PROSPECTIVE AND RETROSPECTIVE STUDY OF SOME ANTHROPOMETRIC AND REPRODUCTIVE CHARACTERISTICS OF GRAVID AND MENOPAUSAL NIGERIAN WOMEN.

BY

CHIGERU WODI
M.Sc/MED/08622/2008-2009

DEPARTMENT OF HUMAN ANATOMY
FACULTY OF MEDICINE,
AHMADU BELLO UNIVERSITY, ZARIA, NIGERIA.

NOVEMBER, 2011

PROSPECTIVE AND RETROSPECTIVE STUDY OF SOME ANTHROPOMETRIC AND REPRODUCTIVE CHARACTERISTICS OF GRAVID AND MENOPAUSAL NIGERIAN WOMEN.

By

CHIGERU WODI, B.Sc (UNIPORT, 2007)
M.Sc./MED/08622/2008-2009)

A THESIS SUBMITTED TO THE POSTGRADUATE SCHOOL AHMADU BELLO UNIVERSITY, ZARIA, NIGERIA.

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF MASTER OF SCIENCE (M.Sc.) DEGREE IN HUMAN ANATOMY

DEPARTMENT OF HUMAN ANATOMY
FACULTY OF MEDICINE
AHMADU BELLO UNIVERSITY,
ZARIA, NIGERIA.

NOVEMBER, 2011.

DECLARATION

I, CHIGERU WODI, declare that work in the thesis entitled prospective and retrospective of some anthropometric and reproductive characteristics of gravid and menopausal Nigerian women has been performed by me in the Department of Human Anatomy, Faculty of Medicine, Ahmadu Bello University, Zaria, Nigeria, under the supervision of Dr. S.S. Adebisi and Dr. B. Danborno. The information derived from the literature has been duly acknowledged in the text and a list of references provided. No part of this thesis was previously presented for another degree or diploma at any University.

CHIGERU WODI _____ _____
Student Sign Date

CERTIFICATION

This thesis entitled "**Prospective and retrospective study of some anthropometric and reproductive characteristics of gravid and menopausal Nigerian women**" by Chigeru Wodi meets the regulations governing the award of the degree of Master of Science of Ahmadu Bello University, Zaria, and is approved for its contribution to knowledge and literacy presentation.

Dr. S.S. Adebisi (B.Sc, M.Sc. Ph.D) *Chairman, Supervisory Committee* *Department of Human Anatomy* *Faculty of Medicine* *Ahmadu Bello University, Zaria.*	Sign	Date
Dr. B. Danborno (B.Sc, M.Sc. Ph.D) *Member, Supervisory Committee* *Department of Human Anatomy* *Faculty of Medicine* *Ahmadu Bello University, Zaria.*	Sign	Date
Dr. B. Danborno (B.Sc, M.Sc. Ph.D) *Head of Department* *Department of Human Anatomy* *Faculty of Medicine* *Ahmadu Bello University, Zaria.*	Sign	Date
Prof. Adebayo .A. Joshua *Dean, Postgraduate School* *Ahmadu Bello University, Zaria.*	Sign	Date
Prof. Dr. Nikolay Dimitrov External Examiner *Department of Anatomy* *Bayero University,Kano*	Sign	Date

DEDICATION

I dedicate this work as service to humanity and to all women who suffered some form of nausea and vomiting of pregnancy.

To my dearest friend, Racheal Nelson Ebimie-Inikio who was a victim of hyperemesis gravidarum and lost several pregnancies and in fond memory of your late husband, father and friend late Mr. Nelson Ebimie-Inikio, who passed on to glory on the 23rd day of March, 2011.

ACKNOWLEDGEMENT

My most gratitude goes to God Almighty for His grace and provisions throughout my study. I am saying a sincere thanks to my supervisors, Dr. S.S Adebisi and Dr. B. Danborno for the sacrifices made and for their unflinching support and constructive critics. I also appreciate Dr. Dahiru who in a short notice came to my rescue and performed my statistical analysis; your kind gesture will not be forgotten in time. To Rilwan Bashir, words cannot express how grateful I am for your help and support. I pray you also find help just in time when you need it. A big thank you to Mrs. Usifo, Rosemary, Rashidath, Rahima, Heoma, Silver, Nkechi and others who despite your schedule, sacrificed so much and served as my research assistants, may the Almighty reward you. And to my entire respondent, who without much persuasion accepted to be part of this study; always remember you are the key to my success.

I also appreciate all my lecturers and staff of the department of Human Anatomy, ABU, Zaria, for their contributing to knowledge and the help they proffered at one stage of my study. Specially saying thank you to Mr. Timbuak and Dr. Umana who were there for me, to advice and encourage when I needed direction and Mr. Iliya who took the pain to process my admission, you are the best! To my dearest friend Mrs Rachael N. Ebimie-Inikio whom at this time was in the deepest of sorrow. I pray you find comfort and your late husband; an eternal rest. And to my friends; Boma, Sadiya, Fareha and my classmates who remained supportive, I am saying thank you. Finally, I am saying a sincere thank you to my parents, Mr. & Mrs Christian Anele Wodi without whose financial help I may not boast of this achievement, I pray the good Lord continues to bless and preserve you, amen. My wonderful siblings Echey,

Chibeoso, Horu and Vanessa are not left out, for their unflinching love, support and encouragement; you remain my most treasured gift on earth.

ABSTRACT

This study investigated some anthropometric and reproductive characteristics associated with nausea and vomiting of pregnancy (NVP) and menopause among Nigerian women. Subjects for this study were drawn from the three major ethnic groups in Nigeria and were divided into two groups viz; a prospective study group (n = 344) which constitute gravid women and a retrospective group (n = 324) which consist of menopausal women. Data was collected through questionnaire via oral interview and recall from these women while anthropometric variables were obtained following standard protocol. The result showed that an early menarcheal age, higher educational level, increased parity and age at menopause significantly ($P<0.05$) association with NVP in one group but not in the other. Although not significant, a higher proportion of women born in wet season, having a higher economic status, an early child birth and carrying female foetuses reported having NVP. So also were variations in the ethnic report of NVP among the study population. This study also suggest a high prevalence (43.71%) of NVP among Nigerian women and an increased incidence over the years with women of Igbo origin having the highest incidence (53.91%) and Hausa's the least incidence (34.80%). NVP was found to impose some limitation and emotional challenge on these women with exposure to certain smell and certain food being the most aggravating factor. Both pharmaceutical and complimentary medicines were used for management of NVP and lying down was a common manoeuvre as management among those who did not use drugs. Factors found to significantly associated with the age at menopause are religion, ethnicity, parity and age at marriage ($P<0.0001$). Other variables that also showed significant association were season of birth, NVP, breastfeeding, contraception,

educational level and number of elder brothers ($P<0.05$). All other variables found no association although age at menopause increased with age at first birth.

TABLES OF CONTENT

Cover page ---------- i

Title page ---------- ii

Declaration ---------- iii

Certification---------- iv

Dedication ---------- v

Acknowledgement ---------- vi

Abstract ---------- viii

Table of Contents ---------- x

List of Tables ---------- xiv

Abbreviations ---------- xv

CHAPTER ONE

1.1 Background of study ---------- 1

1.2 Statement of research problem ---------- 6

1.3 Significance of the study ---------- 6

1.4 Justification ---------- 6

1.5 Aims and objectives of the study ---------- 7

1.6 Study hypothesis ---------- 7

1.7 Limitations ---------- 8

CHAPTER TWO

2.0 Literature review ---------- 9

2.1 Overview of nausea and vomiting of pregnancy ---------- 9

2.2 Aetiology and pathophysiology of nausea and vomiting of pregnancy --------- 9

2.2.1 Hormonal causes ---------- 9

2.2.2 The vestibular system ---------- 13

2.2.3 Gastro intestinal tract (GIT) ---------- 14

2.2.4 Immunology ---------- 17

2.2.5 Behavioural and psychological factors ---------- 18

2.2.6 Nutritional deficiency ---------- 19

2.2.7 Anatomy ---------- 19

2.2.8 Evolutionary view point (adaptation) ---------- 20

2.2.9 Genetic factor ---------- 22

2.2.10 Ethnicity / socio-economic status ---------- 23

2.2.11 Demographic factors ---------- 26

2.3 Effect of nausea and vomiting of pregnancy ---------- 27

2.4 Management options for nausea and vomiting of pregnancy ---------- 29

2.4.1 Non-pharmacologic remedies ---------- 30

2.4.2 Drug therapy ---------- 31

2.4.3 Complementary and alternative management ---------- 32

2.5 Menopause ---------- 33

2.5.1 Factors that influence age at menopause ---------- 35

2.5.1.1 Demographic characteristics ---------- 35

2.5.1.2 Reproductive correlates ---------- 36

2.5.1.3 Anthropometric factors ---------- 38

2.5.1.4 Handedness ---------- 38

CHAPTER THREE

3.0 Materials and method ---------- 40

3.1 Subjects ---------- 40

3.2 Methods ---------- 40

3.2.1 Determination of NVP and menopause ---------- 41

3.2.2 Anthropometry ---------- 41

3.3 Data analysis ---------- 41

CHAPTER FOUR

4.0 Results ---------- 43

CHAPTER FIVE

5.0 Discussions ---------- 68

5.1 NVP and anthropometric characteristics ---------- 68

5.2 NVP and reproductive characteristics ---------- 68

5.3 NVP and socio-demographic factors ---------- 70

5.4 Menstrual status and incidence/prevalence of NVP ---------- 7I

5.5 Effect of nausea and vomiting of pregnancy ---------- 72

5.6 Management option for NVP ---------- 72

5.7 Age at menopause ---------- 73

5.8 Menopause and socio-demographic characteristics ---------- 74

5.9 Menopause and reproduction ---------- 76

CHAPTER SIX

6.0 Summary, conclusion and recommendation---------- 78

6.1 Summary and conclusion ---------- 78

6.2 Recommendation ---------- 80

References ---------- 81

Appendices ---------- 96

LIST OF TABLE

Table 4.1: Descriptive statistics showing socio-demographic characteristics of gravid women ---------- 44

Table 4.2: Descriptive statistics of anthropometric and reproductive characteristics of gravid women ---------- 45

Table 4.3: Student's t-test for anthropometric and reproductive characteristics of gravid women ---------- 46

Table 4.4: Chi-square (x^2) test for association between NVP and socio-demographic characteristics of gravid women ---------- 47

Table 4.5: Chi-square (x^2) test for association between NVP and reproductive characteristics of gravid women---------- 49

Table 4.6: Descriptive statistics of demographic and reproductive characteristic of menopausal women ---------- 50

Table 4.7: Descriptive statistic of some reproductive characteristic of menopausal women ---------- 52

Table 4.8: Chi-square (x^2) test for association between NVP and demographic and reproductive characteristics of menopausal women ---------- 53

Table 4.9: Student's t-test for association between NVP and some reproductive characteristics of menopausal women ---------- 55

Table 4.10: Comparative analysis of menstrual status of study sample ---------- 56

Table 4.11: Summary on incidence of NVP among ethnic group and general prevalence of NVP among study group ----------57

Table 4.12: Self perception, aggravating factor and effect of NVP on gravid women -- ---------- 59

Table 4.13: Management options for NVP among gravid women ---------- 62

Table 4.14: Student's t-test for association between menopause and some demographic and reproductive characteristics ---------- 64

Table 4.15: ANOVA for demographic and reproductive characteristics and menopause ---------- 65

LIST OF ABBREVIATIONS

ANOVA: Analysis of variance

ANM: Age at natural menopause

ART: Assisted reproduction technique

BMI: Body mass index

B_6: Pyridoxine

B_1: Thiamine

COS: Controlled ovarian stimulation

C3: compliment antibody-3

C4: compliment antibody-4

DNA: Deoxyribonucleic acid

EGG: Electrogastrography

E_2: Estradiol

E_3: Estriol

FSH: Follicle stimulating hormone

GIT: Gastrointestinal tract

GTT: Gestational transient thyrotoxicosis

HCG: Human chorionic gonadotropic hormone

β-HCG: β-isoforms of Human chorionic gonadotropic hormone

HG: hyperemesis gravidarum

IgG: Imminoglobulin G

IgM: Immunoglobulin M

IL-6: Interleukin-6

LH: luteinizing hormone

LMP: Last menstrual period

MYA: Million years ago

NVP: Nausea and Vomiting of pregnancy

TNF-α: α-isoform of Tumour necrosing factor

TSH: Thyroid stimulating hormone

T-Helper 1: Thymus helper cell class 1

T-Helper 2: thymus helper cell class 2

T_4: Thyroxin

CHAPTER 1

INTRODUCTION

1.1 BACKGROUND OF STUDY

Anthropometric characteristics have been shown to be possible predictors of reproductive success in human female species and this has been widely studied. Height, weight and body mass index (BMI) has been associated with increased parity, twinning and higher fertility in women (Danborno and Oyibo, 2008; Pollet and Nettle, 2008; Swami *et al*., 2008). Other has also considered certain reproductive characteristics as probable markers for biological determinants of longevity, especially, early fecundity and late menopause (Doblhammer *et al*., 1999). Reproductive history has been tied to and now well known to determine the existence of the female species as the female's reproductive characteristics is known to determine her survival, fitness, adaptation, and aging and to an extent, survival and reproduction of her offspring from evolutionary perspective (Voland and Engel 1986). However, studies have shown that approximately one-quarter of variation could be attributed to genetic factors and three-quarters to unknown environmental factors (Herskind *et al*., 1996). Among other reproductive characteristics, age at menarche, menopause and nausea and vomiting of pregnancy has been proposed by researchers to be influenced by demographic, environmental, anthropometric and other factors (Simondon *et al*., 1997; Danborno and Oyibo, 2008; Parazzini *et al*.1992; Luoto *et al*. 1994) other than the gene.

Nausea and vomiting of pregnancy (NVP) commonly called "*vomitus metatinus gravidarum (morning sickness)"* is known to occur between the 4^{th} and 10^{th} week of gestation and is resolved about the 20^{th} week of gestation. The aetiology of NVP is

poorly understood (Lacasse *et al*., 2009), however, according to Broussard and Richter (1998), its association with pregnancy was documented on papyrus dating as far back as 2000 BC, the earliest reference being recorded in '*Soranus'* Gynaecology from the second century AD. Report has it that about 80% of all pregnant women will experience some form of nausea and vomiting during pregnancy (Verberg *et al*., 2009) and currently, severe nausea and vomiting known as *hyperemesis gravidarum* which is characterized by severe intractable vomiting requiring hospitalization has become the third leading cause of hospitalization during pregnancy due to dehydration, malnutrition, and electrolyte imbalances (Bennett *et al*., 1998) even though the evolutionary adaptation theory proposes that mild degrees of NVP causes no harm to the mother or embryo and therefore may be a beneficial adaptation rather than a disease or disorder which have probably evolved to serve a useful function of protecting the pregnant woman and embryo from food-borne infections and toxins, teratogens and substances capable of terminating pregnancy (Sherman and Flaxman, 2002). Plausible, the evidence showing that women with NVP have a more positive pregnancy outcome, may have provided additional support for the evolutionary adaptation theory and natural selection (Tierson, 1997). However, the book of Genesis says only that women shall labour and deliver in pain but nothing about the immediate distress of conception was mentioned, with the growth of cities and the hybridization of an urbanized human population, nausea and vomiting of pregnancy have emerged as a common phenomenon. It has been observed that in contemporary, widely dispersed foraging groups such as the Bushmen of South western Africa and of some Amazonian Amerindian tribes with well-documented genetic homogeneity, nausea and vomiting of pregnancy are rare. This contrast significantly with similar groups living in more stable, sessile villages with larger populations and wider contacts to

outside people, resulting in diverse, more complex choices for genetically heterogeneous mate selection such as ours, hence, nausea and vomiting of pregnancy has become common and may progress to maternal morbidity and mortality (Richard, 2002) since implantation and placentation now occur in gestations where immunogenetic differences between mother and foetus are not as subtle as they once were in small, genotypically homogeneous tribal groups. Therefore, maternal immunomodulation necessary for successful survival of the foetus is no longer asymptomatic but associated with dysphoria and what we have come to accept as normal "*morning sickness*". Conception has thus, become easier to recognize but harder to accommodate. Profet (1992) defining nausea and vomiting of pregnancy as the presence of food aversions, nausea and or vomiting, also argued that because not all modern toxins emit the cues that are necessary for triggering the aversions of pregnancy sickness and because the plant foods have become less toxic through selective breeding, the selection pressures maintaining the mechanisms for detecting and avoiding Pleistocene toxins during pregnancy may have been decreasing since the advent of agriculture. She also speculated that the variability in pregnancy sickness among women in industrial societies may be due to variations in dietary toxicity or decreasing selection pressures for detecting and avoiding substances that emit Pleistocene cues of toxicity and proposed a comparison of variability among women in industrial societies and among women in hunter-gatherer societies in order to determine whether pregnancy sickness is more variable among the former.

The incidence of NVP varies across different countries (Jordan *et al.*, 1995) and ethnic differences in the reporting of health problems has become vital in order to find out the reason why patients in same environment experience diseases and treatment

differently, and also to expand approaches for the improvement of public health (Burchard *et al*., 2003). Nausea and vomiting of pregnancy has been associated with race and ethnicity and the reason is unknown but it has been proposed that the difference in incidence between ethnic groups could be accounted for by important socioeconomic variables (Klebanoff *et al.*, 1985; Louik *et al*., 2006). Some researchers have also speculated that genetic factors may explain the difference as to why the degree of occurrence varies among ethnic groups (Vilming *et al*., 2000; Viknes *et al*., 2010). Apart from the ethnic difference in the occurrence of NVP, some anthropometric and demographic factors have also been associated with NVP as studies have reported association between maternal age, body weight, parity, sex of foetus, family history and experience in previous pregnancy as factors which bears increased risk of developing severe NVP (Vikanes *et al*., 2008).

In evolutionary history, a long post-reproductive lifespan is a characteristic feature in the life history of human females, which is not shared with other primates. The timing *of* this adaptation has also been proposed since it does not occur in our nearest relative, the chimpanzee, *Pan Troglotytes* in particular the Bonobo, *Pan Paniscus*. Therefore, it seems likely that the *evolutionary* pressure that led to this adaptation, menopause, occurred sometime after we parted company from our common ancestor around six million years ago (6 mya) (Brunet *et al*., 2002). In recent times, mans quest to find answers about him has generated a lot of questions one of which is the ultimate cause of menopause since selection pressures have pushed several species to maximize reproductive success rather than optimizing longevity (Vaupel *et al*., 1998). This has been the focus of much study as our knowledge about the mechanisms underlying menopause has largely been confined to ovarian exhaustion, which

involves the progressive loss of Oocytes beginning before birth and continuing to the age of menopause. However, a number of evolutionary explanations have been generated. Commonly cited is the mother and grandmother hypothesis which propose that menopause was an adaptive response to changes that led to the divergence of humans from their ancestors (Williams, 1957). This was based on observations such as the long-dependency time of human infants, early age of weaning of human neonates, high maternal mortality rate in child birth with increase in age (Grimes, 1994), the supportive role of grandmothers in childcare, and intergroup female transfer. Furthermore, when the human species took up a bipedal gait as an adaptive mechanism, they did so at the expense of their pelvic brim; reducing the antero-posterior diameter of the pelvis which has increased the risk of childbirth which increases with advance in age. Hence, menopause could have ensued as a check to the danger of this adaptation; a bipedal gait.

The average age of menopause among Nigerian was estimated at 49 years which is slightly lower than the typical age of 51 for many developed countries (Ozumba *et al*., 2004). It has been found that mortality risk for women who had their natural menopause before the age of forty is nearly twice as high as for those who experienced menopause at age 50-54 (Snowdon *et al*., 1990). This may account for the short life expectancy of 47.7 years in Nigerian women. A variety of studies (Bromberg *et al*., 1997; Stanford *et al*., 1987; Whelan *et al*., 1990) also demonstrates that, along with other factors, the age at menopause correlates positively with parity. Moreso, Kirchengast (1992) found a positive correlation between age at last and first birth and age at menopause.

1.2 STATEMENT OF RESEARCH PROBLEM

There is increasing interest especially in developing countries on nausea and vomiting of pregnancy and menopause as a recent study proposes that menopause will soon become a mid-life event (Brown, 2010). Also, there is insufficient data on NVP in Nigeria and the complimentary herbal use has not been defined in Nigeria despite the increase use reported among pregnant women.

1.3 SIGNIFICANCE OF THE STUDY

I. This study is to describe a typical reproductive history of a Nigerian female

II. Provide a reference value on the prevalence of nausea and vomiting of pregnancy among Nigerian population and its incidence among sub-ethnic group.

III. Give an idea to what extent the environment contributes to this condition (NVP) when compared with data provided by other researchers for other countries.

1.4 JUSTIFICATION

The increased life expectancy especially in developed countries has re-awakened research into reproductive history as more evolutionary studies propose that there is a trade-off between reproductivity and longitivity. Several investigators reports that there is increased incidence of nausea and vomiting of pregnancy with association to economic status and life style. However, there exist controversies about Blacks or white being most affected. In addition, this study is also based on recommendations of Vikanes *et al.,* (2008) that the difference in incidence between (sub) populations and

the observed pattern of NVP among different ethnic group with respect to their environment should be studied.

1.5 AIMS AND OBJECTIVES OF THE STUDY

I. To determine the prevalence and incidence of nausea and vomiting of pregnancy in Nigeria and its subpopulations based on ethnicity.

II. To determine the association between reproductive characteristic and certain socio-demographic factors with NVP and menopause.

III. To investigate the use of herbal remedies in the management of nausea and vomiting of pregnancy in Nigeria.

1.7 STUDY HYPOTHESIS

I. There is an increase incidence of NVP among gravid women in recent times than year's back.

II. Women of low socio-economic status are less likely to suffer nausea and vomiting of pregnancy than those of higher socioeconomic status.

III. There is no association between ethnicity and nausea and vomiting of pregnancy.

IV. The average menopausal age for Nigerian women will be less than that reported for the black race.

V. Other factors other than age are more determining of menopausal onset.

1.7 LIMITATIONS

Some limitations encountered include;

I. Gaining ethical approval and authorization from some hospitals, institution and community

II. Lack of willingness and cooperation from the women

III. Problem of recalling event on the part of the women and inability of the women to fill out the questionnaires completely.

CHAPTER 2

LITERATURE REVIEW

2.1 OVERVIEW OF NAUSEA AND VOMITING OF PREGNANCY

The majority of pregnant women experience nausea and vomiting during pregnancy (Kouzi, 2003). However, nausea and vomiting in pregnancy is not always nausea and vomiting of pregnancy (NVP). The differential diagnosis of nausea and vomiting in pregnancy can be extensive and the underlying cause can sometimes be difficult to diagnose. However, the timing or onset of the symptoms is important in differentiating nausea and vomiting of pregnancy from other causes. A thorough history and physical examination, with appropriate investigations, is required in symptomatic women (Tabassum *et al*., 2010). Report has shown that the quality of life may be impaired before severe physical symptoms appear (Magee *et al*., 2002). Also, NVP was known to negatively affect the individual's family, employment, and social life, and can impose an economic burden, particularly with productivity loss (Koch and Frissora, 2003). There is evidence indicating that most women with NVP do not receive appropriate pharmacologic or non-pharmacologic treatment for the condition (Mazzotta *et al*., 2000; kouzi, 2003).

2.2 AETIOLOGY AND PATHOPHYSIOLOGY OF NAUSEA AND VOMITING OF PREGNANCY

2.2.1 Hormonal causes

Several hormones has been hypothesized and considered as the pathogenesis of nausea and vomiting of pregnancy. Although the pathways through which these hormones act still remain suggestive. One of such hormones that have been implicated is the human chorionic gonadotopic hormone. The primary reasons for

considering human chorionic gonadotropic hormone (HCG) as likely triggers of nausea and vomiting of pregnancy are due to the close temporal association between peak HCG concentrations and peak NVP symptoms (Kouzi ,2003). Some researchers have reported conditions associated with higher HCG production, such as multiple gestations and hydatidiform mole, as being associated with NVP (Kallen, 2000; Soto-Wright *et al*., 1995), so also are women bearing female offspring as HCG levels are known to be high in pregnancies with a female foetus (O'Brien and Zhou, 1995). Also, chromosomal abnormalities such as Trisomy-21 which is known to be associated with higher maternal HCG concentrations have been shown to more common in severe nausea and vomiting cases (kallen, 2000). This is evidenced as NVP is less common in circumstances known to be associated with low HCG levels, such as smoking (Cuckle *et al*., 1990).

Another reason for the implication of HCG in NVP is that HCG has been shown to stimulate the thyroid gland during pregnancy. Several studies on thyroid hormones in pregnancy have established an association between transient biochemical hyperthyroidism and NVP with the degree of biochemical hyperthyroidism correlating closely with the severity of NVP (Goodwin *et al*., 1992). More so, since hyperthyroidism itself is rarely a cause of nausea and vomiting, these studies provided strong evidence implicating HCG as a triggering factor for NVP. Furthermore, HCG has been shown to have a structural similarity with thyroid-stimulating hormone (TSH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) with the main structural difference being that HCG has a carboxyl terminal moiety which is not present in the others hence, isoforms of HCG lacking the carboxyl terminal group are very similar to TSH and are more thyrotrophic than the intact HCG molecule

(Yoshimura *et al*., 1994). In addition to stimulating the thyroid gland, HCG isoforms stimulate the production of sex steroids by the maternal and, possibly, the foetal gonad. Jordan *et al*., (1999) found that a positive correlation exist between various HCG isoforms, estradiol, thyroxin production, and severity of NVP. Cole (1997) in a comparative study made an attempt to establish the relationship between circulating HCG in women with severe nausea and vomiting of pregnancy and asymptomatic woman. Out of the fifteen published works, eleven showed a significant higher level of serum HCG when compared to control group, eight (8) out of which matched for gestational age. Possible explanation given for negative results in the remaining cases was the different method used in HCG assay and their ability to detect HCG subunits and isoforms or metabolites. In another study by Tsuruta *et al*, (1995) patient with severe nausea and vomiting of pregnancy had significantly increased level of the HCG fraction that contains the asialocarbohydrate chains. Despite much published work on HCG in relation to NVP, the mechanism through which HCG itself would cause nausea and or vomiting remains vague, but it has been proposed that it does this by mechanisms which include a stimulating effect on the secretory process in the upper GIT or by stimulation of thyroid function because of its structural similarities to thyroid stimulating hormone (TSH) (Hershman, 2004).

Researchers have also found an abnormal progesterone level in severe NVP patients with patient with NVP having lower progesterone level. Others however measured a higher progesterone level in patients of related small groups (Yoneyama *et al*., 2002). Conclusions from these studies are not convincing as not all investigators could find a correlation between the level of progesterone and severity of NVP. Even after

progesterone treatment in women with NVP in one study no relief of symptoms was observed (Fairweather, 1968).

The role of oestrogen in pregnancy induced nausea and vomiting has been linked to numbers of conditions associated with high oestrogen level such as higher body mass, first pregnancy, oestrogen therapy and undescended testes in the foetus. Oestrogen has several mechanisms that could modulate factors causing NVP one of which is slowing intestinal transit and gastric emptying which results in an increased accumulation of fluid caused by elevation of steroids and hence a shift in pH (kocak *et al*., 1999). This shift in pH in the GIT could lead to *Helicobacter pylori* infection which could be related to gastrointestinal symptoms (kocak *et al*., 1999). Elevated mean estradiol (E_2) level was found in patients with NVP when compared to control groups (Yoneyema, 2002). Gadsby *et al*., (2003) recorded a strong correlation ($p \leq 0.001$) between those who had nausea with contraceptive pills and those who had NVP in pregnancy. Another retrospective survey, also observed a strong correlation among women suffering from NVP and nausea during the use of contraceptive, an oestrogen-related side effect (Yoneyema, 2002b). Patients who did not tolerate oral contraceptives suffered severe NVP at a considerable higher frequency and longer duration (Gadsby *et al*., 2003). Estriol (E_3) too has been considered in the pathogenesis of NVP but no difference in serum level were observed in two prospective studies (Lagiou *et al*., 2003). Considering the fact that in pregnancies induced by controlled ovarian stimulation (COS) in assisted reproduction technique (ART) when circulating oestrogen levels are very high is not associated with a higher incidence of vomiting of pregnancy, makes it is less likely that increase oestrogen level and progesterone can cause NVP (Verberg *et al*.,2005).

Thyroid gland is physiologically stimulated during early pregnancy leading to gestational transient thyrotoxicosis (GTT) due to deviation of the thyroid hormone secretion from normal range. GTT was observed in two-third of women suffering from hyperemesis gravidarum (Goodwin et al., 1999b). Fifteen comparative studies of thyroxin (T_4) and thyroid stimulating hormone (TSH) level in patient with severe NVP when compared with control subjects, eight was matched with gestational age while eleven showed increased thyroxin (T_4) level. More so, in another thirteen comparative studies of TSH level, nine showed increased TSH level in NVP patients (Verberg *et al*., 2005). Various mechanisms might be involved in the stimulation of thyroid function during pregnancy. Under the influence of oestrogens, the production of thyroid binding globulin increases and T_4 metabolism is slowed, causing a transient decrease in T_4 level (Verberg *et al*., 2005). Higher renal iodine clearance which causes stimulation of the thyroid to compensate for a relative iodine deficiency could be a second mechanism (Glinoer, 1997). A decreased albumin and increased free fatty concentrations which affects the binding of thyroid hormones to their carrier proteins could be a third mechanism (Stockigt, 2001).

2.2.2 The vestibular system

Chronic nausea and vomiting in the non-pregnant adult population is largely attributed to disease of the GIT and the neuro-vestibular system. A number of physiologic changes that occur in normal pregnancy are also known to accompany nausea and vomiting in patients with motion sickness and certain vestibular disorders (Black, 2002). A comparison of the symptom constellation of motion sickness and the symptom pattern of NVP reveals striking similarities (Black, 2002). The gastrointestinal changes associated with NVP (delayed gastric emptying, reduced

oesophageal sphincter pressure, decreased gall bladder motility, and increased gut transit time) are almost identical to changes in the patient with motion sickness. Given the symptomatic similarity between NVP and the nausea and vomiting of motion sickness and the fact that hormonal factors play a role in both conditions, obstetricians have long noted an association between a history of motion sickness susceptibility and the occurrence of NVP (Kouzi, 2003). In a survey of 1000 women between 14 and 28 weeks of gestation, 12% had a history of motion sickness and the frequency of NVP was significantly higher in women with a history of motion sickness than in those without a history of motion sickness (Whitehead *et al*., 1992). Similarities between NVP and motion sickness suggest that the inner ear may influence the incidence and or severity of NVP. Studies related to plasma osmolarity during pregnancy and in women with vestibular disorders have also suggested that vestibular-mediated nausea and vomiting may be induced by hormonally mediated change in osmolarity in early pregnancy. Based on all the evidence, according to Kouzi (2003), participation of the vestibular system in the pathogenesis of NVP may be attributed to either a pre-existing, subclinical vestibular dysfunction that renders a pregnant woman more susceptible to the hormonal trigger for NVP, or a very strong hormonal trigger for NVP that can adversely affect the normal vestibular system of a pregnant woman.

2.2.3 Gastrointestinal tract (GIT)

Gastric motor dysfunction has been implicated in NVP. Women with subclinical gastric motor dysfunction who become pregnant are likely to be more susceptible to NVP (Kouzi, 2003). Using electrogastrography (EGG) to evaluate the prevalence of gastric dysrhythmias in pregnant women, abnormalities were demonstrated in all women with NVP (Koch, 1990). In this study, more than 81% of the pregnant women

had various degrees of nausea and gastric dysrhythmias, 65% had tachygastrias (4 to 9 cycles/min waves), 19% had bradygastrias, and 15% had a flat-line pattern while the pregnant women with minimal or no nausea, all had a normal gastric rhythm (3 cycles per minute). The presence of a dysrhythmia was associated with the report of nausea, whereas the presence of normal EGG pattern was associated with the absence of nausea. In addition, asymptomatic women who were studied after delivery had normal EGG activity, whereas they had a variety of gastric dysrhythmias during the first trimester of pregnancy when nausea was present (Koch, 1990; Kouzi, 2003). The study also found that gastric dysrhythmias and the associated nausea are usually preceded by an increase in plasma vasopressin levels. These findings were further confirmed by other studies (Walsh *et al*., 1996; Jednak *et al*., 1999) that also demonstrated the presence of gastric dysrhythmias in women with NVP. Collectively, studies have indicated that gastric dysrhythmias represent a pathophysiologic mechanism for NVP. The acute loss of normal gastric rhythm during a wave of nausea, the observation that women in the first trimester of pregnancy without nausea had normal EGG rhythms, and the return to normal gastric rhythm after delivery supported the notion that the presence of gastric dysrhythmias is an objective finding related to stomach dysfunction and nausea symptoms (Kouzi, 2003). The mechanisms underlying gastric dysrhythmias are poorly understood however, potential mechanisms that may lead to gastric dysrhythmias include: gastric neuromuscular dysfunction or malfunction, abnormalities in vagal or sympathetic neural activity involving the stomach, neuro-hormonal and vascular changes that occur in the first trimester of pregnancy, hyper and hypothyroidism, which may disrupt intestinal pacemaker activity (Gunsar *et al*., 2001) and also changes in intravascular volume status that affects vasopressin secretion (Kouzi, 2003).

The increased incidence of *Helicobacter pylori* infection observed in severe NVP patients has made it a candidate aetiogical factor. Several works has been done to support this and the most outstanding was reported by Bagis *et al*., (2002) which was considered as a standard test for *Helicobacter pylori*. In this study, *Helicobacter pylori* were tested for using histological examination of mucosal biopsy. Result of this study revealed that 95% of these patients tested positive compared to the control group, with higher *Helicobacter pylori* densities found in gastric antrum of patients with NVP which could be correlated with the severity of symptoms. Erdem *et al*., (2002) on the other hand, did not find a correlation between serum *Helicobacter pylori* immunoglobulin G (IgG) concentration and the duration of NVP symptoms although, he used another method. The factors implicated in the cause of *Helicobacter pylori* infection include a change in gastric pH resulting from accumulation of fluid caused by elevated steroid hormone (Kocak et al., 1999) and pregnancy related change in immune system especially in humeral and cell mediated immunity (Lanciers *et al*., 1999). Report also has it that some women did not respond to standard management until treated for *Helicobacter pylori* (el-Younis *et al*., 1998). Although, Verberg *et al*., (2005) argues that susceptibility to *Helicobacter pylori* is not secondary to steroid level, or changes in immune system does not provide enough evidence for the implication of *H.pylori* in NVP but rather, that damage to the upper GIT due to excessive vomiting most likely increases susceptibility to subclinical *Helicobacter pylori* infection.

2.2.4 Immunology

Increased immune responses (i.e. both humeral and cell-mediated changes) resulting from physiological changes have been observed in pregnancy and considered to probably protect the foetus and decidua from rupture by the maternal immune system with chronic NVP considered a result of an over activated immune system (Minagawa *et al*., 1999). Sekizawa *et al*., (2001) measured an increase in the concentration of foetal DNA in the plasma of NVP patients when compared with those of asymptomatic women both having single male foetus. This suggests a strong relationship between NVP and immune interaction between mother and foetus. A positive correlation was observed between IL-6 (interleukin- 6) and β-hCG in NVP patients (kuscu *et al*., 2003). Interleukin 1, 2, 6, and 8 and tumour necrosis factor-α (TNF-α) at a higher level showed a strong positive correlation between NVP and non-pregnant control (Kaplan *et al*., 2003). Yoneyama *et al*., (2002) studied T-helper 1/ T-helper 2 balance and observed a shift towards T-helper 2 dominance in HG patient accompanied by increased progesterone and oestrogen levels. In another comparative study, Leylek *et al*., (1999) found higher IgG, IgM, C3, C4 levels and lymphocyte count in patients with nausea and vomiting. He observed a positive correlation between IgG and IgM level, β-hCG and lymphocyte count, and IgM and C3. These findings support an activated immune system in severe NVP as opposed to suppression during starvation; hence, the results are also not conclusive but could be interpreted as a compensatory reaction to limit the progression of this condition rather than the cause itself (Verberg *et al*., 2005).

2.2.5 Behavioural and psychological factors

In addition to the plausible biological and pathophysiological theories that have been proposed for the aetiology of NVP, psychological theories also exist. However, methodologically sound studies necessary to establish a psychological component in NVP, particularly a psychosomatic one, are lacking (Kouzi, 2003). NVP was believed to result from resentment against pregnancy or ambivalence of woman ill-prepared for motherhood due to immaturity in personality, strong mother dependence, anxiety and tension related to pregnancy (Ringler *et al*., 1984). The most frequently discussed psychological theories that have been proposed to contribute to the aetiology of NVP include the Psychoanalytic Theory (Deuchar, 1995; Iancu *et al*.,1994) ,Stress Hypothesis, (Georgas *et al*.,1984) ,Coping Skills Theory (Katon *et al*.,1980) and the Behavioural Conditioning Hypothesis. (Callahan *et al*., 1986; Long *et al*., 1986 and Simon and Schwartz, 1999). The assumption is frequently made that women with severe NVP are transforming purely psychic trauma into physical symptoms. Secondary gain has also been suggested to contribute to symptoms as a means to obtain attention and sympathy from family or friends (Iancu *et al*., 1994). Other hypothesis state that NVP is a disorder resulting from sexual aversion (Fairwether, 1968), symptoms of hysteria and neurosis or depression result from psychosocial stress, poverty and marital conflict (el-Mallakh *et al*., 1990; Lub-Moss *et al*., 1997). Investigators have found support for psychological pathogenesis as lower incidence of NVP were said to be observed during times of war and deprivation while differences in incidence were observed between cultures. Furthermore, studies showing that hospital admission away from environmental influences, without partners, family and responsibilities often reduce vomiting support the psychological hypothesis (Shouenborg *et al*., 1992; Lub-Moss *et al*, 1997). According to Kouzi (2003), the

success of hypnosis and other psychotherapeutic approaches in treating NVP does suggest an interaction between physiological, psychological, and socio-cultural factors. The interactions of these factors are unique in a particular patient and will differ from one woman to another.

2.2.6 Nutritional deficiency

Vitamins and trace element deficiency has also been considered in the pathogenesis of vomiting of pregnancy. However, neither could studies show a relationship between the biochemical indicators of vitamin B6 status and the incidence or degree of NVP nor did a placebo controlled studies on pyridoxine therapy in women with NVP show any significant effect on vomiting (Jewell *et al*., 2003). Plasma zinc and copper level have also been studied in severe NVP patients but observed results were contradictory. While Lao *et al*., (1998) reported no plasma difference when zinc and copper level were compared with control in a series of observational cohort studies, Teksen *et al*., (2001) reported low plasma zinc level and normal copper concentration and Dokmeci *et al*., (2004) found elevated plasma zinc level and low copper concentration. These changes in both vitamins and trace elements could be associated with increase in nutritional demand during pregnancy, vomiting and or aggravation of existing NVP however, a casual relationship cannot be completely excluded (Verberg, 2005).

2.2.7 Anatomy

A right sided corpus luteum was observed to be more frequent in a cohort study of patients with NVP (Samsioe *et al*., 1986). Possible explanation for this is difference in venous drainage between the right and left ovary causing a higher concentration of

steroids in the hepatic portal system when corpus luteum is situated on the right side. However, the continuation of symptoms in a woman with severe NVP in whom excision of a right sided corpus luteum was performed at 12 weeks does not support this theory (Thorp *et al*., 1991).

2.2.8 Evolutionary view point (adaptation)

Although the overwhelming majority of clinicians believe that NVP is a real disorder, the possibility that NVP symptoms serve a useful function has emerged as a hypothesis which highlights the adaptive and evolutionary significance of nausea and vomiting during pregnancy. The hypothesis, known as the "Maternal and Embryo Protection" hypothesis, suggests that normal levels of NVP (excluding hyperemesis gravidarum) and the associated temporary taste aversions protect pregnant women and their embryos from harmful substances in food, particularly pathogenic microorganisms in meat products and toxins in strong-tasting plants (Sherman and Flaxman, 2002; Profet, 1992). This hypothesis also indicates that normal levels of NVP will not harm the embryo or mother. Support for this hypothesis came from studies that demonstrated an association between NVP and positive pregnancy outcomes such as decreased risk of miscarriage (Tierson, 1997). Further support for the maternal and embryo protection hypothesis is based on the fact that NVP symptoms peak when the embryonic tissues are most sensitive to toxins and pathogens (weeks 5 to 18 of pregnancy), and that pregnant women in their first trimester reported significantly more food aversions than non-pregnant control subjects. The pattern of selective avoidance of meats and fatty foods is consistent with the ethnographic evidence of little or no nausea and vomiting of pregnancy in population groups relying on grain and fruit diets rather than on meat (Minturn and

Weiher 1984; Mitzi, 2004). Recognizing NVP as an adaptation may, according to the hypothesis, help reassure patients and enable them to pursue new non-invasive ways of avoiding or minimizing NVP symptoms, such as eliminating potential triggering stimuli (e.g. odours from foods that pregnant women find aversive) from the home and work environments during the first trimester of pregnancy (Kouzi ,2003). Supporters (Sherman and Flaxman, 2002; Mitzi, 2004) of the maternal and embryo protection hypothesis believe that uncomplicated NVP is a natural phenomenon and in the vast majority of cases, a normal part of a healthy pregnancy.

Huxley (2000) proposed that nausea and vomiting of pregnancy may have another functional role. He speculates that nausea and vomiting result in lower energy intake and consequently lower levels of anabolic hormones, insulin, insulin growth factor-1, and maternal tissue synthesis. These changes would lead to shunting of scarce nutrients to the developing placenta and foetus. This *"embryo protection"* hypothesis seems plausible in mild cases of nausea and vomiting and may even offer some measure of comfort. However, noting that some first-trimester vitamin deficiencies have been implicated in teratogenesis, Profet (1992) suggested that pregnancy sickness might appear maladaptive because it induces aversions to important sources of foliate and other vitamins and micronutrients, such as some vegetables, that are essential for normal embryonic development. She went on to suggest, however, that the nutritionally adverse effects of pregnancy sickness on embryonic health are probably exacerbated in modern industrial societies as foliate reserves from a normal Pleistocene diet would have been sufficient to withstand the temporary deficiencies of pregnancy sickness because Pleistocene hunter-gatherer women with sufficient fat reserves are unlikely to have been vitamin deficient at conception because much of

their caloric intake prior to conception would have come from vegetables and fruits contrary to the caloric intake of women in modern industrial societies which comes from non-plant foods or processed foods with low vitamins (Profet, 1992). Although, whether a woman vomits or not, the occurrence of NVP does not guarantee a positive outcome of pregnancy, and the absence of NVP symptoms does not signify failure of gestation (Kouzi, 2003).

2.2.9 Genetic factor

The precise relationship between genetics and environment and exact role of genetics itself is complex and uncertain (Harrison *et al*., 1993). Even when all racial and ethnic groups share a genetic variant that causes a disease, studies of different groups may offer important insights (Burchard *et al*., 2003). Some researchers have speculated that genetic factors may explain the difference in the prevalence and severity of NVP between ethnic groups (Vilming *et al*., 2000). A study in Norway showed that the risk of severe nausea and vomiting of pregnancy was 15.2% in second pregnancy if the first pregnancy was affected, 0.7% in the second pregnancy if the first was not affected, 16.0% in the second pregnancy if the first was affected with the same partner and 10.9% in the second pregnancy if the first was affect with a different partner. This suggests that there might be a genetic aspect to NVP possibly involving both maternal and foetal gene even though environmental factors cannot be ruled out (Vikanes *et al*., 2010). Vikanes *et al*., (2010) in their generational study (1967-2008) found that daughters who were born after pregnancy complicated with hyperemesis gravidarum had 3% risk of having it in their own pregnancy, women who are born after an unaffected pregnancy had a 1.3% risk, female partner of sons born after hyperemesis gravidarum complicated pregnancy had a 1.18% risk and 1.13% if the mother did not

suffer it respectively. Furthermore, daughters born after a pregnancy not complicated by severe NVP but whose mother had had a previous (before they were born) or subsequent (after they were born) complicated pregnancy had 3.08% and 2.99% respectively of developing the condition thus, implying that maternal gene may have a stronger influence than the foetal gene (Vikanes *et al*., 2010). This was further buttressed in the consanguinity study of Grjibovski *et al*., (2008) whose result showed that consanguinity did not increase the risk of developing NVP thus, implying that foetal recessive gene does not play a major role in the developing nausea and vomiting of pregnancy. Studies reporting an increased risk across generation suggest genetic involvement, transmitted by mother but caused by shared environmental factors. (Signorello *et al*., 2005; Golberg *et al*., 2007; Cedergren *et al*., 2008; Sandven *et al*., 2009). A strong family history was also reported of two or more affected relative in an online survey administered by the Hyperemesis Education and Research Foundation between 2003-2006 on women whose mother experienced NVP or HG while pregnant with them (Gadsby *et al*., 2003).

2.2.10 Ethnicity / socio-economic status

Profet (1992) acknowledged that the cross-cultural occurrence of pregnancy sickness has important implications on NVP. Contrary to the hypothesis of Richard (2002), that NVP has emerged due to hybridization of urbanization society and indiscriminate selection of sexual partner leading to a more complex heterogeneity, she suggested, pregnancy sickness should be ubiquitous among pregnant women of hunter-gatherer societies because she considered them to represent the closest approximation to Pleistocene hunter-gatherer feeding ecology and that selection pressures for pregnancy sickness would have been most intense in the environment of a Plio-

Pleistocene forager, particularly during periods of scarcity. Similarly, she described current hunter-gatherer feeding ecology as being characterized by experimentation with wide variety of food sources, particularly during dry seasons or drought years when marginal environments necessitate broadening the diet to include, and therefore more toxic, plant foods (Profet, 1992).This on the other hand favourably describes the urbanized societies of today.

Three documented studies that used multivariate analysis to evaluate the association between race/ethnicity and NVP showed contradictory results. The first failed to demonstrate the significant relationship between race/ethnicity and vomiting (Klebanoff, 1985), the second recorded that white women had less NVP than Hispanics and blacks (Weigel and Weigel, 1988) while the third showed that black women had less NVP than whites (Louik *et al*., 2006). Vikanes *et al*., (2008) implicated ethnic differences in the prevalence of NVP. Their study reveals that in New Zealand, the incidence among pacific islanders was higher than in women of European descent. More so, in USA, being non-white was associated with a higher probability of developing severe NVP (Paauw *et al*., 2005) and in Norway, increased risk was associated with non-indigenes as immigrants of Pakistani were 3.7 times more at risk than Norwegian women (Vagen *et al*., 1999). Further study of 900,000 first births in Norway, revealed that all immigrants, except those born in Europe and North America, had a higher prevalence of severe NVP than the ethnic Norwegian women. This was regardless of duration of residence (Vikanes *et al*., 2008). Considering stress as a factor associated with increased risk of developing NVP, given the prevalence in Norway among immigrants, Vikanes *et al*., (2008) hypothesised that their risk of developing severe NVP may decrease with an increase length of residence therefore, in another study, 50,904 women of first generation

immigrants were used. The result of this study showed that women from Central and South America, Middle East, Other African (except North African), Indians and Sri Lanka with residence of greater than five years had a decreased risk (0.99%) of reporting nausea and vomiting of pregnancy in contrast to Iranian, Turkey and north African women who were twice at risk when compared to reference group. They therefore concluded that environmental factors are important in the aetiology of NVP and can notify the genetic risk, although some environmental factors may have a different impact on different ethnic groups (Vikanes *et al*., 2008). Lacasse *et al*., (2009) using a multivariate analysis also studied 367 women of which 81.2% were Caucasians, 10.1% blacks, 4.6% Hispanics and 4.1% Asians and showed that ethnicity was significantly associated with the likelihood of reporting NVP. Gadsby *et al*., (2003) in his literature review stated that vomiting was common in blacks than in whites.In addition, hospitalization was more in blacks than in whites and colored women are apt to be affected more often than white women of the same social class. In contrast, other literatures in their review recorded that black and Asian women have less NVP than Caucasians in the first trimester of pregnancy and that the white ethnicity was associated with increased vomiting (Louik *et al*., 2006; Lacasse *et al*., 2009).

Some studies have also reported an association between socioeconomic status and NVP. According to one report, women having income greater than 40,000Cdn$ per year are less likely to have NVP in the first trimester. In contrast, another study conducted in 2000, showed that household income ranging from 30-40,000 (i.e >30 <40,000) Cdn$ per year was a determinant for NVP in first trimester of pregnancy (Lacroix *et al*., 2000). Karaca *et al*., (2004) also reports that the seropositivity of *H.*

pylori in NVP patients was significantly high in groups of lower socio-economic status which suggests that lower socio-economic status could also be a major risk factor for infection with *H.pylori* in pregnant women.

2.2.11 Demographic factors

The normal sex ratio of female to male newborns is 48.6-51.4% and known to be well conserved. Kallen (1987) was the first to report an increase in female to male sex ratio in pregnancies complicated by severe NVP, 53% females compared with the expected 49%. The percentage of female live births in pregnancies associated with hyperemesis gravidarum in prior studies ranged from 53% to 66% compared with 58% females in their studies (Schiff *et al*., 2004). The incidence of hospitalization for vomiting of pregnancy in a study population was 4.2/1000 live birth with majority of cases occurring in the first trimester, 2.7/1000 live births. However, infant sex ratio also varied by trimester with 50% increased odds of a female infant among women hospitalized in the first trimester (Schiff *et al*., 2004). Sex ratio also varied significantly by severity of this condition as women hospitalized with severe NVP for three days or more had an 80% increased odds of having female infants while those hospitalized for less number of days had 50% increased odds of having a female infant when compared to control (Schiff *et al*., 2004). Previous studies on European and North American population consistently show a higher ratio of female foetuses in women with NVP. A study in an Asian population also showed a significant association between NVP and female foetuses of which 83% of the study population had female foetuses (Tan *et al*., 2006).

Bosso *et al*., (2001) examined twinning and foetal gender in birth of women with a hospital diagnosis of pre-eclampsia or NVP in Denmark between1980-1996. Of 6,277

birth records extracted with NVP and 24,764 with pre-eclampsia, twinning were more frequent in both pregnancies of either condition with male to female sex ratio of 0.87 and 1.04 respectively. Study on twinning had also shown that NVP was more than twice high in monozygous twins than dizygous twins (NORD, 2009)

Maternal age, body weight and parity have been reported as factors associated with increased risk of developing NVP. Maternal age between 20-24 years old, being married, carrying a female foetus or more than one foetus were all socio-demographic characteristics associated with a higher prevalence of vomiting of pregnancy (Vikanes *et al*., 2008). Women of younger age has been shown to be significantly associated with having an increased risk of NVP and this was highest at a mean age of 26 years (Gadsby *et al*., 2003). Association between smaller weight gain in pregnancy and gender of foetus (female) has also been observed with NVP (Vilming *et al*., 2000; Linseth *et al*., 2005). Lacasse *et al*., (2009) observed multiparty as a determinant of more severe NVP symptoms during the first trimester of pregnancy. This also corresponds to existing literatures (Kallen *et al*., 2003; Linseth, 2005). Primgravid or nulliparity is also relatively associated to increased NVP or hyperemesis gravidarum while some literatures record no association between nausea and parity.

2.3 EFFECT OF NAUSEA AND VOMITING OF PREGNANCY

Although several studies have shown that mild nausea and vomiting of pregnancy has little or no effect on the mother and foetus and is in fact, considered as a normal part of pregnancy (Sharman and Flexman, 2002; Kouzi, 2003) associated with favourable pregnancy outcome. Women with HG were found to have a lower risk for foetal loss, lower birth weight, preterm delivery and non syndromic oral cleft defect in foetus

(Czeizel *et al*., 2003; Broussard & Richter, 1998). Broussard & Richter (1998) also reported that although the mean differences in birth weight of infants carried by women with and without vomiting were not significantly different but there was an increased incidence of fetal loss in women who did not vomit when compared with those who did (86/1000 births versus 49/1000 births; Relative Risk 1.83). this condition however is not without adverse effect as nausea and vomiting of pregnancy may progress to a more severe form known as hyperemesis gravidarum which if not checked could be detrimental to the mother and foetus due to complications arising from dehydration, metabolic and electrolyte disturbances (Togay-Isikay *et al*., 2001). Complications reported in patients with severe NVP include lower birth weight, preterm delivery, foetal malformation, neurological and vascular abnormalities, stillbirth and fetal and prenatal mortality (Togay-Isikay *et al*., 2001; NORD, 2009). Elective termination has been performed in approximately 2% of pregnancies complicated by hyperemesis (Mazzotta *et al*., 1996). Higher incidence of testicular carcinoma has also been observed in male offspring of mothers who suffered severe nausea and vomiting of pregnancy (Depue *et al*., 1987). Others have shown children born to mothers with severe NVP have a long term effect; low attention span with about 9% of women with extreme weight loss in pregnancy (>5% of pre- pregnant weight) due to hyperemesis gravidarum reporting having a child with a behavioral disorder (NORD, 2009).

Besides the effect on the foetus and pregnancy outcome, even when the condition is not so severe, symptoms can cause considerable distress and temporary disability (O'Brien and Naber, 1992). For as many as 35% of pregnant women, the NVP symptoms are severe enough to seriously disrupt their lives, causing them to change

their usual activities, of which nearly 50% of employed women believed their work efficiency was substantially reduced by NVP, and as many as 25% required time off from work (Kouzi, 2003). More so, almost one half of women with NVP said that it had adverse effects on their relationships with their spouse, and 55% of pregnant women with NVP felt depressed (Kouzi, 2003).

2.4 MANAGEMENT OPTIONS FOR NAUSEA AND VOMITING OF PREGNANCY

The cause of pregnancy-induced nausea and vomiting remains unknown. As a result, treatments that address the cause of this condition are not available. Management of NVP focuses mainly on alleviating symptoms, however, it is important to rule out other medical condition capable of inducing nausea and vomiting such as gall bladder disease, ulcer disease, hepatitis, gastroenteritis, appendicitis, pyelonephritis, and pancreatitis (Koch, 1998) as current survey (Power *et al*., 2001) revealed that clinicians are willing to treat this condition aggressively for concern of safety and the risk to their foetus even though a majority of pregnant women with NVP do not seek therapy. Obstetric explanations for NVP symptoms should also be considered because NVP is more common in patients with multiple gestations and hydatidiform moles. Once other causes of nausea and vomiting are ruled out, the most commonly recommended therapeutic approach for managing NVP includes non-pharmacologic remedies, drug therapy and complementary and alternative medicine (Broussard and Richter, 1998; Nelson-Piercy, 1998; Murphy, 1998; and Koch, 2000).

2.4.1 Non-pharmacologic remedies

For patients with NVP symptoms, a variety of dietary modifications and other non-pharmacologic remedies are recommended initially (Koch, 2000; Power *et al*., 2001 and Kouzi, 2003). These include the following:

I. Avoiding certain aggravating odours, foods, or beverages that can trigger nausea.

II. Avoiding fatty or spicy foods and eliminating iron supplements from the diet, because they can cause nausea.

III. Eating frequent small meals. The emphasis traditionally has been on bland and dry foods, high-protein snacks, and crackers at the bedside in the morning before arising.

IV. Ingestion of sips of fluids throughout the day to prevent dehydration, drinks that contain salt, glucose, and potassium, or high-protein liquid drinks are usually recommended.

V. Recumbent resting whenever tired or nauseous.

A survey revealed that 63% of respondents identified lying down and remaining still as the best manoeuvre to improve NVP (Dilorio, 1985). O'Brien and Naber (1992) reported that nearly 25% of women in their study also identified recumbent rest as a means of improving NVP in a third survey.

2.4.2 Drug therapy

Many women and health care providers frequently overestimate the teratogenic risk of medications during pregnancy (Mazzotta *et al*., 1999; Mazzotta and Magee, 2000). As a result, a great number of NVP patients do not seek drug therapies that have been proven to be safe and effective. Despite evidence of foetal safety, most anti-emetic

medications are contraindicated during pregnancy. However, a recent risk-benefit analysis of the literature on the safety and efficacy of these agents for the treatment of NVP revealed that some of them can be safely prescribed during pregnancy (Mazzotta and Magee, 2000; Kouzi, 2003). Evidence from controlled trials has shown that the following anti-emetic agents are safe and effective for the treatment of varying degrees of NVP; Bendectin/Diclectin (doxylamine and pyridoxine), antihistamines (H1 blockers), and phenothiazines (Magee *et al*., 2002). As head-to-head comparative studies for individual drugs are not available, it is reasonable, if success is not achieved with one of these agents to switch to another. Many of these agents may also be used in combination along with non-pharmacologic approaches (Kouzi, 2003).

In severe cases of nausea and vomiting of pregnancy known as *hyperemesis gravidarum*, characterized by severe nausea with prolonged and sustained vomiting during pregnancy which can have serious detrimental effects on both mother and foetus, hospitalization is required in more than 1 in 50 women who were affected . Other clinical manifestations of hyperemesis gravidarum include dehydration, weight loss, and/or signs of nutritional deficiencies. The most common treatment options for patients are intravenous hydration and the administration of anti-emetic medications (either IV or suppositories). In some cases, parenteral nutrition is also required (Bennett *et al*., 1998; Power *et al*., 2001; Kouzi, 2003 and Ghani, 2003). Pregnant women with hyperemesis gravidarum who have vomited for more than 3 weeks will likely develop sub-acute vitamin B1 (thiamine) deprivation. Hydration of these patients with intravenous dextrose without prior administration of thiamine will cause Wernicke's encephalopathy, which is a serious neurologic disorder caused by deficiency of thiamine (Gardian *et al*., 1999) as metabolism of the dextrose rapidly consumes the remaining thiamine in these patients, leading to acute encephalopathy

characterized by ataxia, dementia, and nystagmus. Maternal death or permanent neurologic abnormality was shown to have occurred in more than 80% of cases (Gardian *et al*., 1999). Elective termination of approximately 2% of pregnancies complicated by hyperemesis gravidarum has been reported (Mazzotta *et al*., 1996).

2.4.3 Complementary and alternative management

Following the increased incidence of congenital malformation in pregnancy from unknown cause but attributed to certain drug use in pregnancy, many pregnant women are seeking a variety of complementary and alternative therapies to treat NVP (Murphy, 1998; Tsui *et al*., 2001). These therapies include vitamins, botanical dietary supplements, homeopathic remedies, acupuncture, acupressure and acustimulation, hypnotherapy, aromatherapy and behavioural modification. However, there is a dearth of research literature to support or refute the safety and efficacy of many of these alternative approaches (Kouzi, 2003). A study reported that the only predictor of increased use of herbal medicine in their study was increased severity of nausea and vomiting (Hollyer *et al*., 2002) and that women may choose to use herbal supplements than pharmaceutical product because they consider it safer. Herbal treatment has increased severally in nausea and vomiting (Hollyer *et al*., 2002) and a low level of education has been associated with this increase (Gibson *et al*., 2001). Similar work done in the United States (Hepner, 2002), Canada (Westfall, 2004), Norway (Nordeng, 2004) and Nigeria (Gharoro, 2000) supports the increase use of herbal supplement among pregnant women with ginger, chamomile, peppermint and cannabis as common management for nausea and vomiting in pregnancy (Forster *et al*., 2006). However, among these complimentary/herbal remedies, only ginger have been studied in well controlled trials for the treatment of NVP. Two controlled trials

used ginger capsules, 250 mg 4 times daily, in the treatment of NVP (Fischer-Rasmussen *et al*., 1990 and Vutyavanich *et al*., 2001). These trial studies revealed that ginger significantly reduced nausea and the number of vomiting episodes in NVP patients of the ginger group as compared to the placebo group. Ginger has also been shown to reduce postoperative and motion-induced nausea and vomiting (Mowrey and Clayson, 1982; Bone *et al*., 1990). Though with limited data, ginger appears to be an effective alternative treatment for NVP. Since concerns have been raised in some literatures (Fulder and Tenne, 1996; Blumenthal *et al*., 2000) about possible adverse effects of ginger use, ginger should only be recommended as a second-line agent for the treatment of NVP.

2.5 MENOPAUSE

The human life experience is rapidly changing and *menopause* is only one aspect *of* this. Menopause which is defined as the permanent cessation of menstruation and is said to have occurred when there has been one year without a menstrual period. The definition of menopause which has been widely used in research is based on World Health Organization (WHO, 1981) definition which defined menopause as the permanent cessation of menstruation resulting from loss of ovarian follicular activity which is not induced by any drug, clinical or surgical procedure. However, anthropological and cross-cultural studies have challenged the concept of menopause as a universal phenomenon with wide variations in symptom perception and reporting in women from different ethnic origins living in different countries as cultural explanations of these differences need to include lifestyle (diet, exercise, social factors, as well as reproductive patterns) which can affect biological processes (Hunter and Rendell, 2007).

Williams was the first to suggest that *menopause* may be adaptive (Williams, 1957; *Armin and Shanley, 2009)*. This adaptation is in the direction that at some age women may avoid the dangers *of* childbirth, by curtailing their own reproductive effort in favour *of* diverting care to existing kin. Childbirth certainly presents a substantial mortality risk, which increases dramatically with age (Grimes, 1994). The level *of* this risk is unique to humans and is a result, at least in part, *of* a compromise on the dimensions *of* the pelvic aperture, to enable the safe birth *of* a baby with large head and shoulders, while minimizing the impact on an effective bipedal gait *(Armin and Shanley, 2009).*

Reproductive physiology is known to occur under tight control *of* the hypothalamic–pituitary–gonadal (HPG) axis. The process involves the follicle-stimulating hormone and the luteinizing hormone secreted by pituitary gonadotropic hormones, which are then stimulated by the hypothalamic gonadotropin-releasing hormone; stimulate various events in the ovaries such as follicular growth, hormone secretion and ovulation. In the process, there is a plethora *of* positive and negative feedback connections between the ovaries (through their hormones) and the pituitary/hypothalamus as reproductive ageing seems to occur at all levels *of* the HPG axis. Central changes include alterations in pituitary/hypothalamic responsiveness to neurohormonal signals, while changes in the ovaries affect Oocytes survival and ovarian hormonal feedbacks (Wu *et al*., 2005). Oocytes dynamics becomes death process as females are born with an Oocytes reservoir, which is not replenished thereafter. When the number *of* remaining Oocytes falls below a certain threshold (approximately 1000), *menopause* ensues *(Armin and Shanley, 2009)*. Oocytes loss

occurs by entry into the growth phase under tight hormonal control or apoptosis (i.e. atresia), but not necrosis.

2.5.1 Factors that influence age at menopause

2.5.1.1 Demographic characteristics

Although some earlier reports also noted that black women in South Africa and the United States experience menopause somewhat younger than white women (Mac-Mahan &Worcester, 1962; Frere, 1971), attention has focused on the role of other demographic factors as predictors of age at natural menopause, such as education, marital status, and urban-rural living environment. The results of these studies have been largely inconclusive as some investigators have found low educational status to be a risk factor for early menopause (Brambilla and McKinlay, 1989; Luoto *et al*., 1994; Bromberger *et al*., 1997). Other studies have found no link between educational status and age at natural menopause (Brand, 1978; Bernard and Signorello, 2000). Garrido-Latorre *et al*., (1996) observed the factors linked to an early menopause are smoking, malnutrition during infancy or adolescence, poor educational level, living in altitude greater than 3000m above sea level and, in general, living in underdeveloped countries. Education and the socio-economic levels measured in this study by the interviewees' monthly income showed differences in the age of menopause but only the socio-economic level showed a significant difference. For women with high school education, menopause came 1.6 years later than for women with no formal education. Likewise, those of a high socioeconomic level experienced menopause 1.3 years later than those of a low level ($P < 0.05$). Demographic factors are of arguable etiologic significance since, at best, they are surrogates for other exposures which

may have direct physiologic effects on the ovaries, and at worst they are likely to be confounded by other factors.

2.5.1.2 Reproductive correlates

The age at menarche, length of menstrual cycle, parity, and oral contraceptive use are key determinants of lifetime number of ovulatory cycles and the individual effect of these variables on the age at natural menopause (ANM) have been investigated in many studies. Factors encouraging a late menopause are mainly linked to women's reproductive characteristics such as an early onset of menstruation, longer and regular menstrual cycles, multiple births, use of contraceptive hormones and having breastfed (Narayan, 1991; Rhaw, 1992; Garrido-Latorre *et al*., 1996). An early menstrual onset was shown to be associated with an early menopause in one study (Cramer and Xu, 1996), but not in others (Whelan *et al*., 1990; Parazzini *et al*., 1992; Beser *et al*., 1994). A shorter cycle length, particularly during early reproductive years was observed to decrease the age at natural menopause by one to two years (Whelan *et al*., 1990). In the published work of *Nicolás et al*., (2010), there was no significant influence of the age at menarche on the age at natural menopause. This result was consistent with the findings of other epidemiological studies (Hardy and Kuh, 1999). Although no observed differences with the sample of women who had early *menarche at* 11 years, women who reached *menarche at* less than nine years of *age* reached *menopause* earlier than other women *(Nicolás et al*., 2010). This decreased trend in menarche age without corresponding decrease in the age menopause may have led to an increase in the reproductive period of life in most human population. In a multivariate analysis, no statistically significant association was observed between age at menarche and age at menopause (Ubirani *et al*., 2010).

The use of oral contraceptives is a recognized factor in delaying the onset of menopause. A study showed significant differences in the population of women from Mexico City with later menopausal age of 1.7 years, and this was consistent for women who use contraceptive before the age of 35 and not as replacement therapy to alleviate menopausal symptoms (Garrido-Latorre *et al*., 1996).

Another study have shown an earlier age at menopause among women with no history of oral contraceptives use (Harlow and Signorello, 2000) while others found no relationship (Brambilla and McKinlay, 1989; Bromberger *et al*., 1997). Much study have found that nulliparous women are at greater risk of early natural menopause and have observed a trend of later menopause associated with increasing parity (Beser *et al*., 1994; Bromberger *et al*., 1997; Harlow and Signorello, 2000). Other variables that showed important differences were the number of pregnancies and births, where there was a linear trend between women with no pregnancies or births (nulliparas) and those with a child or more. On average, nulliparas experience menopause 2.6 years earlier ($P < 0.05$). These findings are consistent with those reported in other literature and did not change after controlling for other factor (Garrido-Latorre *et al*., 1996). Likewise, having breastfed gave an average age for menopause 2.1 years later than in those women who did not breastfeed ($P < 0.05$). When this variable was broken down by the number of children who were breastfed, the differences were even more marked (Garrido-Latorre *et al*., 1996).

2.5.1.3 Anthropometric factors

A number of epidemiologic studies have investigated the association between increasing body mass index and earlier age at natural menopause with mixed results.

Beser *et al*. (1994) found that obese women (body mass index BMI ≥25 kg/m^2) had a significantly earlier age at natural menopause (about 1 year earlier) than non obese women. Several other studies (Brambilla and McKinlay, 1989; Kriplani and Banerjee, 2005; Harlow and Signorello, 2000; Navarro *et al*., 2010) reported no difference in the median age at natural menopause by quintile of body mass index. Bromberger *et al*., (1997) found no significant difference in the age at natural menopause of women below and above a BMI cut-off of 27.3 kg/m^2, but did observe that women who were currently on a weight reduction diet or who gained at least 27 pounds after the age of 20 experienced menopause about 1 year earlier than women with no such history. Willett *et al*. (1983) reported that lean women had higher rates of menopause than heavy women in the same age group. Weight, whether relative or absolute, has been correlated with smoking, parity, and educational level, and epidemiologic studies focusing on obesity and age at natural menopause have not been consistent in selecting confounders for inclusion in their statistical models.

2.5.1.4 Handedness

Some attention has been paid to the possible association between handedness and an early age of natural menopause, drawing from a previous scientific studies which linked left-handedness to autoimmune and reproductive disorders (Searleman and Fugagli, 1987; Geschwind and Behan, 1984) and the possibility that autoimmune reactions against hormone receptor sites and or Oocytes may play a role in the premature onset of menopause (Rabinowe *et al*., 1989). Also, the theory that the intrauterine hormonal environment is involved in the determination of cerebral lateralization has also been postulated and was taken into consideration (Geschwin and Galaburda, 1989). Study of some Mexican–American women which included

only six left-handed women reported that left-handed women experienced menopause on an average of 5 years earlier than right-handed women (Leidy, 1990). Two later studies (Allaway *et al*., 1991; Pavia *et al*., 1994) found no association between handedness and the age at natural menopause.

CHAPTER 3

MATERIALS AND METHODS

3.1 SUBJECTS

Subjects for this study were recruited via simple random sampling. The eligible population of this study totalled 668. Subjects for the retrospective study numbered 324 and constitute menopausal women who came from settlements in Kaduna, Abia, Rivers and Osun State. While subjects for the prospective study was constituted by gravid women attending antenatal clinic in University of Port-Harcourt teaching hospital (UPTH), Cottage hospital Port-Harcourt, General hospital Funtua, Katsina State and Military hospital Lagos. This group numbered 344.

Inclusion criteria for the retrospective aspect of this study were women who have attained natural menopause which is defined as having missed twelve (12) consecutive menstruations of which neither any drug, clinical or surgical procedure has induced it (WHO, 1981). Women with gestational age of less than or equal to four (≤4) weeks were excluded from the prospective study. Even when women met the condition of gestational age, those with co-existing clinical, obstetrics and gynaecological condition capable of inducing nausea and vomiting in pregnancy were excluded. So also were non-Nigerians and women with mixed race.

3.2 METHOD

The method for this study was both retrospective and prospective study. The study population were grouped into two, menopausal women were target for the retrospective study, whereas, gravid women attending antenatal clinic at the time of this study provided the data for the prospective study. Information required was obtained through standardized questionnaires as designed by Lacasse *et al*., 2009.

Verbal interview of the women was the instrument of data collection to filling out the questionnaires for this study via recall. Questionnaires were also distributed to these women to fill out either individually or in group. This study was carried out with due approval from the ethical committee of the participating hospitals and the consent of the subjects themselves.

3.2.1 Determination of gestational age, NVP and menopause

Information on nausea and vomiting of pregnancy were obtained from the gravid subjects and for some, through recall. Ages at menopausal onset were also given through recall by the menopausal women. Gestational ages were obtained from the subjects as given to them by the attending physician calculated from the date of their last menstrual period (LMP). Foetal sexes were also given by these women as was told them by the sonographer or the outcome after childbirth in the case of retrospective study.

3.2.2 Anthropometry

Height and weight measurements were taken. Height was measured using a stadiometer with subjects standing without shoes and with heels together, toes apart, and the head held in the Frankfort plane to the nearest 0.1cm. Weight was taken with light clothes and barefoot to the nearest 0.1kg.

3.3 DATA ANALYSIS

Data were analysed using Analyse-It for Microsoft excel version 2.22,2011. Data were presented as descriptive statistics, percentages of Mean ± SD. Ethnic incidence and general prevalence of NVP in the subjects was calculated and reported as

percentages. Pearson's chi-square and student t-test was used where appropriate to compare means and calculate for association between nausea and vomiting of pregnancy and the demographic and reproductive characteristics. One way analysis of variance (ANOVA) and student's t-test was also used to compare means and determine association between menopause and other variables considered. The level of significance was valued at $P<0.05$ for all analysis.

CHAPTER 4

RESULTS

The characteristics distributions of the gravid study population are represented on Table 4.1. Each variable under study for the study population differs within the study group. Fewer women reported having vomited during their gestational period.

Presented also on Table 4.2 is a descriptive statistic of anthropometric variables of the study group represented as Mean ± Standard deviation. Within the study group, the mean age of the gravid women was observed to be 29.60 ± 4. On the reproductive characteristics of the gravid women, a low mean menarcheal age of 12.40 ± 2.30 was observed. Other parameters associated with gravidity which was also observed include their pregnancy weight and weight gain, mean systolic and diastolic blood and haemoglobin concentration.

The association between NVP and anthropometric (age, height, pregnancy weight, weight gain) and reproductive parameters (systolic and diastolic blood pressure and age at menarche) for gravid women with and without NVP are given in Table 4.3. Only menarcheal age associated significantly ($P<0.05$) with NVP. There was no significant mean difference in the ages, height and diastolic blood pressure of gravid women with and without NVP. Although, women who suffered NVP had slightly lower weight, weight gain but higher systolic blood pressure (75.45 ± 13.29; 5.17 ±3.57 and 111.40 ± 12.40 respectively) when compared to their counterpart who did not suffer NVP.

Table 4.1: Descriptive statistics showing socio-demographic characteristics of gravid women

Parameters	Frequency (%)	N
NVP		
Yes	164 (49.20)	333
No	169 (50.80)	
Season of birth		
Dry	132 (41.40)	319
Wet	187 (58.60)	
Ethnicity		
Hausa	44 (12.80)	
Igbo	130 (37.80)	344
Yoruba	109 (31.70)	
Others	61 (17.70)	
Religion		
Christian	283 (84.70)	
Muslim	48 (14.40)	334
Others	3 (0.90)	
Educational level		
Tertiary	179 (53.90)	
Secondary	98 (29.50)	
Primary	14 (4.20)	332
Others	37 (11.10)	
None	4 (1.20)	
Occupation		
Working	122 (36.30)	
Student	69 (20.50)	
Others	62 (18.50)	336
None-working	83 (24.70)	
Income		
≤10,000	14 (4.70)	
11-20,000	31 (10.30)	
21-30,000	45 (15.00)	300
31-40,000	59 (19.70)	
>40,000	151 (50.30)	
Parity		
None	158 (48.30)	
1	73 (22.30)	
2	40 (12.20)	327
3	37 (11.30)	
≥4	19 (5.80)	

Table 4.2: Descriptive statistics of anthropometric and reproductive characteristics of gravid women

Parameters	n	Mean ± SD	Minimum value	Maximum value	Range
Ages (yrs)	344	29.60 ± 4.60	18.00	42.00	24.00
Height (cm)	340	162.69 ± 7.11	106.20	188.00	81.80
Age at menarche (yrs)	341	12.40 ± 2.30	10.00	18.00	8.00
Pregnancy age (months)	344	3.60 ± 1.50	3.00	9.00	6.00
Pregnancy weight (kg)	344	76.32 ± 13.45	50.00	121.00	71.00
Weight gain (kg)	323	5.20 ± 3.67	-10.00	20.50	30.50
Systolic beat (mmHg)	344	110.90 ± 12.20	80.00	160.00	80.00
Diastolic beat (mmHg)	344	66.60 ± 9.10	50.00	100.00	50.00
HB concentration (gm/dl)	344	10.91 ± 2.05	6.00	35.00	29.00

Table 4.3: Student's t-test for anthropometric and reproductive characteristics of gravid women

Parameter	NVP Mean ± SD	Without NVP Mean ± SD	t	P
Age (yrs)	29.20 ± 4.50 (n=164)	29.90 ± 4.50 (169)	1.54	0.12
Height (cm)	162.65 ± 8.10 (n=161)	162.71 ± 6.04 (n=168)	0.07	0.94
Pregnancy weight (kg)	75.45 ± 13.29 (n=164)	77.12 ± 13.71 (n=169)	1.13	0.26
Weight gain (kg)	5.17 ± 3.57 (n=154)	5.26 ± 3.79 (n=158)	0.22	0.82
Systolic BP (mmHg)	111.40 ±12.40 (n=164)	110.70 ± 12.10 (n=169)	0.54	0.59
Diastolic BP (mmHg)	66.60 ± 8.50 (n=164)	66.90 ± 9.60 (n=169)	0.61	0.54
Hb conc. (gm/dl)	10.88 ± 2.70 (n=159)	10.92 ± 1.23 (n=166)	0.13	0.90
Menarche age (yrs)	12.00 ± 2.20 (n=163)	12.70 ± 2.40 (n=168)	2.58	0.01*

Table 4.4: Chi-square (x^2) test for association between NVP and socio-demographic characteristics of gravid women

Parameter	NVP (Frequency)	Without NVP (Frequency)	n	X^2	P
Ethnicity					
Hausa	15	28			
Igbo	69	59	333	4.71	0.19
Yoruba	53	53			
Other	27	29			
Educational level					
Tertiary	83	91			
Secondary	50	44			
Primary	6	8	321	2.22	0.70
Other	16	19			
None	3	1			
Religion					
Christian	137	136			
Muslim	18	29	323	2.54	0.28
Other	1	2			
Occupation					
Working	65	54			
Student	32	34	325	2.52	0.47
Other	26	34			
Non-working	37	43			
Season of birth					
Dry	62	64	308	-	0.28
Wet	89	93			
Income (#)					
≤10,000	5	8			
11-20,000	15	15			
21-30,000	28	15	291	5.03	0.28
31-40,000	31	26			
>40,000	71	77			

Investigation on the association between NVP and socio-demographic characteristics of the gravid women are presented on Table 4.4. All the variables considered showed no significant association with NVP.

Represented on Table 4.5 are some other reproductive characteristics considered for association with NVP. NVP was observed to decrease progressively with increase in parity. Nulliparous women reported the highest cases (n = 80) and the multiparous women (parity $\geq$ 4) had the least value (n = 10). So also did women with female foetuses report more incidence of NVP when compared to gravid women with male foetuses although, these were not significant.

Table 4.5: Chi-square (x^2) test for association between NVP and reproductive characteristics of gravid women

Parameter	NVP (Frequency)	Without NVP (Frequency)	n	x^2	P
Parity					
None	80	75			
1	35	37			
2	21	18	320	3.91	0.42
3	12	23			
≥4	10	9			
Foetal sex					
Female	63	-			
Male	33	1	97	1.87	0.17

Table 4.6: Descriptive statistics of demographic and reproductive characteristics of menopausal women

Parameter	Frequency (%)	n
Birth season		
Dry	102 (39.00)	261
Wet	159 (61.00)	
Educational level		
Tertiary	45 (14.20)	
Secondary	84 (26.70)	316
Primary	57 (18.00)	
Others	130 (41.10)	
Ethnicity		
Hausa	136 (42.00)	
Igbo	79 (24.40)	324
Yoruba	88 (27.20)	
Others	21 (6.50)	
Religion		
Christian	166 (52.20)	324
Muslim	152 (47.80)	
Handedness		
Right	297 (94.30)	315
Left	18 (5.70)	
NVP		
Yes	128 (40.90)	313
No	185 (59.10)	
Length of Menstrual flow(days)		
≤3	101 (32.30)	313
4-5	176 (56.20)	
>5	36 (11.50)	
Age at 1st birth (yrs)		
<20	101 (34.00)	
20-25	107 (36.00)	297
26-30	80 (26.90)	
>30	9 (3.00)	
Breast feeding		
Yes	296 (99.00)	299
No	3 (1.00)	
Parity		
1	9 (2.80)	
2	26 (8.00)	
3	40 (12.30)	324
≥4	237 (73.20)	
None	12 (3.70)	
Contraception		
Yes	68 (24.10)	282
No	214 (75.90)	

The menopausal women constitute the group for the retrospective study and have their descriptive characteristics presented on Table 4.6 and 4.7. Going by the season of birth, more women were born in the wet season than in the dry season. For those who reported NVP during their reproductive age, 40.90% of these women reported having suffered NVP in one or more pregnancy while 59.10% never had NVP. It was also observed that more women had an early marriage, early child birth and more children. When compared with women in the prospective study (gravid women), women in this group had a later menarcheal age of 14.30 ± 1.70 and mean menopausal age of the study population was 45.50 ± 3.90.

Table 4.7: Descriptive statistic of some reproductive characteristics of menopausal women

Parameter	n	Mean ± SD	minimum	maximum	Range
Age (Yrs)	323	56.70 ± 8.90	40.00	110.00	70.00
Age at menarche (yrs)	321	14.30 ±1.70	10.00	20.00	10.00
Age at marriage	324	19.60 ± 4.90	10.00	37.00	27.00
Age at menopause (yrs)	321	45.50 ±3.90	30.00	57.00	27.00

Table 4.8: Chi-square (x^2) test for association between NVP and demographic and reproductive characteristics of menopausal women

Parameter	NVP (Frequency)	Without NVP (Frequency)	n	x^2	P
Birth season					
Dry	43	58	252	0.12	0.73
Wet	61	90			
Educational level					
Tertiary	25	20			
Secondary	43	40	305	13.44	0.0002*
Primary	15	40			
Others	42	80			
Ethnicity					
Hausa	42	86			
Igbo	36	43	313	6.79	0.08
Yoruba	42	43			
Others	8	13			
Religion					
Christian	75	88	307	3.55	0.06
Muslim	51	93			
Handedness					
Right	116	172	305	0.01	0.94
left	7	10			
Length of menstrual flow					
≤3days	44	52	303	4.84	0.09
4-5days	62	111			
>5days	18	18			
Age at 1st birth (yrs)					
<20	37	63			
20-25	38	67	292	6.72	0.08
26-30	41	37			
>30	5	4			
Parity					
1	4	1			
2	17	9			
3	16	21	313	11.19	0.02*
≥4	91	144			
None	-	6			

On Table 4.8 are represented the characteristics of the menopausal women. No significant difference was observed in women with NVP by season of birth although more women born in the wet season reported NVP than those born in the dry season. A significant association was observed in the educational level of women and their report of NVP ($P<0.05$). The level of significance was observed between primary and secondary, primary and tertiary, other and secondary, other and tertiary but not between other and primary and secondary and primary. Hence, primary and post-primary level of education was significance in the report of NVP. The parity of these women also showed association between the number of children and the report of NVP, though, no pattern was observed. All other variable considered for association with NVP were not significant, however, the proportion of women reporting for each variable varied.

Tables 4.9 and 4.10 also showed a significant association between NVP and age at menopause and the menstrual status of the study population. Women who did not suffer NVP had an early menopausal age (45.20 ± 4.10) as against women who had NVP (46.10 ± 3.40; $t = 2.18$, $P<0.005$). Grouping the study population into pre-menopausal and menopausal group with the gravid women constituting the pre-menopausal, there was a significant increase in the report of NVP among the two groups such that pre-menopausal women who constituted the prospective study had a higher percentage of NVP cases when compared to those of the menopausal women ($P<0.05$). There was no association found between age at menarche and NVP.

Table 4.9: Student's t-test for association between NVP and some reproductive characteristics of menopausal women

Parameter	NVP Mean ± SD	Without NVP Mean ± SD	t	P
Menarche	14.3 ±1.70 (n=125)	14.30 ± 1.70 (n=185)	0.02	0.98
Age at Menopause	46.10 ± 3.40 (n=127)	45.20 ± 4.10 (n=183)	2.18	0.02*

Table 4.10: Comparative analysis of menstrual status of study sample

Parameter	Freq. (%)	NVP	Without NVP	x^2	P
Menstrual Status					
Pre-menopausal	333 (51.50)	164	169	4.55	0.03*
Menopausal	313 (48.50)	128	185		

Table 4.11: Summary on incidence of NVP among ethnic group and general prevalence of NVP among study group

Ethnicity	Prospective study (Gravid women)	Retrospective Study (Menopausal women)	General prevalence
Hausa	34.80%	32.81%	
Igbo	53.91%	45.57%	
Yoruba	50.00%	49.41%	43.71%
Others	48.21%	38.10%	

The incidence of NVP among ethnic groups and the general prevalence among the study population are recorded on Table 4.11. The trend is such that the prospective study, constituting of gravid women had a general higher incidence when compared with the menopausal women. Within the ethnic groups, the Igbo women were observed to have the highest incidence of NVP (53.91%). Following are the Yoruba's with and the Hausa's having the least incidence of 34.80%. However, the Yoruba's had the highest incidence (49.41%) in the retrospective study, followed by the Hausa's who had the least incidence of 32.81%. For this study, the general prevalence of NVP recorded for the Nigerian study population was 43.71%.

Table 4.12: Self perception, aggravating factor and effect of NVP on gravid women.

Domain	Measure n (%)
Self perception	
NVP	
Mild	61 (39.90)
Moderate	65 (42.50)
Severe	20 (13.10)
Very severe	7 (4.60)
Salivation	
Yes	140 (43.50)
No	182 (56.50)
Salivation	
Mild	38 (28.60)
Moderate	50 (37.60)
Severe	36 (27.00)
Very severe	9 (6.80)
Aggravating factors	
Not eaten for long	15 (11.50)
Exposure to certain smell	45 (34.40)
Exposure to certain food	21 (16.60)
Other factors	18 (13.70)
Combination of two or more factors above	32 (23.80)
Limitations	
Everything is an effort	30 (27.50)
Accomplished less task & took longer time	18 (16.50)
Limited in type of work/activities	5 (4.60)
Difficult maintaining social life/activities	12 (11.00)
Rely on partner/family for everything	6 (5.50)
Difficulty looking after home, shopping etc	21 (19.30)
Combination of two or more factors above	17 (15.60)
Emotional challenge	
Become very emotional	10 (9.60)
Less interested in sex	29 (27.60)
Feeling downhearted, unhappy & frustrated	25 (23.70)
Fed up being sick, can't enjoy pregnancy	17 (16.20)
Others	14 (13.30)
Combination of two or more factors above	10 (9.60)

The ways in which the gravid women perceived their NVP condition and the challenges it imposes on them are presented on Table 4.12. A higher percentage of the gravid women perceived their NVP condition as being mild with only 4.6% considering theirs as being very severe. The women also reported salivating induced by NVP of which majority of them reported being moderate.

On the factors that aggravates nausea and vomiting of pregnancy condition, being exposed to certain smell was identified as the most aggravating factor and for other a combination of two or more factors would worsen theirs. These women also experienced certain limitation which ranged from impaired performance and limited activities to difficulty fulfilling their obligation towards family and friends as well as maintaining their social life. Associated also to NVP was some emotional challenge of which more women reported being less interested in sex while others had other emotional challenges.

Represented on Table 4.13 are the management options for NVP in the prospective study. Among the women who suffered NVP, fewer women would want medication for their NVP condition. Further on the option of medication used, 46.40% indicated using pharmaceutical product, 32.20% admitted using herbal remedies and 3.60% used a combination of both. Among those who did not use any medication, eating, lying down and a short walk was identified as manoeuvre used to relieve nauseating and vomiting. When asked reasons for choice of management options, women's choice were based on safety, accessibility and affordability. Also, in an attempt to find out who influenced their choice for herbal medicine as management option, it was observed that majority were self prescribed. Information presented also showed that these women had complete relieve with herbal use with only 10% reporting having temporary relief.

Table 4.13: Management options for NVP among gravid women.

Characteristics	n (%)
Use of medication	
Yes	24 (11.40)
No	187 (88.60)
What medication?	
Pharmaceuticals	13 (46.40)
Herbal	9 (32. 20)
Others	5 (17.80)
Combination of one or more options above	1 (3.60)
Other ways of relieving NVP	
Eating	15 (16.50)
Lying down	44 (48.40)
Taking a walk	3 (3.30)
Drinking of water	12 (13.20)
others	13 (14.30)
Reason for choice of management	
Safe	8 (44.40)
Easy to access	2 (11.10)
Safe & cheap	1 (5.60)
Combination of one or more options above	7 (39.00)
Whose prescription for herbal use?	
Friends	2 (20.00)
Family	3 (30.00)
Self	4 (40.00)
Health personnel	1 (10.00)
Effectiveness of herb use	
Complete relieve	9 (90.00)
Temporal relieve	1 (10.00)

Some parameters of the retrospective study group considered for association with menopause are represented on Table 4.14. There was a significant ($P<0.05$)

association between age at menopause and the season of birth as women born in the dry season will have a later menopausal age of about one year when compared to those born in the wet season. Religion was also significantly associated with the age at menopause. Christians were observed to have a later mean menopausal age than their Muslim counterpart (P<0.0001). Other variables such as NVP, breastfeeding and the use of contraceptive were also significantly associated with age of menopause. Women who breast fed were observed to have menopausal age about five years later than those that did not breastfeed. No association was observed with handedness.

Table 4.14: Student's t-test for association between menopause and some demographic and reproductive characteristics

Parameter	Mean ± SD	n	t	P
Season of birth				
Dry	46.40 ± 3.70	102	2.48	0.01*
Wet	45.30 ± 3.50	157		
Religion				
Christians	46.70 ± 2.30	164	6.56	<0.0001*
Muslims	44.00 ± 4.70	151		
Handedness				
Right	45.50 ± 3.90	294	0.33	0.74
Left	45.20 ± 3.70	18		
NVP				
Yes	46.10 ± 3.40	127	2.81	0.03*
No	45.20 ± 4.10	183		
Breast feeding				
Yes	45.80 ± 3.60	293	3.07	0.002*
No	39.30 ± 0.60	3		
Contraception				
Yes	46.90 ± 2.40	68	3.20	0.002*
No	45.20 ± 4.20	212		

Table 4.15: ANOVA for demographic and reproductive characteristics and menopause

Parameter	Mean ± SD	n	F	P
Educational level				
Tertiary	46.30 ± 2.50	45		
Secondary	46.60 ± 2.50	84	5.91	0.0006*
Primary	45.50 ± 4.90	56		
Others	44.40 ± 4.30	128		
Ethnicity				
Hausa	43.70 ± 4.70	135		
Igbo	46.60 ± 2.30	78	19.39	<0.0001*
Yoruba	46.60 ± 2.60	88		
Others	48.00 ± 2.00	20		
Length of menstrual flow				
≤3days	45.50 ± 3.50	99		
4-5 days	45.50 ± 4.00	175	0.18	0.83
>5days	45.10 ± 4.60	36		
Age at 1st birth				
<20	45.10 ± 4.70	101		
20-25	46.10 ± 2.80	105	2.59	0.05
26-30	46.20 ± 2.40	79		
>30	47.60 ± 3.70	9		
Parity				
None	39.30 ± 4.30	12		
1	43.20 ± 3.60	9		
2	44.00 ± 4.00	25	12.82	<0.0001*
3	44.90 ± 3.60	40		
≥4	46.10 ± 4.30	235		
Age at menarche				
10-12	45.30 ± 5.30	41		
13-15	45.60 ± 3.40	208	0.64	0.59
16-18	45.00 ± 4.30	66		
>18	47.70 ± 4.50	3		
Age at Marriage				
10-15	43.70 ± 5.60	58		
16-20	44.90 ± 4.10	100		
21-25	46.20 ± 2.40	99	6.95	<0.0001*
26-30	46.70 ± 2.30	60		
>30	48.50 ± 4.20	4		

Parameter	Mean ± SD	n	F	P
No of elder brothers				
<3	45.60 ± 3.30	166		
3-5	45.30 ± 3.50	38	4.81	0.009*
>5	39.70 ± 1.50	3		
No of elder sisters				
<3	45.80 ± 3.40	155		
3-5	45.40 ± 3.80	29	1.40	0.25
>5	48.20 ± 4.90	5		

On Table 4.15, educational level strongly associated significantly (P = 0.0006) with the age at menopause. The level of significance was seen between those who attended other forms of education and those who attended secondary or tertiary education but not with primary. Women who attended post-primary education (secondary and tertiary) have a higher menopausal age than those who attended either primary or other form of non-formal education. The ethnicity of these women was also found to strongly associate significantly (P <0.0001) with the age at menopause within the study group. The level of significance was observed between the Hausa women and women from other ethnic groups. Women who were from tribes other than the three major ethnic group had the highest menopausal of about 48 years. Parity and the age at marriage also strongly associated significantly (P<0.0001) in a progressive manner with the age of menopause as women who had no child had the least menopausal of 39.3 years while women who had ≥4 children had a later menopausal age of 46.1 years. The level of significance for age at marriage lies between women who married between the ages of 10-15 and 20-24 years and also between those who married between the ages of 15-19 and 25-29 years. Furthermore, the number of elder brother was also found to associate significantly (P = 0.009) in a progressive pattern with the age at menopause as menopausal age for women decreased with increase in the number of elder brother but not with elder sisters. There was no association found between length of menstrual flow, age at first birth and age at menarche with age at menopause.

CHAPTER 5

DISCUSSION

5.1 NVP AND ANTHROPOMETRIC CHARACTERISTICS

Results for anthropometric characteristics (such as age, height, pregnancy weight, weight gain) and other parameters as blood pressure and haemoglobin concentration from this study found no association with incidence of NVP among pregnant women. The non significant association with age which is contrary to other works (Gadsby *et al*., 2003; Vikanes *et al*., 2008) that found an association between younger women and NVP may not be unconnected to the fact that the population under study may be of the same age range on the average. However, a lower weight (75.45kg) was observed in women who suffered NVP than those who did not (77.12 kg). This is in agreement with the works of Vilming *et al*., (2000) and Linseth *et al*., (2005) who observed a smaller weight gain in women who suffered NVP. Also the non-significant weight gain observed makes it unlikely that weight can be associated with NVP rather the reduction in weight could have resulted from food aversion as reported by Profet (1992) and Sherman and Flaxman (2002) by these women and also due to nutritional loss and dehydration from excessive vomiting other than the cause itself hence, no association.

5.2 NVP AND REPRODUCTIVE CHARACTERISTICS

Age at menarche was observed to be significantly ($P < 0.05$) associated with nausea and vomiting of pregnancy in the prospective aspect of this study which constitute gravid women but not with the menopausal women who were subjects for the retrospective study. The trend was such women who had early menarche suffered NVP. The possible reason for this observed difference may be tied to the

psychological theory of Ringler *et al*., (1984) who said that NVP was associated to lack of preparedness for motherhood, meaning that women who attained early menarche most likely develop faster and have a higher probability of getting married before they were psychologically and emotionally prepared. Also, the role of the environment cannot be completely ruled out as industrialization and development has contributed negatively by increasing the amount of toxins and pollutants in the environment. Considering also the number of years between menarcheal age and the ages of these menopausal women, it may not be wrong to assume that there could be errors in their recall of the age at menarche hence, the difference.

For association between parity and NVP, this study presents two contradicting results. A significant association between parity and NVP was observed in the retrospective group such that the report of NVP among women increased with increased parity with multiparous women having the highest occurrence. This was consistent with several other works (Kallen *et al*., 2003; Linseth, 2005; Lacasse *et al*., 2009). On the other hand, data collected for the prospective study, though not significant reports a decrease in NVP with increase in parity in that multiparous women had a lower incidence of reporting NVP which is in line with the findings of Gadsby, (2003) and Schiff *et al*., (2004). This observed difference may not be unconnected to genetic involvement in this condition which according to Golberg *et al*., (2007), Cedergren *et al*., (2008) and Sandven *et al*., (2009) is transmitted by mother but caused by shared environmental factors. Moreso, unavailability of the medical records for the women who constitute the retrospective study to ascertain if the NVP condition was caused by other factors other than pregnancy induced cannot completely be ruled out. Foetal sex in this study was also consistent with other studies (Kallen, 1987; Schiff *et al*, 2004; Tan *et al*., 2006) that reported that NVP was associated with female foetuses.

There was also no significant association observed between length of menstrual flow and age at first birth although women whose menstrual flow was between 4-5 days reported more NVP and women who had their first child early also reported having NVP with the highest found among women between 26-30 years as also reported by Gadsby *et al*., (2003).

This study also found a significant association (P = 0.02) between age at menopause and vomiting of pregnancy. Women who suffer NVP had a later menopausal age of one year. High and sustained level of the female sex hormones which has been hypothesized by several studies (Goodwin *et al*., 1992; O'Brien and Zhou, 1995; Kallen, 2000; Verberg *et al*., 2005) as aetiology of NVP could be responsible. Conclusions drawn from this indicate that women with NVP are probably more fertile and have a longer reproductive period.

5.3 NVP AND SOCIO-DEMOGRAPHIC FACTORS

Apart from educational level of women in the retrospective group which significantly associated with NVP, ethnicity, educational level, religion, occupation, season of birth, house hold income showed no significant association with NVP in this study. Going by the two seasons of birth, women who were born in the wet season reported more cases of NVP than those born in dry season. More so, the Igbo and Yoruba women had higher incidence of NVP in the prospective study but not in the retrospective as women from Hausa and Yoruba reported more. This may have been influenced by the sample size for the ethnic groups in each study. Christians had more incidence than their Muslim counterpart. Working women also reported more cases and this could be to linked their educational level and hence, their income and lifestyle. A linear relationship was observed between house income and the cases of

NVP reported. Although not significant but this is in agreement with other works (Lacroix *et al*., 2000; Karaca *et al*., 2004). The lack of statistical significance for these variables is likely related to inadequate statistical power as a result of some of the sample sizes.

5.4 MENSRUAL STATUS AND INCIDENCE/PRVALENCE OF NVP

For the purpose of testing one of the hypothesis of this study, the sample population was grouped by menstrual status into two; the pre-menopausal women constituted by gravid women from the prospective study and menopausal women from the retrospective group. Data analysis for this study showed a significance increase (P = 0.003) of about 3% in NVP among pregnant women in recent times and this might be linked choice of diet and the environment as reported by other studies (Profet, 1992; Richard, 2000; Kouzi, 2003).

Ethnic differences in the incidence of NVP were also observed from both studies. Igbo women had the highest incidence rate of 53.91% in the prospective study, with the least observed among the Hausa women, 34.80%. These were generally higher with what was observed from the retrospective study. Further to this, Minturn and Weiher (1984), Mitzi, (2004) and Pepper and Roberts (2006) provided evidence of little or no nausea and vomiting of pregnancy in population groups relying on grain and fruit diets rather than on meat and vegetables. This is typical for the Nigerian population, although diet varies from one ethnic group to another thus, explaining the varying incidence observed between the ethnic groups. However, the incidence for the Nigerian population is lower than that reported for the population of developed

countries (Gadsby *et al*., 2003; Verberg *et al*., 2005). A high prevalence rate of 43.71% (i.e. 437/1000) was observed among the study population.

5.5 EFFECT OF NAUSEA AND VOMITING OF PREGNANCY

Result from this studies show that more women from the Nigerian population perceive their vomiting of pregnancy as being mild or moderate with only about 4.6% referring to theirs as being very severe. A lower percentage of women salivated (43.50%) of which majority also perceived their condition as being mild or moderate rather than severe. Accepting that uncomplicated NVP is a natural phenomenon and is a normal part of a healthy pregnancy as proposed by Richard (2002) and Mitzi, (2004) would have been responsible for the perception of these women over their condition. A greater proportion of those who had experienced NVP identified being exposed to certain smell or food aggravated their nauseating condition, others identified not eating too long as a factor while for others (23.80%), it was a combination of two more of those mentioned above. Although these women reported varying limitation experienced due to NVP, a small percentage (5.5%) indicating they rely on partner and family members for everything supports the perception of their condition as either being mild or moderate. This was also observed in other studies (Chandra *et al*., 2002; Lacasse *et al*., 2009). More women also reported being less interested in sex and the feeling of being unhappy, downhearted and frustrated as emotional challenge experienced (Kouzi,2003; Lacasse *et al*., 2009).

5.6 MANAGEMENT OPTION FOR NVP

On the management option for NVP, a high proportion (32.20%) of women used herbal medicine as management option as reported by Gharoro and Igbafe (2000),

Hollyer *et al*., (2002) and Forster *et al*., (2006). However, a greater percentage used pharmaceutical product (46.40%). Those who neither used pharmaceutical product nor herbal and alternative medicine identified mainly lying down as a manoeuvre in controlling or relieving NVP symptoms. Others mentioned eating, drinking of water and taking a walk as methods that also relieved symptoms. These methods were also suggested by Kouzi (2003) as a non invasive method in management of NVP.

When asked who informed their choice of herbal use for management, more women reported it was self prescribed (40%), followed by those whose prescription were made by family members. Some alternative remedies used by these women include kola nut, ginger, bitter kola, bitter leaf and lime. As much as 90% of these women who used herbal remedies admitted they were completely relieved of vomiting symptoms while 10% mentioned having temporal relieve. Reasons why women would use pharmaceutical, herbal or manoeuvre were because they considered it safe (44.4%), easy to access (11.10%), safe and cheap (5.60%) while for other, for two or more of the above reasons.

5.7 AGE AT MENOPAUSE

This study reports an mean menopausal age of 45.50 ± 3.90 which is about 4 and 3.1 years lower than that (49 and 48.4 years) reported by Gharoro and Igbafe (2000) and Frederic *et al*.,(2001). Unfortunately, while the developed countries record an increase in menopausal age (Brown, 2010), there seem to be a decrease among Nigerian women. This may not be unconnected to the increased poverty rate and high stress level as stress, exercise and strenuous activities has been found to affect the production of sex hormone by interfering with hormonal levels or interfering with the pathway via production of excessive cortisol at the expense of the sex hormone to

cope with stress (Rivier and Rivest, 1991; Kornstein and Clayton, 2002) thus, the low menopausal age might be a reflection of these, imposed on these women due to increased poverty rate.

Handedness and age at natural menopause was also investigated in this study. Contrary with other studies (Geschwin and Galaburda 1989; Rabinowe *et al*., 1989; Leidy, 1990), there was no significant association observed. This was also reported in some studies (Allaway *et al*., 1991; Pavia *et al*., 1994).

5.8 MENOPAUSE AND SOCIO-DEMOGRAPHIC CHARACTERISTICS

Season of birth was found to be significantly ($P < 0.05$) associated with the age at menopause. Women born in dry season has a significant higher age at menopause of about 1.1 years than those born in the wet season. Similar result was reported by Cagnacci *et al.,* (2005) but contrasting to the findings of Smits *et al*., (1997) and Huber *et al*., (2004). This has been linked to prenatal development and Seasonal environmental factors which may be operative even before conception by influencing Oocyte maturation and may contribute to the development of defective embryos and weak adult individuals (Jongbloet *et al*., 1994). It was also suggested that such a mechanism can explain the influence of season of birth on the timing of menarche, on the occurrence of menstrual irregularities and on the incidence of earlier and later menopause (Jongbloet *et al*., 1994).

Educational level found a significant association with the age at menopause. The level of significance was observed between primary and post-primary education. This may be linked to the economic status of these women as well as their living condition and lifestyle (Garrido-Latorre *et al*., 1996). Several other studies (Brambilla and McKinlay, 1989; Luoto *et al*., 1994; Bromberger *et al*., 1997) also found this

association while some others found no association (Brand, 1978; Harlow and Signorello, 2000).

The reason for the significant association ($P<0.0001$) observed between religion and age at menopause is unknown as Christians were observed to have a later menopausal age of 2.7 years than Muslims. However, this can only probably be explained by certain practices and restriction placed on individual lifestyle by religion as no known study has established this. One of such restriction is the use of contraceptive pills which is forbidden by the Islamic region except in critical medical condition where life is threatened (Shaikh, 2003; Ibrahim, 2010). Another reason that might account for this is the geographical location of the subjects as Garrido-Latorre *et al*., (1996) observed an early menopausal age in women living in an altitude 3000m above sea level which is a characteristic of the geographical location of the Muslims in this study.

Ethnic background also showed a significant association with age at menopause. The level of significance was observed between Hausa women and those form other tribe. This suggests that an average Hausa woman would attain menopause 3 years before an Igbo or Yoruba and about 5 years earlier than women from other tribe. Interplay between the gene, environmental factors and lifestyle would have been responsible for the observed difference (Parazzini *et al*., 1992; Garrido-Latorre *et al*., 1996; Treolar *et al*. 1998).

5.9 MENOPAUSE AND REPRODUCTION

Age at marriage and parity showed a linear significant association ($P<0.0001$). Age at menopause increased with age at marriage so that women who had their first child at above 30 years of age had a later menopausal age of 48.5 years. So also was menopausal age found to increase with increase parity as women who had no child, one and four or more had menopausal ages as 39.3, 43.2 and 46.1 years respectively. This study also found significant association between women who reported having nausea and vomiting of pregnancy in their reproductive days, those who breastfed and women who used contraceptives. Menopausal ages for these groups of women increased by 1.1, 5.5 and 1.7 years respectively when compared to their counterpart who did not. This was consistent with other findings as the sustained level of the female sex hormone due to late child birth has been proposed to be responsible for this later menopausal age (Garrido-Latorre *et al*., 1996; Bromberger *et al*., 1997; Harlow and Signorello, 2000; Sievert *et al*., 2001).

This study found no significant association between menarcheal age, length of menstrual flow and age at first birth. However, age at menopause was observed to increase with increase in age at first birth. This is in agreement with the earlier report from this study on the significant association observed between age at marriage and age at menopause. The non significant association between menarcheal age and menopause was found in other studies (Hardy and Kuh, 1999; *Nicolás et al*., 2010; Ubirani *et al*., 2010) but contrasting to several others (Cramer and Xu, 1996; Simondon *et al*., 1997; Thomas *et al*., 2001). Factors which might have influenced this finding could be error in recall of menarcheal age and the difference in sample size.

Some studies (Cramer *et al*., 1995; Bener *et al*., 1998) have reported association between menopause and consanguinity, the focus was on menopausal age of grandmother, mother and sisters. This study reports the first association between numbers of elder brother and the age at menopause ($P<0.009$). Women born after several male children were observed to have early menopause and this age further reduced with increase in male siblings. This can only be accounted for by increased testosterone level which has been associated with infertility (Šperanda and Papić, 2004). However, these women according to Kldinga *et al*., (1978) and Nicola, (2008) have a higher probability of having more sons than daughters. This association was not observed with increased number of female siblings.

CHAPTER 6

SUMMARY, CONCLUSION AND RECOMMENDATION

6.1 SUMMARY AND CONCLUSION

It was established that interplay between the gene, demographic and socio-economic factors determines a woman's reproductive characteristics. Over the years, nausea and vomiting of pregnancy has increased among Nigerian women as the women in the prospective study had a higher incidence than women in the retrospective group. A significant early menarcheal age was observed to be associated with nausea and vomiting of pregnancy in the prospective study but not in the retrospective study, so also did women without NVP have an early menopausal age. Among the study groups, a non significant low pregnancy weight and weight gain was also observed in women with NVP. Having more children associated significantly with increase in NVP in the retrospective study but not the prospective in which NVP decreased with increase in parity. Moreso, report of NVP was found to be more in women with female foetuses. Frequency of NVP was high in younger women, women who breastfed and those who did not use contraceptive.

Socio-demographic characteristics such as ethnicity, Occupation, season of birth and family income did not reach significance in both studies. Although high frequency of NVP was observed with increase in monthly income, Igbo and Yoruba women also had high frequency with the least observed among Hausa women. Educational level was found to be associated with NVP in the retrospective study but not in the prospective even though the frequency increased with increase in educational level. Seasonal variation in the reporting of nausea and vomiting of pregnancy also did not

reach significance but women born in the wet season reported more NVP than those born in the dry season.

Nausea and vomiting of pregnancy has been accepted as a normal part of pregnancy as most women would not take any form of medication. These women also perceived their condition as being mild or moderate rather than severe. However, smell and certain food aggravated their condition and NVP also placed certain limitation which affected them emotionally and socially.

More women were apt to use pharmaceutical products even though the use of complementary and alternative medicine was high, of which were mainly self prescribed. Lying down has also been identified as a manoeuvre for those who did not want any form of medication.

The mean menopausal age for Nigerian women was established as 45.5 years. Season of birth, religion and educational level associated significantly with age at menopause. Ethnic differences also found a level of significance with women from Hausa decent having the least menopausal age.

Reproductive variables such as nausea and vomiting of pregnancy, breastfeeding and use of contraceptive associated significantly with age at menopause, so also was increased parity and age at marriage. Also, age at menopause increased consistently with age at first birth, though not significant, but can be connected to the age at marriage. Women who had more elder brother had a significant early menopausal age but not with sisters. No association was found between handedness, length of menstrual flow and age at menarche.

6.2 RECOMMENDATION

A repeat of this research is encouraged among other ethnic group in other to establish these findings with other contending factors included. Also, a generational study is advised so as to ascertain if there is a genetic influence and to what extent can the environment mask this influence among Nigerian women.

REFERENCES

Alka Kriplani and Kaberi Banerjee (2005). An overview of age of onset of menopause in northern India. *The European menopausal Journal, Maturitas,* 52:199–204.

Allaway, S., Last, P. and Hale, A. (1991). What determines the age at the menopause? *British Medical Journal*, 303:250.

Armin Rashidi and Daryl Shanley (2009). Evolutions of menopause: life histories and mechanisms. Menopause International, 15:26-30

Bagis, T., Gumurdulu, Y., Kayaselcu, K.F., Yilmaz, E.K., and Tarim, E. (2002). Endoscopy in hyperemesis gravidarum and *Helicobacter pylori* infection. *International Journal of Gynaecology and Obstetrics,* 79:105-109.

Bener, A., Rizk, D.E., Ezimokhai, M., Hassan, M., Micallef, R., and Sawaya,M. (1998). Consanguinity and the age of menopause in the United Arab Emirates. *International Journal of Gynaecology and Obstetrics*, 60 (2):155-60.

Bennett, T.A., Kotelchuck, M., Cox, C.E., Tucker, M.J., Nadeau, D.A., (1998). Pregnancy-associated hospitalizations in the United States in 1991 and 1992: a comprehensive view of maternal morbidity. *American Journal of Obstetrics and Gynaecology*, 178:346-54.

Beser, E., Aydemir, V., and Bozkaya, H., (1994). Body mass index and age at natural menopause. *Gynaecology and Obstetrics Investigation*, 37:40–2.

Black, F.O. (2002). Maternal susceptibility to nausea and vomiting of pregnancy: Is the vestibular system involved? *American Journal of Obstetrics and Gynaecology*, 186:S204-9.

Blumenthal, M., Goldberg, A., and Brinckmann, J. (2000). Herbal Medicine: Expanded Commission E Monographs. Newton, MA: *Integrative Medicine Communications,* 88-102; 153-9.

Brand, P.C. and Lehert, P.H. (1978). A new way of looking at environmental variables that may affect the age at menopause. *Maturitas,* 1:121–32.

Brambilla, D.J. and McKinlay, S.M. (1989). A prospective study of factors affecting age at menopause. *Journal of Clinical Epidemiology*, 42:1031–9.

Bone, M.E., Wilkinson, D.J., Young, J.R., McNeil. J., and Charlton. S. (1990). Ginger root: A new antiemetic. The effect of ginger root on postoperative nausea and vomiting after major gynaecologic surgery. *Anaesthesia,* 45:669-71.

Bromberger, J.T. (1997). Prospective Study of the Determinants of Age at Menopause. *American Journal of Epidemiology,* 145(2): 124-133.

Broussard, C.N. and Richter, J.E. (1998). Nausea and vomiting of pregnancy. *Gastroenterology Clinics,* 27:1.

Brown, S. (2010). Menopause likely to become a truly mid-life event. *Menopause International, 16:156*-161.

Brunet, M., Guy, F. and Pilbeam, D. (2002). A new hominid from the Upper Miocene *of* Chad, Central Africa. *Nature,* 418:145–51.

Burchard, E.G., Ziv, E., Coyle, N., Gomez, S.L., Tang, H., Karter, A.J. (2003). The importance of race and ethnic background in biomedical research and clinical practice. *New England Journal of Medicine*, 348:1170-1175.

Cagnacci,A., Pansini ,S.P., Bacchi-Modena, A., Giulini, N., Mollica, G., De Aloysio, D., Vadora, E., and Volpe, A. (2005). Season of birth influences the timing of menopause. *Human Reproduction*, 20 (8): 2190–2193.

Callahan, E., Burnette, M., DeLawyer, D., Brasted, W., (1986). Behavioural treatment of hyperemesis gravidarum. *Journal of Psychosomatic Obstetrics and Gynaecology,* 5:187-95.

Cedergren, M., Brynhildsen, J., Josefsson, A., Sydsjo, A., Sydsjo, G., (2008). Hyperemesis gravidarum that requires hospitalization and the use of antiemetic drugs in relation to maternal body composition. *American Journal of Obstetrics and Gynaecology,* 198:412-5.

Chandra, K., Magee, L. and Koren, G. (2002). Discordance between physical symptoms versus perception of severity by women with nausea and vomiting of pregnancy (NVP). *BMC pregnancy and childbirth*, 2:5.

Cole L.A. (1997). Immunoassay of human chorionic gonadotropin ,its free subunits and metabolites. *Clinical Chemistry,* 43: 2233-2243.

Cramer, D.W., Xu, H., Harlow, B.L.(1995). Family history as a predictor of early menopause. *Fertility and Sterility,* 64 (4):740-5.

Cramer, D.W. and Xu, H. (1996). Predicting age at menopause. *Maturitas,* 23:319–26.

Cuckle, H.S., Wald, N.J., Densem, J.W., Royston, P., Knight, G.J., Haddow, J.E., (1990). The effect of smoking in pregnancy on maternal serum alpha-fetoprotein, unconjugated oestriol, human chorionic gonadotrophin, progesterone and dehydroepiandrosterone sulphate levels. *British Journal of Obstetrics and Gynaecology*, 97:272-6.

Czeizel, A.E., Sárközi, A. and Wyszynski, D.F. (2003). Protective effect of hyperemesis gravidarum for non-syndromic oral clefts. *Obstetrics and gyneacology,* 101:737-744.

Danborno, B and Oyibo, J.E (2008). Anthropometric and menstrual characteristics of girls from Nigeria and Niger Republic. *The internet Journal of Biological Anthropology*, 2(1):

Davis, M. (2004). Nausea and Vomiting of Pregnancy: An Evidence-based Review. *Perinatal Neonatal Nursing,* 18(4):312-328.

Depue, R.H., Bernstein, L., Ross, R.K., Judd, H.L. and Henderson, B.E. (1987). Hyperemesis gravidarum in relation to estradiol levels, pregnancy outcome, and other maternal factors: a seroepidermologic study. *American Journal of Obstetrics and Gyneacology,* 156: 1137-1141.

Deuchar, N. (1995). Nausea and vomiting in pregnancy: A review of the problem with particular regard to psychological and social aspects. *British Journal of Obstetrics and Gynaecology*, 102:6-8.

Dilorio, C. (1985). First trimester nausea in pregnant teenagers: Incidence, characteristics and intervention. *Nurse Research*, 34:372-4.

Doblhammer, G. and Vaupel, J.W. (1999). Reproductive History and Mortality Later in Life for Austrian Women. Max Planck Institute for Demographic Research Germany.

Dokmeci, F., Engin-Ustun, Y., Ustun, Y., Kavas, G.O. and Kocaturk, P.A. (2004). Trace element status in plasma and erythrocytes in hyperemesis gravidarum .*Journal of Reproductive Medicine*, 49:200–204.

el-Mallakh, R.S., Liebowitz, N.R. and Hale, M.S. (1990). Hyperemesis gravidarum as conversion disorder. *Journal of Nervous and Mental Disease,* 178:655–659.

el Younis, C.M., Abulafia, O. and Sherer, D.M. (1998). Rapid marked response of severe hyperemesis gravidarum to oral erythromycin. *American Journal of Perinatology,* 15:533-534.

Erdem, A., Arslan, M., Erdem, M., Yildirim, G. and Himmetoglu, O. (2002). Detection of *Helicobacter pylori* seropositivity in hyperemesis gravidarum and correlation with symptoms. *American Journl of Perinatology,* 19:87–92.

Fairweather, D.V. (1968). Nausea and vomiting in pregnancy. *American Journal of obstetrics and gyneacology,* 102: 135-175.

Frederic, T., François, R., Eric, B. and Thierry de, M. (2001). International Variability of Ages at Menarche and Menopause: Patterns and Main Determinants. *Human Biology*, 73 (2): 271-290.

Frere, G. (1971). Mean age at menopause and menarche in South Africa. *South Africa Journal of Medical Science*, 36:21–4.

Fischer-Rasmussen, W., Kjaer, S.K., Dahl, C., and Asping, U. (1990). Ginger treatment of hyperemesis gravidarum. *European Journal of Obstetrics and Gynaecology Reproduction Bio,* 38:19-24.

Forster, D.A., Angela, D., Gemma, W., Melissa, B. and Elizabeth, M. (2006). Herbal medicine use during pregnancy in a group of Australian women. *BMC Pregnancy and Child birth,* 6:21.

Fulder, S. and Tenne, M. (1996). Ginger as an anti-nausea remedy in pregnancy and the issue of safety. *Herbal Gram*, 38:47-50.

Gadsby, R., Barnie-Adshead, A.M. and Jagger C. (1993). A prospective study of nausea and vomiting during pregnancy. *British Journal of General Practitioners*, 43:245-248.

Gardian, G., Voros, E., Jardanhazy, T., Ungurean, A. and Vecsei, L. (1999). Wernicke's encephalopathy induced by hyperemesis gravidarum. *Acta Neurologica Scandinavica,* 99:196-8.

Garrido-Latorre, F., Lazcano-Ponce, E.C., Lbpez-Carrillo, L. and Hernhdez-Avila, M. (1996). Age of natural menopause among women in Mexico City. *International Journal of Gynaecology and Obstetrics,* 53:159-166.

Georgas, J., Giakoumaki, E., Georgoulias, N., Koumandakis, E., and Kaskarelis, D. (1984). Psychosocial stress and its relations to obstetrical complications. *Psychotherapy and Psychosomatics,* 41:200-205.

Geschwind, N. and Behan, P. (1984). Laterality, hormones, and immunity. In: Geschwind N, Galaburda AM. *Cerebral Dominance: the Biological Foundations*. Harvard University Press Cambridge, Massachusetts, PP. 211–24.

Geschwind, N., and Galaburda, A.M. (1985). Cerebral lateralization, Biological mechanisms, associations, and pathology: A hypothesis and a program for research. *Archives of Neurology.,* 42:428–59.

Ghani, R. (2003). The use of total parenteral nutrition in protracted hyperemesis gravidarum. *Journal of Obstetrics and Gynaecology,* 23:199–201.

Gharoro, E.P. and Igbafe, A.A. (2000). Pattern of drug use among antenatal patients in Benin City, Nigeria. *Medical Science Monitor,* 6:84-87.

Gibson, P., Powrie, R. and Star, J. (2001). Herbal and alternative medicine use during pregnancy: a cross sectional survey. *Obstetrics and Gynaecology,* 97**:**s44-s45.

Glinoer, D., de Nayor, P., Bourdoux, P., Lemone, M., Robyn, C., Van Steirteghem, A., Kinthaert, J., and Lejeune, B. (1990).Regulation of maternal thyroid during pregnancy. *Journal of Clinical Endocrinology and Metabolism,* 71:276-287.

Grimes, D.A. (1994). The morbidity and mortality of pregnancy – still risky business. *American Journal of Obstetrics and Gynaecology*, 170:1489–94.

Grjibovski, A.M., Vikanes, A., Stoltenberg, C., and Magnus, P.(2008). Consanguinity and the risk of hyperemesis gravidarum in Norway. *Acta Obstetricia et Gynecologica Scandinavica,* 87:20-25.

Golberg, D., Szilagyi. A., and Graves, L. (2007). *Hyperemesis gravidarum and Helicobacter pylori infection: a systematic review. Obstetrics and Gynaecology*, *110:*695-703.

Goodall, J. (1986). The Chimpanzees *of* Gombe: Patterns *of* Behavior. *Cambridge: Harvard University Press*.

Goodwin, T.M., Montoro, S., Mestman, J.H. (1992). The role of chorionic gonadotropin in transient hyperthyroidism of hyperemesis gravidarum. *Journal of Clinical Endocrinology and Metabolism*, 75:1333-7.

Gunsar, F., Yilmaz, S., Bor, S., Kumanlioglu, K., Cetinkalp, S. and Kabalak, T. (2001). Effect of hypo- and hyper-thyroidism on gastric myoelectrical activity and gastric emptying. *Neurogastroenterology Mot*., 13:266.

Hardy, R. and Kuh, D. (1999). Reproductive characteristics *and* the *age at* inception of the peri*menopause* in a British N*at*ional Cohort. *American Journal of Epidemiol*ogy, 149:612–20.

Harrison, D.A., Gdula, D.A., Coyne, R.S. and Corces, V.G. (1993). A leucine zipper domain of the suppressor of Hairy-wing protein mediates repressive effect on enhancer function. *Genes and Development*, 7:1966–1978.

Harlow,B.L. and Signorello, L.B. (2000).Factors associated with early menopause. *The European Journal of menopause: Maturitas,* 35:3–9.

Hershman, J.M. (2004). Physiological and pathological aspect of the human chorionic gonadotropin on the thyroid. *Best Practice and Research Clinical Endocrinology and Metabolism*, 18:249-265.

Herskind, A.M (1996). The heritability of human longevity: a population based study of 2872 Danish twin pairs born 1870-1900". *Human Genetics,* 97:319-323.

Herpner, D.L., Harnett, M., Segal, S., Camann, W., Bader, A. and Tsen, L. (2002). Herbal use in parturients. *Anesthesia and Analgesia.,* 94:690-693.

Hollyer, T., Boon, H., Georgousis, A., Smith, M., and Einarson, A. (2002). The use of CAM by women suffering from nausea and vomiting during pregnancy. *BMC Complimentary and Alternative Medicine*, 2:1-6.

Huber S., Fieder M., Wallner B., Iber K. and Moser G. (2004). Effects of season of birth on reproduction in contemporary humans: brief communication. *Human Reproduction*, 19,445–447.

Hunter, M. and Rendall, M. (2007). Bio-psycho-socio-cultural perspectives on menopause *Best Practice & Research Clinical Obstetrics and Gynaecology*, 21: 261-274.

Huxley, R.R. (2000). Nausea and vomiting in early pregnancy: its role in placental development. *Obstetrics and Gynaecology,* 95: 779-82.

Iancu, I., Kotler M., Spivak B., Radwan, M., and Weizman, A. (1994). Psychiatric aspects of hyperemesis gravidarum. *Psychotherapy and Psychosom*atics, 61:142-149.

Ibrahim, A. (2010). Birth control and modern issues,sharia.April 16, 2010. Islamic learning materials.

Jednak, M.A., Shadigian, E.M., Kim, M.S., Woods, M.L., Hooper, F.G., and Owyang, C. (1999). Protein meals reduce nausea and gastric slow-wave dysrhythmic activity in first trimester pregnancy. *American Journal of Physiol*ogy, 277:G855-861.

Jewell, D. and Young, G. (2003). Intervention for nausea and Vomiting in early pregnancy. *Cochrane Data base system Review,* 4, CD000145.

Jongbloet, P.H., Kersemaekers, W.M., Zielhuis, G.A. and Verbeek, A.L. (1994) .Menstrual disorders and month of birth. *Anne Human Biology,* 21: 511–518.

Jordan, V., MacDonald, J., Crichton, S., Stone, P. and Ford, H. (1995). The incidence of hyperemesis gravidarum is increased among Pacific Islanders living in Wellington. *The New Zealand Medical Journal*, 105:342-344.

Jordan, V., Grebe, S.K.G., Cooke, R.R., Ford, H.C., Larsen, P.D., and Stone, P.R. (1999). Acidic isoforms of chorionic gonadotropin in European and Samoan women are associated with hyperemesis gravidarum and may be thyrotrophic. *Clinical Endocrinology*, 50:619-27

Kallen, B. (2000). Hyperemesis gravidarum during pregnancy and delivery outcome: A registry study. In: Koren G, Bishai R, eds. Nausea and Vomiting of Pregnancy: State of the Art. *Toronto: Motherisk, the Hospital for Sick Children*, 36-40.

Kallen, B., Lundberg, G. and Aberg, A. (2003). Relationship between vitamin use, smoking and nausea and vomiting of pregnancy. *Acta Obstetricia Gynecologica Scandinavica,* 82: 916-920.

Kaplan, P.B., Gucer, F., Sayin, N.C., Yuksel, M., Yuce, M.A. and Yardim, T. (2003). Maternal serum cytokine levels in women with hyperemesis gravidarum in the first trimester of pregnancy. *Fertility and sterility*, 79:498-502.

Karaca, C., Guler, N., Yazar, A., Camlica, H., Demir, K. and Yildirim, G. (2004). Is lower socio-economic status a risk factor for *Helicobacter pylori* infection in

pregnant women with hyperemesis gravidarum? *Turkish Journal of Gastroenterology*, 15:86–89.

Katon, W., Ries, R., Bokan, J., and Kleinman, A. (1980). Hyperemesis gravidarum: A biopsychosocial perspective. *Psychiatry Medicine*, 10:151-62.

Kirchengast, S. (1992). Relations between Fertility, Body Shape and Menopause in Austrian Women". *Journal of biosocial Science,* 24: 555-559.

Klebanoff, M.A., Koslowe, P.A., Kaslow, R. and Rhoads, G.G. (1985). Epidemiology of vomiting in early pregnancy. *Obstetrics and Gynaecology*, 66:612–616.

Klinga, K., Bek, E. and Runnebaum, B. (1978). Maternal peripheral testosterone levels during the first half of pregnancy. *American Journal of Obstetrics and Gynaecology*, 1(131):60-2.

Kuscu, N.K., Ylidirim, Y., Koyuncu, F., Var, A. and Uyanik, B.S. (2003). Interleukin-6 levels in hyperemesis gravidarum. *Archives of Gynaecology and Obstetrics*, 269.13-15.

Koch, K.L. (1998). Review article: Clinical approaches to unexplained nausea and vomiting. *Adv Gastroenterology Hepatology and Clinical Nutrition*, 3:163-78.

Koch, K.L., Stern, R.M., Vasey, M., Botti, J.J., Creasy, G.W. and Dwyer, A. (1990). Gastric dysrhythmias and nausea of pregnancy. *Digestive Disease Science,* 35:961-8.

Koch, K.L. (2000). Therapy of nausea and vomiting. In: Wolfe, M.M, ed. *Therapy of Digestive Disorders*. Philadelphia, PA: *W.B. Saunders*, 731-46.

Koch, K. and Frissora, C. (2003). Nausea and vomiting during pregnancy. *Gastroenterology Clinical North America*, 32:201–34.

Kocak, I., Akcan, Y., Ustun, C., Demirel, C., Cengiz, L. and Yanik, F.F. (1999). *Helicobacter pylori* seropositive in patient with hyperemesis gravidarum. *International Journal Gynaecology and Obstetrics*, 66: 251-254.

Kornstein, S.G. and Clayton, A.H. (2002). Women's Mental Health: A Comprehensive Textbook. (ed. Version) Guilford press, New York. Pp 8-18.

Kouzi, S. (2003). Nausea and Vomiting of Pregnancy. *American Journal of Pharmaceutical Education*, 67(2): 66.

Lacasse, A., Rey, E., Ferreira, E., Morin, C. and Bérard, A. (2009). Epidemiology of nausea and vomiting of pregnancy: prevalence, severity, determinants and the importance of race/ethnicity. *BMC Pregnancy and Childbirth,* 9:26.

Lacroix, R., Eason, E. and Melzack, R. (2000). Nausea and vomiting during pregnancy: A prospective study of its frequency, intensity and patterns of change. *American Journal of Obstetrics and Gynaecology*, 182:931-937.

Lagiou, P., Tamimi, R., Mucci, L.A., Trichopoulos, D., Adami, H.D. and Hsieh, C.C. (2003). Nausea and vomiting in pregnancy in progesterone: A prospective study. *Obstetricia and Gynecologica Scandinavica*, 83:916-920.

Lanciers, S., Despinasse, B., Mehta, D.I. and Blecker, U. (1999). Increased susceptibility to *Helicobacter pylori* infection in pregnancy. *Infectious Disease*, *Obstetrics and Gynaecology*, 7:195-198.

Lao, T.T., Chin, R.K., Mak, Y.T. and Panesar, N.S. (1988). Plasma zinc concentration and thyroid function in hyperemetic pregnancies. *Acta Obstetricia Gynecologica Scandinavica*, 67:599–604.

Leidy, L.E. (1990). Early age at menopause among left-handed women. *Obstetrics and Gynaecology,* 76:1111–4.

Leylek, O.A., Toyaksi, M., Erselcan, T. and Dokmatas, S. (1999). Immunologic and biochemical factors in hyperemesis gravidarum with or without hyperthyroxinemia. *Gynaecology and Obstetrics Investigation*, 47:229-234.

Linseth, G. and Vari, P. (2005). Nausea and vomiting in pregnancy. *Health Care Women International,* 26:372-386.

Long, M.A.D., Stephen, S.S. and Tucher, J.J. (1986). Outpatient treatment of hyperemesis gravidarum with stimulus control and imagery procedures. *Journal of Behavioural Therapy and Experimental Psychiatry,* 2:105-9.

Louik, C., Harnandez-Diaz, S., Werler. M.M. and Mitchell. A.A. (2006). Nausea and vomiting in pregnancy: maternal characteristics and risk factors. *Paediatrics and Perinatal Epidemiology,* 20:270-278.

Lub-Moss, M.M. and Eurelings-Bontekoe, E.H. (1997) Clinical experience with patients suffering from hyperemesis gravidarum (severe nausea and vomiting during pregnancy): thoughts about subtyping of patients, treatment and counselling models. *Patient Education and Counselling,* 31:65–75.

Luoto, R., Kaprio, J. and Uutela, A. (1994). Age at natural menopause and socio-demographic status in Finland. *American Journal of Epidemiology*, 139:64–76.

MacMahan, B. and Worcester, J. (1962.). Age at menopause: United States. In: *US Vital and Health Statistics*. 1960–62. Washington DC: Government Printing Office, Series I: No19.

Magee, L., Mazzota, P. and Koren, G. (2002). Evidence-based view of safety and effectiveness of pharmacological therapy for nausea and vomiting. *American Journal of Obstetrics and Gynaecology*, 186:S256–S261.

Mazzotta, P., Magee, L. and Koren, G. (1996). Therapeutic abortions due to severe morning sickness: an unacceptable combination. *The Mother sick Newsletter Fall*, 1–3.

Mazzotta, P., Magee, L.A., Maltepe, C., Lifshitz, A., Navioz, Y. and Koren, G. (1999). The perception of teratogenic risk by women with nausea and vomiting of pregnancy. *Reproductive Toxicology*, 13:313-319.

Mazzotta, P. and Magee, L.A. (2000). A risk-benefit assessment of pharmacological and nonpharmacological treatments for nausea and vomiting of pregnancy. *Drugs,* 59:781-800.

Mazzotta, P., Maltepe, C., Navioz, Y., Magee, L.A. and Koren, G. (2000). Attitudes, management and consequences of nausea and vomiting of pregnancy in the United States and Canada. *International Journal of Gynaecology and Obstetrics*, 70:359–65.

Minagawa, M., Narita. J., Tada, T., Bannai, M., Oya, H., Hatakeyama, K. and Abo, T. (1999). Mechanism underlying immunologic states during pregnancy: Possible association of the sympathetic nervous system. *Cell Immunology*, 196:1-13.

Minturn, L. and Weiher, A. (1984). The influence of diet on morning sickness: a cross culture study. *Medical Anthropology,* 8:71-75.

Morabia. A. and Costanza, M.C. (1998). The World Health Organization Collaborative Study of Neoplasia and Steroid Contraceptives: International variability in ages at menarche, first live birth and menopause. *American journal of Epidemiology,* 148:1195–1205.

Mowrey, D.B. and Clayson, D.E. (1982). Motion sickness, ginger and psychophysics. *Lancet*, 1:655-7.

Murphy, P.A (1998). Alternative therapies for nausea and vomiting of pregnancy. *Obstetrics and Gynaecology,* 91:149-155.

Narayan, H. (1991). What determines the age at menopause. *British Medical Journal,* 302: 1540.

National organization for rare diseases (2009). National organization for rare disease (NORD) database 2009.

Navarro, M.C., Sosa, M., Saavedra, P., Gil-Antullano, S.P., Castro, R., Bonet, M., Travesí, I., and Miguel, E. (2010). Anthropometric and gynaecological history according to the socioeconomic status of postmenopausal women: poverty and the menopause. *Menopause International*, 16: 12–17.

Nelson-Piercy, C. (1998). Treatment of nausea and vomiting in pregnancy: When should it be treated and what can safely be taken. *Drug Safety*, 19:155-164.

Nicolás, M., Daniela, G., Alberto, S., Juan, E.R.C., Juan, M., Rafael, S., Francisco, Q., Francisco, V. and Txantón, M. (2010). Lowering the *age at menarche and* risk of early *menarche* in a popul*a*tion of Spanish postmenopausal women during the past two decades*. Menopause International, 16:111-114.*

Nicola Pearson (2008).Women with high testosterone may be more likely to have sons. The Sunday times, March 24, 2008.

Nordeng, H. and Havnen, G. (2004). Use of herbal drugs in pregnancy:A survey among 400 Norwagian women. *Pharmacoepidermiology and Drug Safety*, 13:371-380.

O'Brien, B. and Naber, S. (1992). Nausea and vomiting during pregnancy: Effects on the quality of women's lives. *Birth*, 19:138-143.

O'Brien, B. and Zhou, Q. (1995). Variables related to nausea and vomiting during pregnancy. *Birth*, 22:93-100.

Ozumba, B.C., Obi, S.N., Obikili, E. and Waboso, P. (2004). Age, Symptoms, and Perception of Menopause among Nigerian women. *Journal of Obstetrics and Gynaecology India*, 54:575-578.

Paauw, J.D., Bierlings, S., Cook, C.R. and Davis, A.T. (2005). Hyperemesis gravidarum and foetal outcome . *JPEN Journal of Parenteral and Enteral Nutrition,* 29:93-96.

Parazzini, F., Negri, E., and LaVecchia, C. (1992). Reproductive and general lifestyle determinants of age at menopause. *Maturitas*, 15:141–9.

Pavia, M. H., Ekbom, A., Adami, H.O. and Trichopoulos, D. (1994). Handedness, age at menarche, and age at menopause. *Obstetrics and Gynaecology*, 83:579–82.

Pepper, G.V. and Roberts, S.C. (2006). Rates of nausea and vomiting in pregnancy and dietary characteristics across populations. *Proceedings of the Royal Society of Biological sciences,* 273: 2675-2679.

Pollet, T.V and Nettle, D (2008). Taller women do better in a stressed environment: height and reproductive success in rural Guatemalan women. *American Journal of Human Biology*, 10: 102.

Power, M.L., Holzman, G.B. and Schulkin, J. (2001). A survey on the management of nausea and vomiting in pregnancy by obstetrician and gynaecologists. *Primary Care Update on Obstetrics and Gynaecology,* 8:69-72.

Profet, M. (1992) Pregnancy sickness as adaptation: A deterrent to maternal ingestion of teratogens. In Barkow J.H. Cosmides, L. and Tooby, J. (eds): *The Adapted Mind. Evolutionary Psychology and the Generation of Culture.* New York, Oxford University Press, pp. 327-365.

Rabinowe, S.L., Ravnikar, V.A., Dib, S.A., George, K.L. and Dluhy, R.G. (1989). Premature menopause: monoclonal antibody defined T-lymphocyte abnormalities and antiovarian antibodies. *Fertility and Sterility,* 51:450–4.

Rhaw, K.T. (1992). Epidemiology of the menopause. *British Medical Bulletin*, 48(2): 249-261.

Ringler, M. and Krizmanits, A. (1984). Psychosomatic aspects of emesis gravidarum: somatic and psychosocial status of females in early pregnancy. *Z Geburtshilfe Perinatolo*, 188:234–238.

Rivier, C. and Rivest, S. (1991). Hypothalamic-pituitary-gonadal axis: peripheral and central mechanisms. *Biology of reproduction* 45:523-532.

Samsioe, G., Crona, N., Enk, L. and Jarnfelt-Samsioe, A. (1986). Does position and size of corpus luteum have any effect on nausea of pregnancy*? Acta Obstetricia et Gynecologica Scandinavica,* 65:427–429.

Sandven, I., Abdelnoor, M., Nesheim, B.I. and Melby, K.K. (2009). *Helicobacter pylori* infection and hyperemesis gravidarum: a systematic review and meta-analysis of case-control studies. *Acta Obstetricia et Gynecologia Scandinavica*, 88**:**1190-1200.

Searleman, A. and Fugagli, A.K. (1987). Suspected autoimmune disorders and left-handedness: evidence from individuals with deabetes, Crohn's disease and ulcerative colitis. *Neuropsychologia*, 25:367–74.

Sekizawa, A., Sudito, Y., Iwasaki, M., Watanabe, A., Jimbo, M., Hoshi, S., Saito, H. and Okai, T. (2001). Cell-free foetal DNA is increased in plasma of women with hyperemesis Graviarum. *Clinical Chemistry*, 47:2164-2165.

Schiff, M.A., Reed, S.D. and Daling, J.R. (2004). *The sex ratio of pregnancies complicated by hospitalisation for hyperemesis gravidarum. BJOG: An international Journal of Obstetrics and Gynaecolog, 111:*27-30.

Schouenborg, L.O., Honnens de Lichtenberg, M., Djursing, H. and Sorensen, J. (1992). Hyperemesis gravidarum. *Ugeskr Laeger*, 154:1015–1019.

Shaikh, S. (2003). Contraception. In: *Maguire, D (Ed) the case of contraception and abortion in world religion*. Oxford university press.Pp 3.

Sherman, P.W. and Flaxman, S.M. (2002). Nausea and vomiting of pregnancy in an evolutionary perspective. *American Journal of Obstetrics and Gynaecology*, 186(5 suppl):S190-7.

Sievert, L.L., Waddle, D. and Canali, K. (2001). Marital status and Age at Natural Menopause: Considering Pheromonal Influence. *American Journal of Human Biology* 13:479–485.

Signorello, L.B., Harlow, B.L., Wang, S. and Erick, M.A. (1998). Saturated fat intake and the risk of severe hyperemesis gravidarum. *Epidemiology,* 9:636-40

Simon, E.P. and Schwartz, J. (1999). Medical hypnosis for hyperemesis gravidarum. *Birth*, 26:248-54.

Simondon, K.B., Simon,I., and Simondon, F. (1997). Nutritional status and age at menarche of Senegalese adolescents. *Annuals of Human Biology,* 24:521–532.

Smits, L.J., Van Poppel, F.W., Verduin, J.A., Jongbloet, P.H., Straatman, H. and Zielhuis, G.A. (1997). Is fecundability associated with month of birth? An analysis of 19th and early 20th century family reconstitution data from The Netherlands. *Human Reproduction,* 12: 2572–2578.

Soto-Wright, V., Bernstein, M., Goldstein, D.P. and Berkowitz, R.S. (1995). The changing clinical presentation of complete molar pregnancy. *Obstetrics and Gynaecology*, 86:775-779.

Stanford, J.L. (1987). Factors influencing the age at menopause. *Journal of Chronical Diseases*, 40: 995-1002.

Stockigt, J.R. (2001).Thyroid hormone measurement: A critical appraisal. *Endocrinology Metabolism Clinics of North America,* 30:265-289.

Swami, V., Miller, R., Penke, L., Tovee, M.J. and Furnham, A (2008). The influence of men's sexual strategy on Peerceptions of women's bodily attractiveness, health and fertility. *Perspective and Individual Difference*, 44: 98-107.

Šperanda, Ž and Papić, Z. (2004). Effect of increased testosterone level on women's infertility. *Diabetologia Croatica*, 33:2.

Tabassum Firoz, Caroline Maltepe, Adrienne Einarson, (2010). Nausea and Vomiting in Pregnancy Is Not Always Nausea and Vomiting of Pregnancy. *Journal of Obstetrics and Gynaecology Canada*, 10:970–972.

Tan, P.C., Jacob, R., Quck, K.F. and Omar, S.Z. (2006). The foetal sex ratio and metabolic, biochemical, haematological and clinical indicators of severity of hyperemesis gravidarum. *BJOG : An international Journal of Obstetrics and Gynaecology,* 113:733-737.

Teksen, F., Dokmeci, G., Kavas, P., Aribal, K. L. and Cengiz, F. (2001). Copper, zinc and magnesium status in hyperemesis gravidarum. *Journal of Obstetrics and Gynaecology,* 21:46–48.

Thomas, F., Renaud, F., Benefice, E., and Meeus, T. (2001). International Variability of Ages at Menarche and Menopause: Patterns and Main Determinants. *Human Biology*, 73(2): 271-290 (Article).

Thorp, J.M., Watson, W.J. and Katz, V.L. (1991). Effect of corpus luteum position on hyperemesis gravidarum. A case report. *Journal of Reproductive Medicine*, 36:761–762.

Tierson, F.D. (1997). Pregnancy, dietary cravings and aversions. Encyclopedia of Human Biology. 2nd Ed. Academic Press, 7: 57-9.

Togay-Isikay, C., Yigit, A. and Mutluer, N. (2001). Wernicke's encephalopathy due to hyperemesis gravidarum:an under-recognised condition. *Australian and New Zealand Journal Obstetrics and gynaecology*, 41:453-456.

Treolar, S.A., Do, K.A. and Martin, N.G., (1998). Genetic influences on the age at menopause. *Lancet,* 35:1084–1085.

Tsui, B., Dennehy, C.E. and Tsourounis, C. (2001). A survey of dietary supplement use during pregnancy at an academic medical center. *American Journal of Obstetrics and Gynaecology,* 185:433-7.

Tsuruta, E., Tada, H., Tamaki, H., Kashiwai, T., Asahi, K., Takeoka, K., Mitsuda, N., and Amino, N. (1995). Pathogenic role of asialo human chorionic gonadotropin in gestational thyyroxicosis. *Journal of Clinical Endocrinology Metabolism,* 18:350-355.

Ubirani, B.O., Dóra, C., Marilia-Sá, C., Eduardo, F., Cláudia de, S.L. and Guilherme, L.W. (2010). Lack of association between age at menarche and age at menopause. *An International journal of midlife health and beyond*: *Maturitas***,** 67 (3):245-250.

Vagan, S., Stoltenderg, C. and Stray-Pedersen, B. (1999). Complaint and complication in pregnancy: a study of ethnic Norwagian and ethnic parkistani women in Oslo. *Ethnicity and Health,* 4:19-28.

Verberg, M.F., Gillott, D.J., Al-Fardan, N. and Grudzinskas, J.G. (2005). Hyperemesis gravidarum, a literature review. *Human Reproductive Update*, 11:527-539.

Vilming B and Nesheim BI (2000). Hyperemesis in a contemporary population in *Oslo. Acta Obstetricia et Gynecologica Scandinavica*, 79:640-643.

Vikanes, A.V., Grjibovski, A., Vangen, S. and Magnus, P. (2008). Length of residence and the risk of developing hyperemesis gravidarum amongst first generation immigrants to Norway. *European Journal of Public Health*, 18:460-465.

Vikanes, A., Skjærven, R., Grjibovski, A.M., Gunnes. N., Vangen, S. and Magnus, P. (2010). Recurrence of hyperemesis across generations: population based cohort study. *British Medical Journal,* 340: c2050.

Voland, E. and Engel, C. (1986). Ist das postmenopausale Sterbealter Variable einer fitness-maximierenden Reproduktionsstrategie?. *Anthropologischer Anzeiger,* 44:19-34.

Vutyavanich, T., Kraisarin, T. and Ruangsri, R.A. (2001). Ginger for nausea and vomiting in pregnancy: A randomized, double-masked, placebo-controlled trial. *Obstetrics and Gynaecology,* 97:577-82.

Walsh, J.W., Hasler, W.L., Nugent, C.E. and Owyang, C. (1996). Progesterone and estrogen are potential mediators of gastric slow-wave dysrhythmias in nausea of pregnancy. *American Journal of Physiology*, 270:G506-514.

Weigel, M.M. and Weigel, R.M. (1988). The association of reproductive history, demographic factors and alcohol and tobacco consumption with the risk of developing nausea and vomiting in early pregnancy. *American Journal of Epidemiology,* 127:562-570.

Westfall, R.E. (2004). Use of anti-emetic herb in pregnancy: Women's choices and the question of safety and efficacy. *Complementary Therapies in Nursing and Midwifery,* 10:30-36.

Whelan, E.A. (1990). Menstrual and reproductive characteristics and age at natural menopause. *American Journal of Epidemiology,* 131: 625-32.

Willett, W., Stampfer, M.J. and Bain, C. (1983). Cigarette smoking, relative weight, and menopause. *American Journal of Epidemiology*, 117:651–8.

Williams, G.C. (1957). Pleiotropy, natural selection, and the evolution of senescence. *Evolution*, 11:398–411.

Whitehead, S.A., Andrews, P.L.R and Chamberlain, G.V.P. (1992). Characterization of nausea and vomiting in early pregnancy: A survey of 1000 women. *Journal of Obstetrics and Gynaecology*, 12:364-369.

World Health Organisation (1981). Research on Menopause. Report of a WHO Scientific group. WHO technical report N670. *WHO Geneva.*

Wu, J.M., Zelinski, M.B., Ingram, D.K. and Ottinger, M.A. (2005). Ovarian aging and *menopause*: current theories, hypotheses, and research models. *Exprimental Biology and Medicine*, 230:818–28

Yoneyama, Y., Sawa, R., Suzuki, S., Yoneyama, K., Doi, D., Otsubo, Y. and Araki, T. (2002). The T-helper 1/ T-helper 2 balance in peripheral blood of women with hyperemesis gravidarum. *Clinical Biochemistry,* 35:561-564.

Yoshimura, M., PeKary, A.E. and Pang, X.P. (1994). Thyrotropic activity of basic isoelectric forms of human chorionic gonadotropin extracted from hydatidiform mole tissues. *Journal of Clinical Endocrinology and Metabolism*, 78:862-4.

APPENDIX I

LETTER OF CONSENT

This letter is to give you information in the hope that you will participate in a study for a dissertation as part of my MSc anatomy program. This study seeks to find out the incidence of emesis gravidarum and its associating factors in Nigeria and its subpopulation.

Participation is voluntary. It involves collection of certain information about you and your pregnancy. The information collected via questionnaire and personal interview will only be used for the above objectives and scientific publications.

I assure you that this study has been reviewed and approved by my supervisors and the university committee on ethics. Thank you for your understanding.

Yours Sincerely,

Wodi Chigeru
Department of Anatomy
Faculty of Medicine
Ahmadu Bello University, Zaria.

I have read the information presented in the information letter about a study being conducted by Wodi Chigeru for her MSc thesis.

I have also had the opportunity to ask questions related to my personal information and have received satisfactory answers to my questions and any additional detail.

I was also informed that I may withdraw my consent at any time.
With full knowledge of all foregoing, I agree to participate in this study.

Participants Signature/Date ——————————————

Interviewer Name/Date ——————————————
Interviewer Signature: ——————————————

APPENDIX II

Questionnaire for prospective study on socio-demographic characteristics of women with NVP and herbal use in treatment of nausea and vomiting in pregnancy among pregnant women.

Part I

1. How old are you ? .....
2. Birthday day and month. (Day.....) And (Month.....)
3. Tick your age grouping.

   (A) 18-22yrs (B) 23-27yrs (C) 28-32yrs (D) 33-37yrs (E) 38yrs and above
4. What is your ethnicity (paternal)?

   (A) Hausa (B) Igbo (C) Yoruba (D) Others specify.....
5. What is your religious background? (A) Muslim (B) Christian (C) Tradition

   (D) Others
6. Educational level attained?

   (A) Tertiary (B) Secondary (C) Primary (D) None (E) Others
7. What is your occupation?

   (A) Working (B) Non-working (C) Student (D) Others
8. Household income per month (in Naira).

   (A) ≤10,000 (B) 11,000-20,000 (C) 21,000-30,000 (D) 31,000-40,000 (E) Above 40,000
9. Age at menarche (first menses) .....
10. How old is your pregnancy? .....
11. Pregnancy weight (Kg).....
12. Pregnancy weight gain (Kg).....
13. Height (cm).....

14. Blood pressure (SBP/DBP mmHg).....

15. Blood HB concentration (mg/dl).....

16. How many children do you have (parity)?

(A) None (B) One (1) (C) Two (2) (D) Three (3) (E) Four (4) and above

17. Do you experience nausea and vomiting? (A) Yes (B) No

18. How many times do you vomit in a day?.....

19. How serious is it? (A) Mild (B) Moderate (C) Severe (D) Very severe

20. Do you also salivate? (A) Yes (B) No

21. Rate your salivation. (A) Mild (B) Moderate (C) Severe (D) Very severe

Aggravating factor and effect on lifestyle. *(More than one option can be chosen in this section).*

22. What worsens your nausea and vomiting condition?
(A) Not eaten for longer than you would like
(B) Worse when exposed to certain smells
(C) Worse when exposed to certain foods
(D) Other specify.....

23. What emotional challenge do you face with nausea and vomiting of pregnancy?
(A) Become very emotional
(B) Less interested in sex
(C) Downhearted, unhappy, depressed, gloomy & Frustrated
(D) Fed up with being sick, Can't enjoy your pregnancy
(E) Others specify.....

24. What limitation does nausea and vomiting of pregnancy place on you?
(A) Everything is an effort
(B) Accomplished less than you would like, Took longer to get things done than usual
(C) Difficult or took extra effort to perform, and/or limited in types of work and other activities
(D) Difficulty maintaining your normal social activities with family, friends, neighbours, or social groups
(E) Rely on your partner an family members to do things that you would normally do for family
(F) Difficulty looking after home, Difficulty shopping for food, Difficulty preparing or cooking meals.

Alternative medicine in use for nausea and vomiting of pregnancy

Part B

1. In present pregnancy, do you suffer nausea and vomiting? A) Yes B)No

2. Do you use any form of medication for your nausea and vomiting? (A) Yes (B)No

3. If yes (to Q2 above), what type of medication do you use?
   A) Orthodox B) Herbal C) pharmaceutical D) Others specify.....

4. If No (to Q2 above), how do you relieve your nausea and vomiting?
   (A)Eating (B) lying down (C) Take a walk (D) Drink water (E) Other

5. Give reason for the use (Q3) above? (A) Safe (B) Cheap (C) easy to access (D)other

6. If herbs, which herb do you take? .....

7. Who prescribed it?
   (A) Friends (B) Family (C) Self prescription (D) Health personnel (E) Others

8. Do you feel better after taking these herbs? (A)Yes (B) No (C) Somehow.

Questionnaire for retrospective study on socio-demographic characteristics of women with NVP, menopausal and reproductive history.

Part II

Personal information

1. How old are you?.....
2. Give your birthday day and month. (Day.....) And (Month.....)
3. Tick your age grouping.

   (A) 18-22yrs (B) 23-27yrs (C) 28-32yrs (D) 33-37yrs (E) 38yrs and above
4. Educational level? (A)Tertiary (B)Secondary (C) Primary (D)Other
5. What is your ethnicity (paternal)?

   (A) Hausa (B) Igbo (C) Yoruba (D) Others specify.....
6. What is your religious background? (A) Muslim (B) Christian (C) Tradition (D) Others
7. Which hand do you use (handedness)? (A) Right (B) Left

Reproductive history

8. Age at menarche (first menses) .....
9. Length of menstrual flow (A) ≤ 3days (B)4-5 days (C)Above 5days
10. Age at marriage.....
11. Age at first birth? (A) <20 (B) 20-25 (C) 26-30 (D) Above 30
12. Did you Breast feed? (A) Yes (B)No
13. How many children do you have? (A) None (B) One (1) (C) Two (2) (D) Three (3) (E) Four (4) and above

14. Did you experience nausea and vomiting during your reproductive days?

    (A) Yes (B) No

15. If yes, in how many pregnancies?.....

16. Give the present age(s) of each child/children..... ....

17. What was the pregnancy outcome (sex) of each?..... ....

18. What was your management option then for nausea and vomiting of pregnancy?

    (A) Orthodox B) Herbal C) pharmaceutical D) Others specify.....

19. Did you us oral contraceptive for family planning? (A) Yes (B) No

20. Age at last child birth? (A) <30 (B) 30-35 (C) 36-40 (D)Above 40

21. Age at onset of menopause.....

Family background

22. Number of sibling in your family.....

23. Position occupied in family (siblings).....

24. Number of elder brother(s).....

25. Number of elder sister(s).....