Pérusse, L., Bouchard, C. and Rao, D.C. (1996). Familial clustering of abdominal visceral fatand total fat mass: the Quebec Family Study. *Obesity Resource,* 4: 253–261

Robinson, S. J., and Manning, J. T. (2000). The ratio of 2nd to 4th digit length and male homosexuality. *Evolution Hum. Behav*. 21, 333– 345.

Romaguera, D., Norat, T., Mouw, T. et al. (2009). Adherence to the Mediterranean diet is associated with lowerabdominal adiposity in European men and women. *Journal of Nutrition,*139: 1728–1737

Romano, M., Leoni, B. and Saino, N. (2006). Examination marks of male university students positively correlate with finger length ratios (2D:4D). *Biological Psychology*. 71(2):175-82.

Romanski, S.A., Nelson, R.M and Jensen, M.D. (2000). Meal fatty acid uptake in adipose tissue: gendereffects in nonobese humans. *America Journal of Physiology, Endocrinology and Metabolism,*279: 455 – 462.

Ronalds, G., Phillips, D.I, Godfrey, K.M., Manning, J.T. (2002).The ratio of second to fourth digit lengths: a marker of impaired fetal growth? *Early Human Development,* 68: 21–26.

Rosner, W., Auchus, R.J., Azziz, R., Sluss, P.M. and Raff, H. (2007). Position statement: utility, limitations,and pitfalls in measuring testosterone: an Endocrine Society position statement. *Journal of ClinicalEndocrinology and Metabolism,* 92: 405–413

Ross, R. and Janiszewski, P.M. (2006). Is weight loss the optimal target for obesity-related cardiovasculardisease risk reduction? *Canadian Journal of Cardiology,* 24: 25–31.

Ross, R., Freeman. J., Hudson, R. and Janssen, I. (2002). Abdominal obesity, muscle composition, and insulin resistance in premenopausal women. *Journal of Clinical Endocrinology and Metabolism*, 87(11):5044 – 51.

Ryan, A.S., Berman, D.M., Nicklas, B.J., Sinha, M., Gingerich, R.L., Meneilly, G.S., Egan, J.M and Elahi, D. (2003). Plasma adiponectin and leptin levels, body composition, and glucose utilization in adult women with wide ranges of age and obesity. *Diabetes Care*, 26: 2383–2388.

Sabin, M.A., Crowne, E.C., Stewart, C.E, Hunt, L.P, Turner, S.J., Welsh, G.I., Grohmann, M.J.,Holly, J.M. and Shield, J.P. (2007). Depot-specific effects of fatty acids on lipid accumulation inchildren's adipocytes. *Biochemical and BiophysicalResearch Commununication*,361: 356–361.

Sabir, A..A., Isezuo, S.A. Ohwovoriole., O. A. Fasanmade, S. A. Iwuala, A. S. Umar, M.T. (2013). Rural-urban difference In plasma lipid levels and prevalence ofdyslipidemia in Hausa-Fulani of North-Western Nigeria. *Ethnicity & Disease.* 23(3):374–378)

Salomon, E.G., Hizon, C. E. and Raboca, J. C. (2011). Minimum waist circumferenceand visceral fat values by ultrasonography to identifyadult urban Filipinos at risk for metabolic syndrome.*Philipp Journal of Internal Medicine*, 49(1): 15-21.

Samaras, K., Botelho, N.K., Chisholm, D.J and Lord, R.V. (2010). Subcutaneous and visceral adipose tissue gene expression of serum adipokines that predict type 2 diabetes. *Obesity*, 18: 884–889.

Santos, J.L., Saus, E. and Smalley, S.V. (2012). Copy number polymorphism of the salivary amylase gene: implications in human nutrition research. *Journal of Nutrigenetics Nutrigenomics*, 5(3):117–131.

Sanya, A.O., Ogwumike, O.O., Ige A.P. and Ayanniyi, O.A. (2009) Relationship of waist-hip ratio and body mass index to blood Pressure of individuals in Ibadan North Local Government.*Africa Journal of Pure and applied Science.* 1**:** 7-11

Saunders, T. J., Palombella, A., McGuire, K.A., Janiszewski, P.M., Despres, J.P. and Ross,R. (2012). Acute exercise increases adiponectinlevels in abdominally obese men. *Nutrition and Metabolism*, Article ID148729, 6 pages.

Scheen, A.J. (2009). The endocannabinoid system: a promising target for the management oftype 2 diabetes. *Current Protein and Peptide Science*,10: 56–74

Scherer, P.E., Williams, S., Fogliano, M., Baldini, G. and Lodish, H.F. (1995). A novel serum protein similar to C1q, produced exclusively in adipocytes. *Journal of Biological Chemistry*, 270: 26746–26749

Schmidt, M.I., Duncan, B.B., Watson, R.L., Sharrett, A.R., Brancati, F.L. and Heiss, G. A. (1996). metabolic syndrome in whites and African-Americans. *Diabetes Care*, 19:414–418.

Schnohr, P., Scharling, H. and Jensen, J.S (2007). Intensity versus duration ofwalking, impact on mortality: the Copenhagen City Heart Study. *European Journal Cardiology, Prevention and Rehabilitation*, 14:72–8.

Schulze MB, Thorand B, Fritsche A, Ha¨ ring HU, Schick F, et al. (2012) Bodyadiposity index, body fat content and incidence of type 2 diabetes. *Diabetologia,* 55: 1660–1667.

Schuster, J., Vogel, P., Eckhardt C. and Morelo, S.D.B. (2014) Applicability of the visceral adiposity index (VAI) in predicting components of metabolic syndrome in young adults. *Nutrition Hospitals*, 30(4):806-812

Seckl, J.R. and Walker, B.R (2001). Minireview: 11beta-hydroxysteroid dehydrogenase type 1- atissue-specific amplifier of glucocorticoid action. *Endocrinology,*142: 1371–1376.

See, R., Abdullah, S.M. and McGuire, D. K. et al. (2007). The association of differing measures of overweight and obesity with prevalent atherosclerosis: the Dallas Heart Study. *Journal of American College of Cardiology,* 50:752-759.

Seidell, J.C, Cigolini, M., Deslypere, J.P., Charzewska, J., Ellsinger, B.M., Cruz, A. (1991) Body fat distribution in relation to serum lipids and blood pressure in 38-year-old European men: the European fat distribution study. *Atherosclerosis*, 86:251–260.

Sengier A. (2005). Multifactorial etiology of obesity: nutritional and central aspects. *Medical Review of Bruxelles*, 26:211-214.

Shao, J., Yu, L., Shen, X., Li, D and Wang, K. (2010). Waist-to-height ratio, an optimal predictor for obesity and metabolic syndrome in Chinese adults. *Journal of Nutrition, Health and Aging,*14: 782–785.

Shaw, J.E., Sicree, R.A., Zimmet, P.Z. (2010). Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Research and Clinical Practice,* 87:4–14

Shi, H. and Clegg, D.J. (2009). Sex differences in the regulation of body weight. *Physiology and Behaviour,*97: 199–204

Shi, H., Strader, A.D., Woods, S.C. and Seeley, R.J. (2007). Sexually dimorphic responses to fat loss aftercaloric restriction or surgical lipectomy. *America Journal of Physiology, Endocrinology and Metabolism*, 293: 316– 326.

Shillabeer, G. and Lau, D.C. (1994). Regulation of new fat cell formation in rats: the role of dietaryfats. *Journal of Lipid Research,*35: 592–600

Shimomura, I., Matsuda, M., Hammer, R.E., Bashmakov, Y., Brown, M.S. and Goldstein, J.L. (2000). Decreased IRS-2 and increased SREBP-1c lead to mixed insulin resistance and sensitivity in liver of lipodystrophic and *ob*/*ob* mice. *Molecoular Cell*, 6: 77–86.

Sigurjonsdottir, H.A., Koranyi, J., Axelson, M., Bengtsson, B.A. and Johannsson, G. (2006). GH effect onenzyme activity of 11betaHSD in abdominal obesity is dependent on treatment duration.*European Journal of Endocrinology,* 154: 69–74.

Siminnialayi, I.M., Emem-Chioma, P.C., Dapper, D.V. (2008). The prevalence of obesity as indicated byBMI and waist circumference among Nigerianadult attending family medicine clinics asoutpatients in Rivers state. *Nigeria Journal of Medicine*, 17:340–345.

Simmons, R. K., Alberti, K. G., Gale, E. A. et al. (2010). The metabolic syndrome: useful conceptor clinical tool? Report of a WHO Expert Consultation. *Diabetologia*, 53:600-605.

Slumming, V. A. and Manning, J. T. (2000) Second to fourth digit ratio in elite musicians: evidence for musical ability as an honest signal of male fitness. *Evolution and Human Behaviour*, 21: 1–9.

Smemo, S., Tena, J.J. and Kim, K.H (2014). Obesity associated variants within FTO form long-range functional connections with IRX3. *Nature*, 507(7492):371–375.

Smith, S.C. and Haslam, D. (2007). Abdominal obesity, waist circumference and cardiometabolic risk: awareness among primary care physicians, the general population and patients at risk – the shape of the nations survey. *Current Medical Research and Opinion,* 23: 379–84.

Sniderman, A.D., Bhopal, R., Prabhakaran, D., Sarrafzadegan, N., Tchernof, A. (2007). Why mightSouth Asians be so susceptible to central obesity and its atherogenic consequences?The adipose tissue overflow hypothesis. *International Journal of Epidemiology*,36: 220–225

Sobngwi E., Mbanya J. C. and Unwin, N. C., et al. (2004). Exposure over the life course to an urbanenvironment and its relation with obesity,diabetes, and hypertension in rural andurban Cameroon. *International Journal of Epidemiology*, 33:769–776

Speakman, J., Hambly, C., Mitchell, S. and Król, E (2007). Animalmodels of obesity. *Obesity Review*, 1: 55-61 .

Speliotes, E.K., Willer, C.J. and Berndt, S.I (2010). Association analyses of 249,796 individuals reveal18 new loci associated with body mass index. *Nature Genetics,* 42: 937–948

Stamatakis, E., Hamer, M., Tilling, K. and Lawlor, D.A. (2002). Sedentary time in relation tocardio-metabolic risk factors: differential associations for self-report vsaccelerometry in working age adults. *Internal Journal of Epidemiology,* 41:1328–37.

Stanhope, K.L. and Havel, P.J. (2008). Endocrine and metabolic effects of consuming beverages sweetened with fructose, glucose, sucrose, or high-fructose corn syrup. *American Journal of Clinical Nutr*ition, 88: 1733–1737

Stanhope, K.L. and Havel, P.J. (2010). Fructose consumption: recent results and their potentialimplications. *Annal of NewYork Academy of Science,*1190: 15–24

Stanhope, K.L., Schwarz, J.M., Keim, N.L., Griffen, S.C., Bremer, A.A., Graham, J.L., Hatcher, B.,Cox, C.L., Dyachenko, A., Zhang, W., McGahan, J.P., Seibert, A., Krauss, R.M., Chiu, S., Schaefer, E.J., Ai, M., Otokozawa, S., Nakajima, K., Nakano, T., Beysen, C., Hellerstein, M.K., Berglund, L. and Havel, P.J. (2009). Consuming fructose-sweetened, not glucose-sweetened, beverages increasesvisceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *Journal of Clinical Investigation,* 119: 1322–1334

Stefan, N., Stumvoll, M., Vozarova, B., Weyer, C., Funahashi, T., Matsuzawa, Y., Bogardus, C and Tataranni, P.A. (2003). Plasma adiponectin and endogenous glucose production in humans. *Diabetes Care,* 26: 3315 - 3319.

Stefan, N., Vozarova, B and Funahashi, T. (2002). Concentration is associated with skeletal muscle insulin receptor tyrosine phosphorylation, and low plasma concentration precedes a decrease in whole-body insulin sensitivity in humans. *Diabetes,* 51:1884- 1888

Steinhagen-Thiessen, E., Peter, B. and Christian, L. (2008). Dyslipidemia in primary care – prevalence,recognition, treatment and control: data fromthe German Metabolic and CardiovascularRisk Project (GEMCAS).*Cardiovascular Diabetology*, 7:31.

St-Pierre, A.C., Cantin, B., Dagenais, G.R., Mauriège, P., Bernard, P.M., Després, J.P. and Lamarche, B. (2005). Low-density lipoprotein subfractions and the long-term risk of ischemic heartdisease in men: 13-year follow-up data from the Quebec Cardiovascular Study. *Arteriosclerosis, Thrombosis and Vascular Biology,* 25: 553–559

St-Pierre, J., Lemieux, I., Miller-Felix, I., Prud'homme, D., Bergeron, J., Gaudet, D., Nadeau, A., Després, J.P. and Vohl, M.C. (2002). Visceral obesity and hyperinsulinemia modulate the impact ofthe microsomal triglyceride transfer protein_493G/T polymorphism on plasma lipoproteinlevels in men. *Atherosclerosis* 160: 317–324.

St-Pierre, J., Miller-Felix, I., Paradis, M.E., Bergeron, J., Lamarche, B., Després, J.P., Gaudet, D. and Vohl, M.C. (2003). Visceral obesity attenuates the effect of the hepatic lipase _514C_Tpolymorphism on plasma HDL-cholesterol levels in French-Canadian men. *Molecoular Genetics andMetabolism,*78: 31–36

Talaei, M., Sadeghi, M., Marshall, T., Thomas, G. N., Iranipour R., et al. (2013). Anthropometric indices predicting incident type 2 diabetes in an Iranian population: The Isfahan Cohort Study. *Diabetes and Metabolism,*39: 424–31.

Tao, Y.X. (2010). Mutations in the melanocortin-3 receptor (MC3R) gene: Impact on human obesity or adiposity. *Current Opinion and Investigation Drugs,* 10: 1 092-1 096.

Tao,Y.X. (2009). Mutations in melanocortin-4 receptor and human obesity.*Progress in Molecoular Biology and Translational Science*, 88:1 73-204

Tappy, L. and Le, K.A (2010). Metabolic effects of fructose and the worldwide increase in obesity.*Physiology Review,*90: 23–46.

Taro, Y., Masahiro, U. and Ryutaro, O (2001). Influence of urbanisation on physical activity and dietarychanges in Huli-speaking population: a comparativestudy of village dwellers and migrants in urban settlements. *British Journal Nutrition*, 85:65–73.

Taskinen, M.R. (2003). Diabetic dyslipidaemia: from basic research to clinical practice. *Diabetologia*, 46: 733–749.

Taskinen, M.R. (2003). Diabetic dyslipidaemia: from basic research to clinical practice. *Diabetologia*, 46: 733–749

Taskinen, M.R. (2005). Type 2 diabetes as a lipid disorder. *Current Molecoular Medicine, 5:* 297–308

Taskinen, M.R. (2005). Type 2 diabetes as a lipid disorder. *Current Molecoular Medicine,* 5: 297–308

Taskinen, M.R., Adiels, M., Westerbacka, J., Soderlund, S., Kahri, J., Lundbom, N., Lundbom, J.,Hakkarainen, A., Olofsson, S.O, Orho-Melander, M. and Boren, J (2011). Dual metabolic defects arerequired to produce hypertriglyceridemia in obese subjects. *Arteriosclerosis, Thrombossis and VascularBiology,*31: 2144–2150

Tchernof, A. and Labrie, F. (2004). Dehydroepiandrosterone, obesity and cardiovascular diseaserisk: a review of human studies. *European Journal of Endocrinology,*151: 1–14

Tchernof, A. and Després, J.P. (2013)**.** Pathophysiology of human visceral obesity: An update.*Physiology Review,* 93: 359– 404.

Tchernof, A., Bélanger, C., Morisset, A.S., Richard, C., Mailloux, J., Laberge, P. and Dupont, P. (2006).Regional differences in adipose tissue metabolism in women: minor effect of obesityand body fat distribution. *Diabetes,*55: 1353–1360

Tchoukalova, Y.D., Koutsari, C., Karpyak, M.V., Votruba, S.B., Wendland, E. and Jensen, M.D. (2008). Subcutaneous adipocyte size and body fat distribution. *American Journal of Clinical Nutrition,*87(1):56-63.

Teff, K.L., Grudziak, J., Townsend, R.R., Dunn, T.N., Grant, R.W., Adams, S.H., Keim, N.L.,Cummings, B.P., Stanhope, K.L. and Havel, P.J. (2009). Endocrine and metabolic effects of consumingfructose- and glucose-sweetened beverages with meals in obese men and women:influence of insulin resistance on plasma

triglyceride responses. *Journal of Clinical Endocrinology and Metabolism,* 94: 1562–1569

Tjønna, A. E. (2009).Aerobic interval training reduces cardiovascular risk factors more than a multitreatment approach in overweight adolescents. *Clinical Science of London,*116: 317–326.

Topolski, T.D., Logerfo, J., Patrick, D.L., Wiliams, B., Walwick, J. and Patrick, M.B (2006). The rapid assessment of physical activity among adults. *Preventing Chronic Diseases*, 3:(4)118

Traurig, M., Mack, J. and Hanson, R.L (2009). Common variation in *SIM1* is reproducibly associated with BMI in Pima Indians. *Diabetes*, 58(7):1682–1689.

Tremblay, A.J., Despre´s, J.P., Piche,´ M.E, Nadeau, A., Bergeron, J and Alme´ras, N (2004). Associations between the fatty acid content of triglyceride, visceral adipose tissue accumulation, and components of the insulin resistance syndrome. *Metabolism*, 53(3):310-7, http://dx.doi.org/10.1016/j. metabol.2003.10.011.

Trinder, P. (1969). Determination of serum glucose. *Annals of Clinical Biochemistry,* 6:24-27.

Tsai, E.C., Matsumoto, A.M., Fujimoto, W.Y. and Boyko, E.J (2004). Association of bioavailable, free,total testosterone with insulin resistance: influence of sex hormone-binding globulinand body fat. *Diabetes Care,*27: 861–868

Tulloch-Reid, M.K., Williams, D.E., Looker, H.C., Hanson, R.L. and Knowler, W.C (2003). Do measures of body fat distribution provide information on the risk of type 2 diabetes in addition to measures of general obesity? Comparison of anthropometric predictors of type 2 diabetes in Pima Indians. *Diabetes Care,* 26: 2556–2561

Umut. H., Zeynep, S., Özhan, P., Ferdi, G., Burak, K. and Hüseyin, E. (2015). Relationship between second to fourth digit ratios and obesity, muscle mass. *Journal of Clinical and Analytical Medicine*, 10:4328-3846

Van Anders, S.M and Hampson, E. (2005). Testing prenatal androgen hypothesis: measuring digit ratios, sexual orientation and spatial abilities in adults. *Hormones and Behavior,* 47:92-98

Van Cauwenberg, J., Van Holle, V., De Bourdeaudhuij, I., Owen, N.and Deforche, B. (2014). Older adults' reporting of specific sedentary behaviors: validity andreliability. *BMC Public Health,* 14:734.

Van der Klaauw ,A.A., Biermasz, N.R., Feskens, E.J., Bos, M.B, Smit, J.W., Roelfsema, F.,Corssmit, E.P., Pijl, H., Romijn, J.A., Pereira, A.M. (2007). The prevalence of the metabolic syndromeis increased in patients with GH deficiency, irrespective of

long-term substitutionwith recombinant human GH. *European Journal of Endocrinology,*156: 455–462

Van Harmelen, V., Lonnqvist, F., Thorne, A., Wennlund, A., Large, V., Reynisdottir, S. and Arner, P. (1997). Noradrenaline-induced lipolysis in isolated mesenteric, omental and subcutaneousadipocytes from obese subjects. *International Journal of Obesity and Related Metabolic Disorders,*21: 972–979

Varlamov, O., Somwar, R., Cornea, A., Kievit, P., Grove, K.L. and Roberts, C.T. (2010). Single-cellanalysis of insulin-regulated fatty acid uptake in adipocytes. *American Journal of Physiology, Endocrinology andMetabolism,*299: 486 – 496.

Varley, R. (1995). Lexical semantic deficits following right hemisphere damage: Evidence from verbal fluency tasks. *European Journal of Disorders of Communication,* 30:362–371.

Vartanian, L.R., Schwartz, M.B. and Brownell, K.D. (2007). Effects of soft drink consumption onnutrition and health: a systematic review and meta-analysis. *American Journal of Public Health,*97:667–675.

Veldhuis, J.D., Erickson, D., Mielke, K., Farhy, L.S., Keenan, D.M. and Bowers, C.Y (2005). Distinctiveinhibitory mechanisms of age and relative visceral adiposity on growth hormonesecretion in pre- and postmenopausal women studied under a hypogonadal clamp. *Journal of Clinical Endocrinology and Metabolism,*90: 6006–6013

Veldhuis, J.D., Hudson, S.B., Erickson, D., Bailey, J.N., Reynolds, G.A., Bowers, C.Y. (2009). Relativeeffects of estrogen, age, visceral fat on pulsatile growth hormone secretion in healthywomen. *American Journal of Physiology, Endocrinology and Metabolism,* 297: 367–374

Venables, M.C. and Jeukendrup, A.E. (2008). Endurance training and obesity: effect on substrate metabolism and insulin sensitivity. *Medical Science of Sports and Exercise,*40: 495–502

Vermeulen, A., Verdonck, L. and Kaufman, J.M. (1999). A critical evaluation of simple methods forthe estimation of free testosterone in serum. *Journal of ClinicalEndocrinology and Metabolism*, 84: 3666–3672

Vissers, D., Hens, W., Taeymans, J., Baeyens, J.P., Poortmans J. and van Gaal, L. (2013). Theeffect of exercise on visceral adipose tissue in overweight adults: a systematic review and meta-analysis," *PLoS ONE*, 8(2); e56415

Vogel, C.I., Greene, B. and Scherag, A (2009). Non-replication of an association of *CTNNBL1* polymorphisms and obesity in a population of Central European ancestry. *Biomedical Central Medical Genetics*, 10:14.

Voracek, M. and Dressler, S.G. (2007). Digit ratio (2D:4D) in twins: Heritabilityestimates and evidence for a masculinized trait expression inwomen from opposite-sex pairs. *Psychological Reports,*100:115-26.

Votruba, S.B. and Jensen, M.D. (2007). Sex differences in abdominal, gluteal, and thigh LPL activity.*America Journal of Physiology, Endocrinology and Metabolism,* 292: 1823 –1828

Wajchenberg, B.L. (2000). Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. *Endocrinology Review,* 21: 697–738.

Walters, R.G., Coin, L.J. and Ruokonen, A. (2013). Rare genomic structural variants in complex disease: lessons from the replication of associations with obesity. *Public Library of Science One,* 8(3):58048.

Walters, R.G., Jacquemont, S. and Valsesia, A. (2010). A new highly penetrant form of obesity due to deletions on chromosome 16p11.2. *Nature,* 463(7281):671–675.

Wang, J., Thornton J.C., Bari, S., Williamson, B., Gallagher, D., Heymsfield, S.B., Horlick, M., Kotler, D., Laferrere, B., Mayer, L., Pi-Sunyer, F.X., Pierson, R.N. (2003). Comparisons of waist circumferences measured at 4 sites. *American Journal of Clinical Nutrition*, **77**:379 –384.

Wang, Y., Rimm, E.B., Stampfer, M.J., Willett, W.C, Hu, F.B. (2005). Comparison of abdominal adiposity and overall obesity in predicting risk of type 2 diabetes among men. *American Journal Clinical Nutition*, 81:555–563.

Wannamethee, S.G. (2010). High adiponectin and increased risk of cardiovascular disease and mortality in asymptomatic older men: does NT-proBNP help to explain this association? *European Journal of Cardiovascular Prevention and Rehabilitation,*Advance online publication. doi: 10.1097/HJR.0b013e32833b09d9..

Wannamethee, S.G., Shaper, A.G., Morris, R.W and Whincup, P.H (2005). Measures of adiposity in the identification of metabolic abnormalities in elderly men. *American Journal of Clinical Nutrition,* 81: 1313–1321.

Welborn, T.A., Dhaliwal, S.S. and Bennett, S.A. (2003). Waist-hip ratio isthe dominant risk factor predicting cardiovascular death inAustralia. *Medical Journal of Austeralia,*179:580-5.

Weltman, A., Després, J.P., Clasey, J.L., Weltman, J.Y., Wideman, L., Kanaley, J., Patrie, J.,Bergeron, J., Thorner, M.O., Bouchard, C. and Hartman, M.L. (2003). Impact of abdominal visceral fat,growth hormone, fitness, and insulin on lipids and lipoproteins in older adults. *Metabolism,* 52: 73–80

Weyer, C., Funahashi, T and Tanaka, S. (2001). Hypoadiponectinemia in obesity and type 2 diabetes: Close association with insulin resistance and hyperinsulinemia. *Journal of Clinical Endocrinology and Metabolism,* 86:1930-1935.

Whitlock, G., Lewington, S., Sherliker, P. et al. (2009). Prospective Studies Collaboration.Body-mass index and cause-specific mortality in 900 000 adults: collaborative analysesof 57 prospective studies. *Lancet,* 373:1083-1096.

Williams P.T. (1997). Relationship of distance run per week to coronary heart disease risk factors in 8283male runners. The National Runners' Health Study. *Archieves of Internal Medicine,* 157:191–8.

Williams, T.J., Pepitone, M.E., Christensen, S.E., Cooke, B.M., Huberman, A.D. and Breedlove, N.J. (2000). Finger-length ratios and sexual orientation.*Nature,*404:455-6.

Wolf, A.M., Hunter, D.J. and Colditz, G.A. (1994). Reproducibility and validity ofa self-administered physical activity questionnaire. *International Journal of Epidemiology,*23:991–9.8

World Health Organization (2014). Obesity and overweight. Official publication of WHO; *Fact Sheet,* 27:743

Wu, X.L.,Yang, D.Y.,Chai, W.H.,Jin, M.I.,Zhou, X.C.,Peng, L. (2013). The ratio of second to fourth digit length (2D:4D) and coronary artery disease in a Han Chinese population. *International Journal of Medical Science,* 10: 1584-8

Wu, X.W., Muzny, D.M., Lee, C.C. and Caskey, C.T. (1992). Two independent mutational events in the loss of urate oxidase during hominoid evolution. *Journal of Molecoular Evolution,*34:78-84..

Wybenga, D.R., Pileggi, V.J., Dirstine, P.H. and Di Giorgio, J.(1970). Methods of measuring serum lipids. *Clinical Chem*istry, 16:980

Xi ,H., Li, M., Fan, Y. and Zhao, L. A. (2014). comparison of measurement methods and sexual dimorphism for digit ratio (2D:4D) in Han ethnicity. *Archives of Sexual Behavior*, 43(2):329-33.

Xu, Y. and Zheng, Y. (2015). The digit ratio (2D:4D) in China: a metaanalysis.*American Journal of Human Biology,* 27:304-309.

Yahagi, N., Shimano, H. and Hasty, A.H. (2002). Absence of sterol regulatory element-binding protein-1 (SREBP-1) ameliorates fatty livers but not obesity or insulin resistance inLep(*ob*)/Lep(*ob*) mice. *Journal of Biological Chemistry,*277: 19353–19357.

Yamauchi, T., Kamon, J. and Minokoshi, Y. (2002). Adiponectin stimulates glucose utilization and fattyacid oxidation by activating AMP-activated protein kinase. *Nature Medicine,* 8: 1288–1295.

Yamauchi, T., Nio,Y. and Maki, T. (2007). Targeted disruptionof AdipoR1 and AdipoR2 causes abrogation of adiponectin binding and metabolic actions. *Nature Medicine*, 13(3) 332–339

Yki-Jarvinen, H. and Westerbacka, J. (2005). The fatty liver and insulin resistance. *Current Molecoular Medicine,*5:287–295

Yusuf, S., Hawken, S. and Ounpuu S. (2005). INTERHEART Study Investigators. Obesityand the risk of myocardial infarction in 27,000 participants from 52 countries: acase-control study. *Lancet,* 366:1640-1649.

Zhang, C., Dang, J., Pei, L., Guo, M., Zhu, H. and Qu, L. (2013a). Relationship of 2D:4D finger ratio with androgen receptor CAG and GGN repeat polymorphism. *American Journal of Human Biology*, 25(1):101-06.

Zhang, Z. Q., Deng, J., He, L. P., Ling, W. H. and Su Y. X. (2013b). Comparison of various anthropometric and body fat indices in identifying cardiometabolic disturbances in Chinese men and women. *PLoS ONE 8(8):* e70893. doi:10.1371/journal.pone.0070893

Zhang, Z.Q., Liu, Y.H., Xu, Y., Dai, X.W., Ling, W.H. and Su, Y.X. (2013c). The validity of the body adiposity index in predicting percentage body fat and cardiovascular risk factors among Chinese.*Clinical Endocrinology*, 81: (3) 356 – 362

Zhao, D., Li, B., Yu,K. and Zheng, L. (2012) Digit ratio (2D:4D) and hand grip strength in subjects of Han ethnicity: Impact of sex and age. *American Journal of Physical Anthropology*, 149:266-71.

Zheng, Z. and Cohn, M.J. (2011). Developmental basis of sexually dimorphic digit ratios. *Proceedings of National Academy of Science, U S A*, 108:16289-94.

Zheng, H., Orsini, N. and Amin, J. (2009). Quantifying the dose-response ofwalking in reducing coronary heart disease risk: meta-analysis. *European Journal of Epidemiology,*24:81–192.

APPENDIX I:

TABLES OF MULTIPLE COMPARISON OF PA

Table 1: Multiple comparison of effect of physical activity on adiposity indices

				Male			Female		
Variables	Exercise categories			MD	SE	P value	MD	SE	P value
BMI	Inactive	versus	Mild	0.68	0.75	1	3.59	0.83	0.00016
	Inactive	versus	Moderate	2.80	0.61	<0.001	5.80	0.65	<0.001
	Inactive	versus	Optimal	2.68	0.63	<0.001	6.98	0.88	<0.001
	Mild	versus	Moderate	2.12	0.72	0.02	2.21	0.82	0.043884
	Mild	versus	Optimal	2.00	0.74	0.043	3.38	1.01	0.004591
	Moderate	versus	Optimal	-0.12	0.60	1	1.18	0.86	1
WC (cm)	Inactive	versus	Mild	4.30	1.87	0.133	9.60	2.22	0.000142
	Inactive	versus	Moderate	11.06	1.52	<0.001	16.91	1.72	<0.001
	Inactive	versus	Optimal	15.82	1.59	<0.001	21.18	2.32	<0.001
	Mild	versus	Moderate	6.76	1.79	0.001	7.31	2.16	0.005257
	Mild	versus	Optimal	11.52	1.85	<0.001	11.58	2.67	0.000141
	Moderate	versus	Optimal	4.76	1.50	0.01	4.27	2.27	0.373017
HC (cm)	Inactive	versus	Mild	0.09	1.53	1	3.97	2.14	0.392932
	Inactive	versus	Moderate	1.45	1.25	1	2.81	1.66	0.54847
	Inactive	versus	Optimal	3.68	1.30	0.03	3.34	2.25	0.832983
	Mild	versus	Moderate	1.36	1.47	1	-1.16	2.09	1
	Mild	versus	Optimal	3.60	1.52	0.111	-0.63	2.58	1
	Moderate	versus	Optimal	2.23	1.23	0.423	0.53	2.20	1
NC (cm)	Inactive	versus	Mild	1.05	0.41	0.071	1.45	0.48	0.017493
	Inactive	versus	Moderate	2.35	0.34	<0.001	2.39	0.37	<0.001
	Inactive	versus	Optimal	2.25	0.35	<0.001	2.71	0.50	<0.001
	Mild	versus	Moderate	1.30	0.40	0.007	0.93	0.47	0.288192
	Mild	versus	Optimal	1.20	0.41	0.022	1.26	0.58	0.188348
	Moderate	versus	Optimal	-0.10	0.33	1	0.32	0.49	1
W/H	Inactive	versus	Mild	0.05	0.01	<0.001	0.07	0.02	0.000332
	Inactive	versus	Moderate	0.11	0.01	<0.001	0.16	0.01	<0.001
	Inactive	versus	Optimal	0.14	0.01	<0.001	0.21	0.02	<0.001
	Mild	versus	Moderate	0.06	0.01	<0.001	0.09	0.02	<0.001
	Mild	versus	Optimal	0.09	0.01	<0.001	0.14	0.02	<0.001
	Moderate	versus	Optimal	0.03	0.01	0.001	0.05	0.02	0.028049
W/Ht	Inactive	versus	Mild	0.03	0.01	0.113	0.06	0.01	<0.001
	Inactive	versus	Moderate	0.06	0.01	<0.001	0.11	0.01	<0.001
	Inactive	versus	Optimal	0.09	0.01	<0.001	0.14	0.01	<0.001
	Mild	versus	Moderate	0.04	0.01	0.003	0.05	0.01	0.001227
	Mild	versus	Optimal	0.06	0.01	<0.001	0.07	0.02	<0.001
	Moderate	versus	Optimal	0.02	0.01	0.038	0.03	0.01	0.25272

BMI: body mass index, WC: waist circumference, HC: hip circumference, NC: neck circumference, W/H: waist-to-hip ratio, W/Ht: waist-to-height ratio, MD: mean difference, SE: standard error. BAI: body adiposity index

Table 2: Multiple comparison of effect of physical activity on the BAI, blood pressure and Digit ratio

				Male			Female		
Dependent Variables	Exercise categories			MD	SE	P value	MD	SE	P value
BAI	Inactive	versus	Mild	0.07	0.74	1.000	2.37	0.99	0.105
	Inactive	versus	Moderate	0.38	0.60	1.000	2.07	0.77	0.055
	Inactive	versus	Optimal	0.81	0.63	1.000	2.34	1.04	0.152
	Mild	versus	Moderate	0.32	0.71	1.000	-0.30	0.97	1.000
	Mild	versus	Optimal	0.75	0.73	1.000	-0.03	1.19	1.000
	Moderate	versus	Optimal	0.43	0.59	1.000	0.27	1.02	1.000
DBP	Inactive	versus	Mild	7.08	1.83	0.001	13.71	1.74	<0.001
	Inactive	versus	Moderate	14.91	1.49	<0.001	20.91	1.35	<0.001
	Inactive	versus	Optimal	21.83	1.56	<0.001	27.07	1.83	<0.001
	Mild	versus	Moderate	7.82	1.76	<0.001	7.20	1.70	0.0002
	Mild	versus	Optimal	14.74	1.81	<0.001	13.36	2.10	<0.001
	Moderate	versus	Optimal	6.92	1.47	<0.001	6.16	1.79	0.004
SBP	Inactive	versus	Mild	12.45	2.72	<0.001	21.37	2.79	<0.001
	Inactive	versus	Moderate	28.08	2.21	<0.001	37.39	2.16	<0.001
	Inactive	versus	Optimal	38.06	2.31	<0.001	44.71	2.93	<0.001
	Mild	versus	Moderate	15.63	2.61	<0.001	16.02	2.72	<0.001
	Mild	versus	Optimal	25.61	2.69	<0.001	23.34	3.36	<0.001
	Moderate	versus	Optimal	9.98	2.18	<0.001	7.32	2.86	0.068
R2D:4D	Inactive	versus	Mild	0.01	0.01	1.000	0.00	0.01	1.000
	Inactive	versus	Moderate	0.03	0.01	<0.001	0.01	0.01	1.000
	Inactive	versus	Optimal	0.04	0.01	<0.001	0.02	0.01	0.004
	Mild	versus	Moderate	0.02	0.01	0.030	0.01	0.01	0.925
	Mild	versus	Optimal	0.03	0.01	<0.001	0.03	0.01	0.006
	Moderate	versus	Optimal	0.01	0.00	0.156	0.02	0.01	0.067
L2D:4D	Inactive	versus	Mild	0.01	0.01	0.198	0.01	0.01	0.857
	Inactive	versus	Moderate	0.02	0.01	<0.001	0.02	0.00	0.006
	Inactive	versus	Optimal	0.04	0.01	<0.001	0.03	0.01	0.0004
	Mild	versus	Moderate	0.01	0.01	0.891	0.01	0.01	1.000
	Mild	versus	Optimal	0.02	0.01	0.003	0.02	0.01	0.128
	Moderate	versus	Optimal	0.01	0.01	0.052	0.01	0.01	0.606

BAI: body adiposity index, R: right hand, L: left hand, 2D:4D: second to fourth digit ratio, SBP: systolic blood pressure, DBP: diastolic blood pressure, MD: mean difference, SE: standard error

Table 3: Multiple comparison of effect of physical activity on the uric acid and adiponectin in males and female

				Male			Female		
Dependent Variable	Exercise categories			MD	SE	P value	MD	SE	P value
Uric Acid	Inactive	versus	Mild	1.69	0.40	<0.001	0.49	0.83	1.00
	Inactive	versus	Moderate	3.13	0.31	<0.001	3.96	0.66	<0.001
	Inactive	versus	Optimal	3.62	0.33	<0.001	4.15	0.66	<0.001
	Mild	versus	Moderate	1.44	0.38	0.002	3.48	0.96	0.005
	Mild	versus	Optimal	1.93	0.40	<0.001	3.66	0.96	0.003
	Moderate	versus	Optimal	0.49	0.31	0.676	0.19	0.82	1.00
Adiponectin	Inactive	versus	Mild	-4.97	1.25	0.001	-3.14	1.36	0.157
	Inactive	versus	Moderate	-8.87	0.96	<0.001	-12.86	1.08	<0.001
	Inactive	versus	Optimal	-11.13	1.03	<0.001	-16.79	1.08	<0.001
	Mild	versus	Moderate	-3.90	1.21	0.01	-9.72	1.57	<0.001
	Mild	versus	Optimal	-6.16	1.26	<0.001	-13.65	1.57	<0.001
	Moderate	versus	Optimal	-2.26	0.97	0.132	-3.93	1.34	0.034

MD: mean difference, SE: standard error

Table 4: Multiple comparison of effect of Physical Activity on FBG and VAI in males and females

				Male			Female		
Dependent Variable	Exercise categories			MD	SE	P value	MD	SE	P value
FBG	Inactive	versus	Mild	21.40	5.52	0.001	9.56	12.84	1.000
	Inactive	versus	Moderate	35.86	4.25	<0.001	55.16	10.23	<0.001
	Inactive	versus	Optimal	43.19	4.54	<0.001	57.09	10.23	<0.001
	Mild	versus	Moderate	14.46	5.31	0.045	45.60	14.86	0.024
	Mild	versus	Optimal	21.79	5.55	0.001	47.53	14.86	0.017
	Moderate	versus	Optimal	7.33	4.29	0.542	1.93	12.67	1.000
VAI	Inactive	versus	Mild	1.42	0.36	0.001	1.41	0.52	0.058
	Inactive	versus	Moderate	2.63	0.27	<0.001	3.26	0.41	<0.001
	Inactive	versus	Optimal	3.16	0.29	<0.001	3.11	0.41	<0.001
	Mild	versus	Moderate	1.21	0.34	0.003	1.85	0.60	0.023
	Mild	versus	Optimal	1.74	0.36	<0.001	1.69	0.60	0.046
	Moderate	versus	Optimal	0.53	0.28	0.346	-0.16	0.51	1.000

VAI; visceral adiposity index, Fasting blood glucose, MD: mean difference, SE: standard error

Table 5:Multiple comparison of effect of PA on serum lipid

				Male			Female		
Dependent Variable	Exercise categories			MD	SE	P value	MD	SE	P value
TC	Inactive	versus	Mild	28.03	6.85	<0.001	25.85	13.17	0.340
	Inactive	versus	Moderate	46.75	5.28	<0.001	72.98	10.49	<0.001
	Inactive	versus	Optimal	60.73	5.64	<0.001	85.24	10.49	<0.001
	Mild	versus	Moderate	18.72	6.60	0.032	47.13	15.24	0.023
	Mild	versus	Optimal	32.70	6.89	<0.001	59.39	15.24	0.002
	Moderate	versus	Optimal	13.98	5.33	0.059	12.26	12.99	1.000
HDL–C	Inactive	versus	Mild	-3.83	1.30	0.024	-4.40	1.50	0.033
	Inactive	versus	Moderate	-9.67	1.00	<0.001	-13.80	1.19	<0.001
	Inactive	versus	Optimal	-11.54	1.07	<0.001	-12.56	1.19	<0.001
	Mild	versus	Moderate	-5.84	1.25	<0.001	-9.40	1.73	<0.001
	Mild	versus	Optimal	-7.71	1.31	<0.001	-8.16	1.73	0.0002
	Moderate	versus	Optimal	-1.88	1.01	0.398	1.24	1.48	1.000
TG	Inactive	versus	Mild	22.70	7.09	0.011	21.55	7.68	0.048
	Inactive	versus	Moderate	43.24	5.47	<0.001	55.96	6.12	<0.001
	Inactive	versus	Optimal	56.39	5.84	<0.001	54.99	6.12	<0.001
	Mild	versus	Moderate	20.54	6.83	0.019	34.41	8.89	0.0025
	Mild	versus	Optimal	33.70	7.13	<0.001	33.44	8.89	0.004
	Moderate	versus	Optimal	13.15	5.51	0.112	-0.97	7.58	1.000
LDL–C	Inactive	versus	Mild	27.32	6.82	0.001	25.95	12.51	0.271
	Inactive	versus	Moderate	47.77	5.25	<0.001	75.59	9.97	<0.001
	Inactive	versus	Optimal	60.99	5.61	<0.001	86.80	9.97	<0.001
	Mild	versus	Moderate	20.45	6.56	0.014	49.65	14.48	0.009
	Mild	versus	Optimal	33.68	6.85	<0.001	60.86	14.48	0.001
	Moderate	versus	Optimal	13.22	5.30	0.084	11.21	12.34	1

MD; mean difference, SE: standard error, TC: total cholesterol, HDL–C: high density lipoprotein cholesterol, LDL–C: low density lipoprotein cholesterol

APPENDIX II

CONSENT FORM

Consent to Participate in the Research

Study of anthropometric and visceral indices of adiposity in relation to metabolic syndrome components and its serum biomarkers among Hausa of Kano

You are please requested to participate in this study conducted by ABDULLAHI ASUKU YUSUF from Department of Human Anatomy, Faculty of Basic Medical Sciences, ABU, Zaria,

If you have any question or concerns about the research, please feel free to contact ABDULLAHI ASUKU YUSUF, Department of Human Anatomy, Faculty of Medicine, ABU, Zaria, 08032878100

1. **Purpose of the Study**

The study is to assess relationship between anthropometric and visceral indices of adiposity with metabolic syndrome

2. **Procedures**

The data collection will involve collecting information with regard to bio-data, here the participant will be asked to provide some information relevant to his/her bio-data. This can be done in less than 1minute.

In the second phase of the study, information regarding medical history including current medications will be obtained.

The last phase will involve taking of participants blood samples and some physical measurements. The participant will be required to abstain from eating and drinking for at least 8 hours before blood sample is taken. This can be achieved easily by overnight fasting, that is not taking anything in the morning following the dinner of the preceeding night.

3. Potential Risk and Discomfort

There is no significant risk associated with this procedure. However, there might be slight discomfort during physical measurements and blood sampling

4. Potential Benefits to the Participant and/or to Society

This research may be of potential benefit to the participant and/or society in the following ways.

i. Opportunity to know your blood pressure, glucose and lipids levels and risk assessment for or incidental diagnosis of metabolic syndrome.

ii. The participant may have an opportunity to come in contact with the equipment used in the study as well as gaining knowledge about the names and uses of such equipment.

iii. Measuring the anthropometric indices of adiposity provides room for establishment of indicators and diagnostic criteria for metabolic diseases which is a useful information for clinicians.

5. **Incentives**

Incentives in the form of free drugs and refreshment will be offered to the participant after participation.

6. Confidentiality

Every effort will be made to ensure confidentiality of any identified information that is obtained in connection with this study. The variables and information collected will only be used for the aim and objectives of the study as well as scientific publications. I assure you that your information will be kept in strict confidence.

7. **Participation and Withdrawal**

Participant can choose whether to be in this study or not. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. You may exercise the option of removing your data from the study.

Participant may also refuse to answer any questions you don't want to answer and still remain in the study. The researcher may withdraw you from this research if circumstances arise that warrant doing so.

8. Right of Research Participants

Participant may withdraw their consent at any time and discontinuous participation without penalty. You are waiving any legal claims, right or remedies because of your participation in this research study. This study has been reviewed and received ethics clearance through Ethics of Ahmadu Bello University Teaching Hospital, Zaria.

9. Signature of Research Participants/Legal Representative

I have read the information provided for the study titled "Effect of Body Adiposity Indices, Digit Ratio and Level of Physical Activity on Metabolic Syndrome and Serum Biomarkers Among Hausas of Kano State, Nigeria" as described herein. My questions have been answered to my satisfaction, and I agree to participate in this study. I have been given a copy of this form

_____

Name of the participant

_____ _____

Signature of the participant Date

_____

Name of the witness

_____ _____

Signature of the witness Date

APPENDIX III

STUDY QUESTIONNAIRE

QUESTIONNAIRE FOR A STUDY OF THE EFFECT OF BODY ADIPOSITY INDICES, DIGIT RATIO AND LEVEL OF PHYSICAL ACTIVITY ON METABOLIC SYNDROME AND SERUM BIOMARKERS AMONG HAUSAS OF KANO STATE, NIGERIA.

Please tick or circle the appropriate letter where necessary below:

DEMOGRAPHY OF PARTICIPANT

1. Research I.D. _____
2. How old are you?_____ (yrs)
3. When are you born? _____/_____/_____(DD/MM/YYYY)
4. Where were you born? _____

5. Order of birth _____

6. Ethnic group _____

ETHNIC BACKGROUND

1. Mother's Ethnic Group _____
2. Grand Mother's Ethnic Group _____
3. Father's Ethnic Group_____
4. Grand Father's Ethnic Group _____

MEDICAL HISTORY

S/N	
1	Reason for hospital visit
2	Hypertensive
3	Diabetic
4	Hypertensive/diabetes
5	Current medications
6	Other established metabolic disorders

ANTHROPOMETRIC AND BLOOD PRESSURE MEASUREMENTS

1	Height
2	Weight
3	Body mass index(BMI)
4	Waist circumference
5	Hip circumference
6	Neck circumference
7	Waist-to-hip ratio
8	Waist-to-height ratio
9	Diastolic blood pressure
10	Systolic blood pressure

SERUM BIOCHEMICAL ANALYSIS

S/N	Variable
1	Uric acid
2	Adiponectin
3	Fasting glucose
4	Total cholesterol
5	HDL cholesterol
6	LDL cholesterol
7	Triglycerides

HAND ANTHROPOMETRY

1. Length of digits (mm)

Hand						
	I	II	III	IV	V	2D:4D
Right						
Left						

RAPID ASSESSMENT OF PHYSICAL ACTIVITY QUESTIONAIRE FOR ASSESSING PHYSICAL ACTIVITY (Topolski *et al.*, 2006)

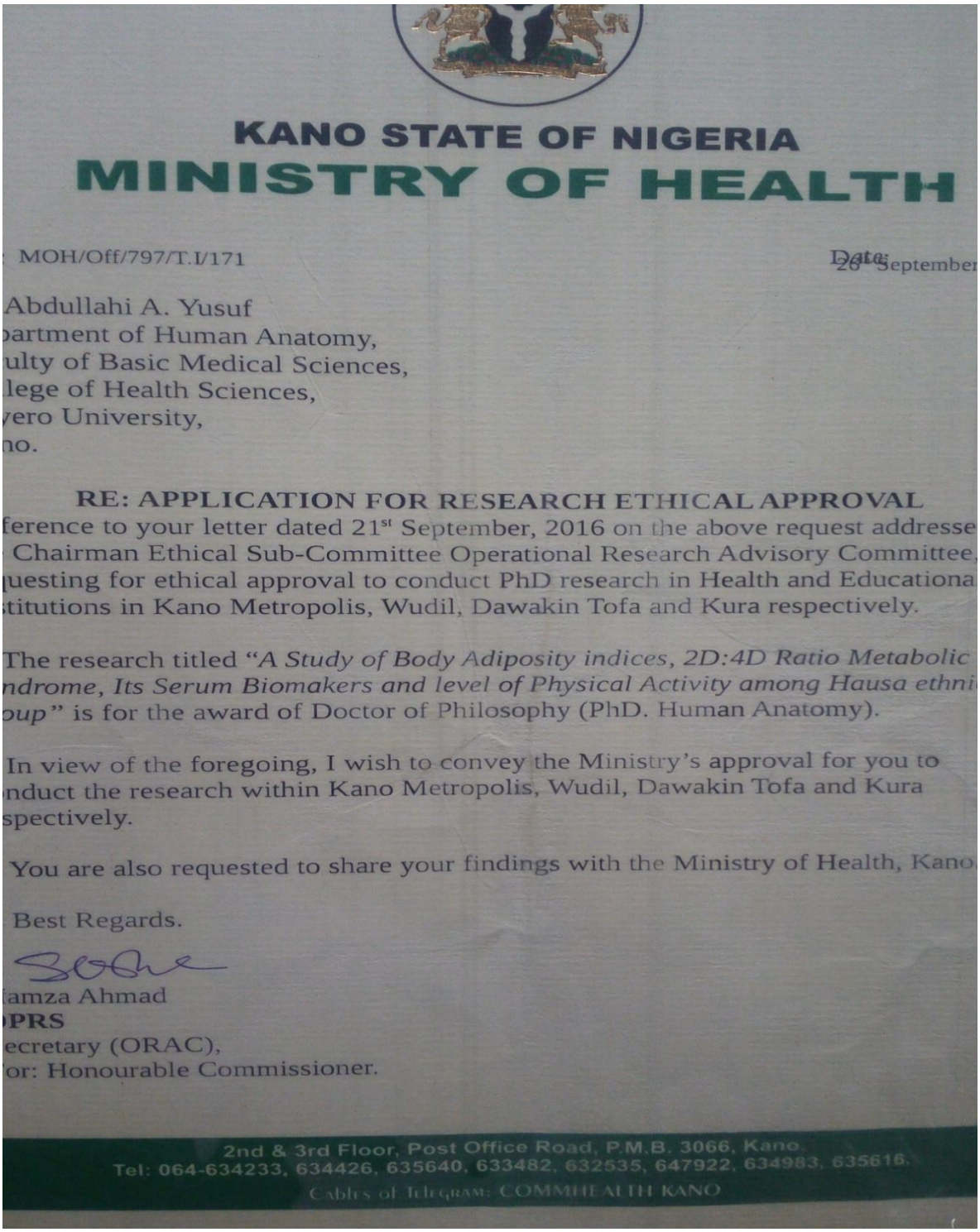
Physical activities are activities which increase your heart and respiratory rates above their resting rate, whether you do them for pleasure, work or transportation.

The following questions ask about the amount of physical activity you usually do. Please mark yes for the one that best describes your activity level in the last one year.

Questions	Response
I rarely or never do any physical activities	
I do some light or moderate physical activities, but not every week	
I do some light physical activities every week	
I do moderate physical activities every week but less than 30minutes a day or five days a week	
I do vigorous physical activities every week but less than 20minutes a day or three days a week	
I do 30minutes or more a day of moderate physical activities five or more days a week	
I do 20minutes or more a day of vigorous physical activities three or more days a week	

APPENDIX III

ETHICAL CLEARANCE



KANO STATE OF NIGERIA
MINISTRY OF HEALTH

MOH/Off/797/T.I/171 Date: 20th September

Abdullahi A. Yusuf
partment of Human Anatomy,
ulty of Basic Medical Sciences,
llege of Health Sciences,
ero University,
no.

RE: APPLICATION FOR RESEARCH ETHICAL APPROVAL

ference to your letter dated 21st September, 2016 on the above request addresse
Chairman Ethical Sub-Committee Operational Research Advisory Committee,
uesting for ethical approval to conduct PhD research in Health and Educationa
stitutions in Kano Metropolis, Wudil, Dawakin Tofa and Kura respectively.

The research titled *"A Study of Body Adiposity indices, 2D:4D Ratio Metabolic ndrome, Its Serum Biomakers and level of Physical Activity among Hausa ethni oup"* is for the award of Doctor of Philosophy (PhD. Human Anatomy).

In view of the foregoing, I wish to convey the Ministry's approval for you to nduct the research within Kano Metropolis, Wudil, Dawakin Tofa and Kura spectively.

You are also requested to share your findings with the Ministry of Health, Kano.

Best Regards.

amza Ahmad
PRS
ecretary (ORAC),
or: Honourable Commissioner.

2nd & 3rd Floor, Post Office Road, P.M.B. 3066, Kano.
Tel: 064-634233, 634426, 635640, 633482, 632535, 647922, 634983, 635616.
Cables or Telegram: COMMHEALTH KANO