EFFECTS OF SEX, AGE, BODY MASS INDEXAND SEASONON SERUM THYROID HORMONES AND THYROID STIMULATING HORMONE IN RED SOKOTO AND SAHEL GOATS

BY

Buhari, HABIBU (D.V.M., 2010)
MSc/VET-MED/9536/2011-2012

A THESIS SUBMITTED TO THE SCHOOL OF POSGRADUATE STUDIES

AHMADU BELLO UNIVERSITY, ZARIA

IN PARTIAL FULFILMENT FOR THE AWARD OF A DECREE OF MASTERS OF SCIENCE IN VETERINARY PHYSIOLOGY

DEPARTMENT OF PHYSIOLOGY
AHMADU BELLO UNIVERSITY, ZARIA, NIGERIA

JUNE, 2015

DECLARATION

I hereby declare that the work in this thesis titled **"Effects of sex,age, body mass indexand seasonon serum thyroid hormones and thyroid stimulating hormone in Red Sokoto and Sahel goats"** was performed by me in the Department of Veterinary Physiology, Ahmadu Bello University, Zaria. No part of this work has been presented elsewhere for the award of a degree or diploma in any institution. The works of other researchers referred to in this study were duly acknowledged in the text and list of references.

……. …… ……..

Buhari HABIBU Signature Date

CERTIFICATION

This thesis titled**"Effects of sex,age, body mass indexand seasonon serum thyroid hormones and thyroid stimulating hormone in Red Sokoto and Sahel goats"**by Buhari HABIBU 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 scientific knowledge and literary presentation.

…… ……... ……

Chairman, Supervisory Committee Signature Date

Dr.M.U. Kawu

…… ……. ……...

Member, Supervisory Committee Signature Date

Dr. T. Aluwong

…… ……. ……

Member, Supervisory Committee Signature Date

Dr. H.J. Makun

…… …… ……

Head of Department Signature Date

Dr.M.U. Kawu

…… …… ……

Dean, School of Postgraduate Studies Signature Date

Prof. A.Z Hassan

ACKNOWLEDGEMENT

For life, faith, health, knowledge, and other revealed and unrevealed privileges given to me by the Almighty Allah, I show my sincere appreciation and thanks to Him, and express my love to the Holy Prophet Muhammad (S.A.W).

This work came to reality because it was well supervised by the capable supervisors. Without my team of supervisors, I would not have been well informed scientifically as I am today. May the almighty increase you and your families in faith and bless you with paradise and fulfil the best desires of your hearts, Ameen.

It shall be acknowledgement unfulfilled if my colleagues in the Department of Veterinary Physiology and Department of Veterinary Pharmacology and Toxicology are not appreciated. My thanks goes to Drs L.S. Yaqub, M. Tauheed, T. Dzenda, Chief E. Nwosu, Mal Sani Abdulrazak and all other staff for their scientific, technical, moral and social support. Similar appreciation goes to the staff of Small Ruminant Research Program, National Animal Production Research Institution (NAPRI), Ahmadu Bello University, Shika, Zaria, for their immeasurable technical support during the course of the study. I am particularly indebted tothe Director of NAPRIfor allowing me to use their animals.Special thanks toDr H.J. Makun, Mal. Mamuda and other NAPRI staff too numerous to mention for their corporation and assistance during my field work.

In life, everyone is expected to have someone to give his/her unconditional love and somewhere to call home. I thank Allah for giving me the best of the best. Special thank goes to my wonderful wife, Dr Hajarah Uwale Yusuf and children, Habib Walid Buhari and Maryam Habib Buhari for their corporation and understanding. The love of my parents, Mallam Habibu Aliyu and Mallama Maryam Yakubu blows freely in my heart all the time.Their prayers and love from cradle to date is what has made me who I am. Thank you “Umma” and “Abba”.

Seasons go and seasons come but my sisters (Sadiya, Aisha, Amina and Rukayyah) made the season of love persistent. Never will I forget my nephews and nieces. My wishes of Allah’s blessing go to my paternal and maternal grandmothers, Amina (Tetu) and Mariya, respectively. I hope the blessings of the Almighty will shine on all my teachers and friends, Auwal U. Kandarawa, Hassan Abubakar, Aliyu Muh’d andNi’imatullah Abdurrahman.Barr. Samuel Zibiri, I say thank you for being there when it matters most, you shall always be appreciated.

DEDICATION

I dedicate this thesis to my beloved parents, Mal. Habibu Aliyu and Malama Maryam Yakubu, wife, Dr. Hajarah U. Buhari and children, Habib Walid Buhari and Maryam Habib Buhari.

Table of contents

Title Page ---------- i

Declaration ---------- ii

Certification ---------- iii

Acknowledgement---------- iv

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

Table of Contents ---------- vi

List of Tables ---------- xii

List of Figures ---------- xiii

List of Appendices---------- xv

Abbreviation, Definitions, Glossary and Symbols---------- xvi

Abstract---------- xvii

1.0 INTRODUCTION---------- **1**

1.1Statement of Research Problem ---------- **5**

1.2 Justification of the Study---------- **6**

1.3 Aims of the Study---------- **7**

1.4 Objectives of the Study---------- **7**

1.5 Null Hypothesis ---------- **7**

2.0 LITERATURE REVIEW ---------- **8**

2.1 Goat Production ---------- **8**

2.2 Breeds of Goats---------- 9

2.2.1 Red Sokoto breed goats ---------- 11

2.2.2 Sahel goats ---------- 11

2.3 Seasons in Nigeria---------- 12

2.4 The Thyroid Gland---------- **14**

2.5 Biosynthesis and Metabolism of Thyroid Hormones ---------- **15**

2.6. Physiologic Effects of Thyroid Hormones---------- **16**

2.7.Thyroid Hormone Receptors Activity---------- **17**

2.8Thyroid Hormones Deiodinase Enzymes---------- **18**

2.9Thyroid Hormones Transporters ---------- **20**

2.10 Thyroid Hormones Metabolism and Excretion ---------- **20**

2.11Role of Thyroid Hormones in Reproduction---------- **21**

2.11.1 Female reproduction---------- 21

2.11.2Male reproduction---------- 25

2.12 Factors Influencing Plasma Concentrations of Thyroid Hormones ---------- **26**

2.12.1Ambient temperature---------- 26

2.12.2 Photoperiod---------- 27

2.12.3 Effect of breed on serum thyroid hormones concentration ---------- 29

2.12.4 Influence of age on thyroid activity---------- 29

2.12.5 Influence of sex on thyroid activity ---------- 31

2.12.6 Relationship between circulating thyroid hormones and nutrition,

feed in-take and weight gain ---------- 31

2.12.7 Influence of minerals and vitamins on serumthyroid hormones concentration-- 35

2.12.8 Effect of stress on serum thyroid hormonesconcentration---------- 38

2.12.9 Influence of thyroid hormones on body temperature---------- 40

2.12.10 Effect of reproductive status on serum the concentration---------- 42

2.13Disorders ofThyroid Function in Ruminants---------- **45**

2.13.1 Hypothyroidism ---------- 45

2.13.2 Hyperthyroidism ---------- 47

2.13.3 Other diseases that affects thyroid hormornes ----------48

3.0 MATERIALS AND METHODS---------- 50

3.1 Experimental Location---------- 50

3.1.1 Housing, feeding, breed identification and animal health status ---------- 50

3.2 Experimental Animals Grouping---------- 51

3.3 Body Mass Index ---------- 51

3.4Ageing of Animals---------- 53

3.5Seasons of the Study---------- 53

3.6Meteorological Parameters---------- 53

3.7Blood Sample Collection---------- 54

3.8Analysis of Serum Total Thyroxine, Total Triiodothyronine and Thyroid Stimulating Hormones---------- 54

3.8.1Principles of total triiodothyronine (T_3)assay---------- 54

3.8.2 Principles of total thyroxine(T_4) assay ---------- 54

3.8.3 Principles of thyroid stimulating hormone assay---------- 57

3.9Statistical Analysis---------- 58

4.0 RESULTS---------- 60

4.1 Meteorological Parameters during the Study Period ---------- 60

4.2 Mean Serum Concentrations of $T_3$and T_4in Red SokotoandSahel Goats--- 62

4.3Meanof Serum Concentrations of TSH and T_3:T_4in RedSokoto and Sahel Goats---------- 64

4.4 Percentages of Serum Thyroid Hormones that are in Form of$T_3$and

T_4 in Red Sokoto and Sahel Goats ---------- 66

4.5Effect of Sex on Serum T_3 and T_4 Concentrations in Red Sokotoand Sahel Goats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 68

4.6Effect of Sex on Serum TSH and T_3:T_4Concentration in Red Sokoto and Sahel Goats during the Cold-dry, Hot-dry and Rainy Seasons ----------70

4.7Effect of Age on Serum Concentration of $T_3$and T_4in Red Sokoto and SahelGoats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 72

4.8Effect of Age on Serum TSH and T_3:T_4in Red Sokoto and Sahel Goats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 74

4.9Effects of Breed and Season on Serum T_3in Buck-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons---------- 76

4.10Effects of Breed and Season on Serum T_3in Adult Bucks of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 78

4.11Effects of Breed and Season on Serum T_3in Doe-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 80

4.12Effects of Breed and Season on Serum T_3in Adult Does of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons---------- 82

4.13Effects Of Breed And Season on Serum T_4In Buck-Kids Of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons----------84

4.14Effects of Breed and Season on Serum T_4in Adult Bucks of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 86

4.15Effects of Breed and Season on Serum T_4in Doe-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons---------- 88

4.16Effects of Breed and Season on Serum T_4in Adult Does of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons---------- 90

4.17Effects of Breed and Season on Serum TSHin Buck-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons---------- 92

4.18Effects of Breed and Season on Serum TSHin Adult Bucks of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons---------- 94

4.19Effects of Breed and Season on Serum TSHin Doe-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 96

4.20Effects of Breed and Season on Serum TSHin Adult Does of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 98

4.21Effects of Breed and Season on T_3:T_4in Buck-Kids of RS and SH Goats during The Cold-dry, Hot-dry and Rainy Seasons ----------100

4.22Effects of Breed and Season on T_3:T_4 in Adult Bucks of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 102

4.23Effects of Breed and Season on T_3:T_4in Doe-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons---------- 104

4.24Effects of Breed and Season on T_3:T_4in Buck-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons ----------106

4.25Effect of Breed n Body Mass Index Red Sokotoand SahelGoats---------- 108

4.26Coefficient of Correlation between BMI and Serum Concentrations of T_3, T_4, TSH and T_3:T_4in Young Red Sokoto and SahelGoats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 110

4.27Coefficient of Correlation Between BMI and Serum Concentrations of T_3, T_4, TSH and T_3:T_4in Adult Red Sokoto and Sahel Goats during the Cold-dry, Hot-dry and Rainy Seasons ---------- 112

5.0 DISCUSSION---------- 114

6.0 CONCLUSION AND RECOMMENDATION----------122

6.1 Conclusion---------- **122**

6.2 Recommendations---------- **122**

REFERENCES ---------- 123

APPENDICES---------- 153

List of Tables

Table 4.1: Mean values (± SEM) of meteorological parameters in the monthsof December (CDS), April (HDS) and August (RAS) during the period of the study---------- 61

Table 4.2: Mean values of serum concentration of T_3, and T_4 in Red Sokoto and Sahel goats---------- 63

Table 4.3: Mean (± SEM) of serum concentration of TSH and T_3:T_4 in Red Sokoto and Sahel goats----------65

Table 4.4: Percentages of serum T_3 and T_4 in Red Sokot oand Sahel goats ---------- 67

Table 4.5: Effect of sex on serum T_3 and T_4 concentrations in Red Sokoto and Sahel goats during the cold-dry, hot-dry and rainy seasons ---------- 69

Table 4.6: Effect of sex on values of serum TSH and T_3:T_4 in Red Sokoto and Sahel ----- 71

Table 4.7: Effect of age on serum T_3 and T_4 concentrations in Red Sokoto and Sahel goats during the cold-dry, hot-dry and rainy seasons ---------- 73

Table 4.8: Effect of age on serum concentration of TSH and T_3:T_4 in Red Sokoto and Sahel goats during the cold-dry, hot-dry and rainy seasons ---------- 75

Table 4.9: Mean (±SEM) values of body mass index in young and adult RS and SH Goats---------- 109

Table 4.10: Pearson's correlation between BMI and circulating concentrations of T_3, T_4, TSH and values of T_3:T_4 for young goats ---------- 111

Table 4.11: Pearson's correlation between BMI and circulating concentrations of T_3, T_4, TSH and values of T_3:T_4 for adult goats---------- 113

List of Figures

Figure 2.1: Map of West Africa indicating the geographical areas and transportation of Sahel goats ---------- 13

Figure 3.1: Animal grouping and subgrouping of RS (Red Sokoto) and SH (Sahel) Goats sampled during the cold-dry seasons (CDS), hot-dry seasons (HDS) and rainy seasons (RAS) ----------52

Figure 4.1: Mean (±SEM) serum concentrations of T_3 in buck-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 77

Figure 4.2: Mean (±SEM) serum concentration of T_3 in adult bucks of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 79

Figure 4.3:Mean (±SEM) serum concentrations of T_3 in doe-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons. ---------- 81

Figure 4.4: Mean (±SEM) serum concentrations of T_3 in adult does of RS and SH goats during the cold-dry, hot-dry and rainy seasons---------- 83

Figure 4.5: Mean (±SEM) serum concentrations of T_4 in buck-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 85

Figure 4.6: Mean (±SEM) serum concentrations of T_4 in adult bucks of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10) ---------- 87

Figure 4.7: Mean (±SEM) serum concentrations of T_4 in doe-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 89

Figure 4.8: Mean (±SEM) serum concentrations of T_4 in adult does of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 91

Figure 4.9: Mean (±SEM) serum concentrations of TSH in buck-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 93

Figure 4.10: Mean (±SEM) serum concentrations of TSH in adult bucks of RS and

SH goats during the cold-dry, hot-dry and rainy seasons ---------- 95

Figure 4.11: Mean (±SEM) serum concentrations of TSH in doe-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 97

Figure 4.12: Mean (±SEM) serum concentrations of TSH in adult does of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 99

Figure 4.13: Mean (±SEM) values of T_3:T_4 in buck-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons---------- 101

Figure 4.14: Mean (±SEM) values of T_3:T_4 in adult buck of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 103

Figure 4.15: Mean (±SEM) values of T_3:T_4 in doe-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 105

Figure 4.16: Mean (±SEM) values of T_3:T_4 in adult does of RS and SH goats during the cold-dry, hot-dry and rainy seasons ---------- 107

List of Appendices

Appendix I: Effect of sex and age on serum concentration of T_3, T_4, TSH and T_3:T_4 in Red Sokoto and Sahel goats during the cold-dry season---------- 152

Appendix II: Effect of sex and age on serum concentration of T_3, T_4, TSH and T_3:T_4 in Red Sokoto and Sahel goats during the hot-dry season ---------- 153

Appendix III: Effect of sex and age on serum concentration of T_3, T_4, TSH and T_3:T_4 in Red Sokoto and Sahel goats during the rainy season ---------- 154

Abbreviations and Symbols

Abbreviations

Abbreviation	**Translation**
AT	Ambient temperature
BAT	Brown adipose tissue
BMI	Body mass index
CDS	Cold-dry season
Dio 1	Deiodinase 1
Dio 2	Deiodinase 2
Dio 3	Deiodinase 3
FSH	Follicle-stimulating hormone
GnRH	Gonadotropin-releasing hormone
HCl	Hydrochloric Acid
HDS	Hot-dry season
MBH	Mediobasal hypothalamus
MCTs	Monocarboxylate transporters
LD	Long days
RAS	Rainy season
RH	Relative Humidity
RS	Red Sokoto
RSG	Red Sokoto Goats
rT_3	Reversed triiodothyronine
RXRs	9-cis retinoic acid receptors
SD	Short days

SHG Sahel Goats

TREs Thyroid response elements

TRs Thyroid hormone receptors

TSH Thyroid stimulating hormone

TSHB Beta-subunit of thyroid-stimulating hormone

TSHR TSH receptors

T_3 Triiodothyronine

T_3:T_4 Triiodothyronine-Thyroxin ratio

T_4Thyroxin

TBG Thyroid binding globulin

TH Thyroid hormones

TMB 3,3',5,5'-Tetramethylbenzidine

Symbols

Symbols Full meaning

% Percentage

kg Kilograms

cm Centimetres

µIU/mL Micro- international unit per millilitre

ng/mL Nano-gram per millilitre

Abstract

Thyroid hormones are the most important hormones involved in the regulation of cellular metabolism, reproductive seasonality, voluntary feed intake and thermogenic adaptation to changes in ambient temperature in mammals and birds. This study was aimed at evaluating the influence of sex, age, body mass index (BMI) and season on serum thyroxin (T_4), triiodothyronine (T_3), thyroid stimulating hormone (TSH) and T_3:T_4 of Red Sokoto (RSG) and Sahel (SHG) goat kids. A total of 240 blood samples were collected from apparently healthy goat kids at the peak of each of the three seasons of the year, that is the cold-dry (CDS), hot-dry (HDS) and rainy (RAS) seasons. In each season, 80 goats were sampled as follows: RS buck-kids (n=10), RS bucks (n=10), RS doe-kids (n=10), RS does (n=10), SH buck-kids (n=10), SH bucks (n=10), SH doe-kids (n=10) and SH does (n=10). The T_3:T_4 was calculated and used as an indirect measure of the conversion of T_4 to T_3. The HDS had significantly higher ($P < 0.05$) temperature-humidity index (84.62) than the RAS (79.63) and CDS (74.45). The results of this study revealed that the overall mean values of circulating concentrations of T_3, T_4 and TSH in these breeds of goats were 2.14 ± 0.087 ng/mL, 45.90 ± 1.90 ng/mL and 0.80 ± 0.036 µIU/mL. Irrespective of season, sex and age, mean serum concentrations of T_3 and T_4 were significantly higher ($P < 0.05$) in RS than SH goats. The RS kids had higher ($P < 0.05$) T_3:T_4 than SH goat kids during the RAS. In RS, female goats had higher ($P < 0.05$) serum T_3 and T_4 than males in the RAS. Similarly, female SH goats had higher ($P < 0.05$) T_3 and T_4 than males in the CDS and RAS, respectively. In the RS, serum TSH (HDS) and T_3:T_4 (CDS) were significantly higher in males than female goats. In SH goats, however, females had higher ($P < 0.05$) T_3:T_4 than males. In both breeds, kids had significantly higher ($P < 0.05$) serum T_3 and T_4 than adult goats. In contrast, adult RS goats had significantly higher ($P < 0.05$) serum TSH than goat kids. The T_3:T_4 was significantly higher ($P < 0.05$) in RS kids than adult goat during the HDS. Irrespective of age and breed,

serum T_3 levels were significantly lower ($P < 0.05$) during the HDS compared to CDS and RAS. The SH goats had lower ($P < 0.05$) serum TSH during the HDS compared to RAS. In both RS and SH kids, mean T_3:T_4 value was significantly lower ($P < 0.05$) during the HDS compared to CDS and RAS. There was a significantly negative correlation ($r = -0.776$; $P < 0.05$) between T_3 and BMI in kids of SH goats during the HDS. A positive correlation ($r = 0.619$; $P < 0.05$) was recorded between TSH and BMI in SH goat kids (HDS), while the correlation was negative ($r = - 0.575$; $P < 0.05$) in the RS goat kids (RAS). The correlation between T_3:T_4 and BMI was positive ($r = 0.900$; $P < 0.05$) in female kids of RS goats in CDS. However, it was negative ($r = 0.749$; $P < 0.05$) in SH goats kids during the HDS. In adult RS goats, the correlation between T_3 and BMI was positive ($r = 0.611$; $P < 0.05$) in the CDS; positive ($r = 0.620$; $P < 0.05$) for T_4 and BMI in CDS; and negative ($r = 0.545$; $P < 0.05$) for T_4 and BMI in HDS. In adult SH goats, the correlation between T_4 and BMI was negative ($r = -0.795$; $P < 0.05$) in male goats during the RAS and negative ($r = - 0.862$; $P < 0.05$) between TSH and BMI in females goats during the HDS. It is concluded that breed, sex, age, BMI and season affects serum concentrations of thyroid hormones and TSH in RS and SH goats reared in Zaria in the Northern Guinea Savannah zone of Nigeria.

CHAPTER ONE

INTRODUCTION

Goats account for 30% of Africa's ruminant livestock and have an estimated population of 147 million in sub-Saharan Africa (Lebbie, 2004). The relatively highprotein and low fat content of goat meat and milk, indicates that goat products would be a nutritionally desirable alternative to other livestock products (Johnson *et al.,* 1995).Distribution of goat breeds in West Africa indicates that the Red Sokoto goats(RSG) are common to the Guinea savannah region of Nigeria and the Niger Republic, while the Sahel goats (SHG) are found around the Sahel belt of West Africa, south of the Sahara(Doutressoulle 1947; Habibu *et al*., 2014). However, adaptation of Sahel goats to the Northern Guinea savannah of Nigeria has been observed over the years (Habibu *et al*., 2015).

The thyroid gland of small ruminants is located on the dorsolateral aspect of the trachea posterior to the larynx. It has an almond shaped and a slightly pointed posterior end. The isthmus connects the caudal poles of the two lobes of the gland (Bhardwaj *et al.,* 2006). The thyroid gland is made-up of follicular cells that are cuboidal to columnar in shape. The synthesis of thyroid hormones (3,5,3'-triiodothyronine [T_3] and 3,5,3',5'-tetraiodothyronine or thyroxine [T_4]) occur within the follicular lumen on a protein backbone called the thyroglobulin. Some of the essential raw materials required for the synthesis of thyroid hormones (TH) are tyrosine and iodide which are obtained from the systemic circulation. Attachment of iodine to the tyrosyl residue on thyroglobulin forms monoiodotyrosine (MIT) and diiodotyrosine (DIT). The MIT and DIT combine to form 3,5,3'-triiodothyronine (T_3) and 3,5,3',5'-tetraiodothyronine (thyroxine or T_4). Thyroid stimulating hormone (TSH), which is secreted by the anterior pituitary gland regulates the synthesis and the secretion of TH(Capen and Martin, 2003; Todini, 2007). The hypothalamus secretes thyrotrophin

releasing hormone (TRH), which regulates pituitary TSH secretion. Negative feedback control of TH secretion is coordinated by the response of adenohypophysis and hypothalamic nuclei to circulating levels of TH (Capen and Martin, 2003).

In plasma, TH are either protein-bound or free, but only the free hormone is responsible for the biological activity; the protein-bound hormones function as a prompt usable storage (Bartalena, 1990). Most physiologic effects of TH are mediated by binding to nuclear receptors of target tissues, stimulating the utilization of oxygen and the production of heat in all cells of the body. The basic physiologic effects of TH are to increase basal metabolic rate, increase cellular glucose availability, stimulate protein synthesis, increase lipid metabolism and stimulate cardiac and neural function (Todini, 2007).

Deiodinase enzymes control the intracellular and plasma action of TH (Salvatore, 2011). Since T_4 has a long half-life (1 week in humans and 1 day in rats), the role of hypothalamus–pituitary–thyroid axis in the regulation of T_4 bioavailability is complemented by the expression and activity of iodothyronine deiodinases. Deiodinase type 1 (D_1) or type 2 (D_2) activate the inactive T_4 by deiodinating it to T_3 (Williams and Bassett, 2011). This reaction is responsible for the production of about 80% of T_3 present in circulation in a healthy subject. Another deiodinase, deiodinase type III (D_3), deiodinate the inner ring of both T_3 and T_4, thereby inactivating and converting them to 3,3'- diiodothyronine (T_2) and reverse 3,3',5'-triiodothyronine (rT_3), respectively (Kaiser *et al*., 1986;Dentice and Salvatore, 2011). For this reason, D_3 is considered to be the major physiological inactivator and terminator of TH actions at peripheral level (Salvatore, 2011). It has been found that photoperiod regulates the expression of type II deiodinase gene in the mediobasal hypothalamus of the Saanen goat,

hence seasonally affecting the bioavailability of TH at the reproductive neuroendocrine axis (Yasuo *et al.,* 2006).

Previously, it was assumed that the lipophilic nature of TH facilitate their passive diffusion through membrane lipid bilayer. However, specific transport mechanisms have been demonstrated for T_4 and T_3 in a variety of cultured cellular systems (Bernal, 2006). Several membrane transporters for cellular entry of THs have been identified and they are now considered among the factors on which TH biological activity could depend (Friesema *et al.,* 2005). An X-linked mutation in one of the TH transporters, monocarboxylate transporter 8 (*MCT8*), causes an unusual abnormality of thyroid function characterized by high serum T_3 and low T_4 and reversed triiodothyronine (rT_3)in humans(Dumitrescu*et al.,* 2006). Thyroid hormone transporter proteins, including system-L (L-type amino acid transporter 1 and CD98), MCTs 8 and 10, organic anion-transporting polypeptides 1A2 and 4A1, found on the syncytiotrophoblast (the primary barrier to maternal-fetal exchange, which lies in direct contact with maternal blood), have been shown to be capable of rapid uptake of TH at a similar rate (Loubière*et al.,* 2012).

Thyroid hormones levels were reported to be higher in growing goats than in adults (Colavita *et al.,* 1983),while lower values were found in old subjects (Ravaglia e*t al.,* 2000).. Seasonality of T_4 in sheep indicated that maximum values were observed during the winter (cold months) and minimum values during the summer (hot months). Spring (increasing day length) showed high T_4 profile and the autumn (decreasing day length) showed low profile. (Menegatos *et al.,* 2006). In Savanna Brown goats, higher serum T_4 was observed during the cold-dry than early rainy season (Kawu, 2011). Plasma concentration of TH is significantly influenced by breed and sex (Bhooshan *et al.,* 2010).

Triiodothyronine is involved in the seasonal regulation of appetite and body weight in hamsters which naturally shows seasonality in appetite, weight gain and reproduction (Murphy *et al.,* 2012). Blood level of TH is regarded as a good indicator of nutritional status of animals (Riis and Madsen, 1985). The nutritional status index of goats can be calculated using the goat body mass index (BMI) (Tanaka *et al.,* 2002). Both serum TH levels and BMI have been used as indicators of the nutritional status of animals (Riis and Madsen, 1985; Estrade-Cortes *et al*., 2009). In humans, change in TH was described to be the consequence rather than the cause of weight gain (Soriguer *et al.,* 2011). Higher plasma TH concentrations were observed in lactating Angora does and their kids supplemented with energy and protein compared to control (Todini *et al*., 2005), while ewes fed low energy diet experienced a decrease in serum T_3 (Rae *et al*., 2002).

Although there is paucity of information on the use of TH agonist to improve animal production, some thyromimetics such as GC-1 and KB2115 have been shown to reduce serum cholesterol independent of low density lipoprotein receptors (LDLRs). They induce cholesterol 7 alpha-hydroxylase (cholesterol 7-alpha-mono-oxygenase or cytochrome P450-7A1or CYP7A1) expression and stimulate the conversion and excretion of cholesterol in bile (Lin *et al.,* 2012). Also, another thyromimetic, 3,5-diiodothyropropionic acid (DITPA) was produced with the aim of managing cardiac disorders (Pennock *et al.,* 1992), considering the tremendous effect of TH on cardiac function.

Goitre has been reported in goats (Al-Ani *et al*., 1998). The main mechanism responsible for the development of thyroid hyperplasia include:iodine-deficient diet, goitrogenic compounds (e.g. propylthiouracil and carbimazole), which interfere with hormone synthesis; dietary iodine excess and genetic defects in biosynthesis of TH. Goitre in goats could be hyperplastic

(Capen and Martin, 2003), congenital dyshormonogenetic (de Vijlder *et al.,* 1981) or colloidal, with enlargement of the cranio-ventral neck region (Cheema *et al.,* 2010). Abortion, delivery of still born or weak kids, myxoedema and hair loss are common signs of goiter in goats (Bires *et al.,* 1996).

1.1 Statement of Research Problem

The increased incidence of dystocia and stillborn in hypothyroid does, myxedema, hair loss and high mortality rate in congenitally goiterous kids (Bires *et al.,* 1996),result in substantial economic loss to a goat farmer. For this reason, determination of normal TH values in our environment will assist in the diagnosis of TH abnormalities and selection of reputable breeding stocks for goat production.Regardless of the influence of TH on reproduction (Dahl *et al.,* 1995), and that of endotoxin release on serum TH levels (Jánosi*et al*.,1998), a comprehensive data on reference values of TH is yet to be established in Nigeriangoats. Determination of normal profiles of serum TH will serve as a foundation upon which information on how TH affect other production parameters and interference by endotoxins (particularly inendotoxin mastitis) on thyroid gland function in goats can be evaluated and managed.

In addition to the paucity of baseline data on serum TH in the two major goat breeds (RSG and SHG) in the Northern Guinea Savannah zone of Nigeria information on the influence of breed, sex, age, BMI and season on the baseline values may be of importance to clinicians, researchers and livestock farmers. Furthermore, such information, if available, could serve as an important input in the diagnosis and management of thyroid related disorders, and enhance the understanding of endocrine thermoregulatory adaptation in RSG and SHG.

1.2 Justification of the Study

Eighty percent of the world goat population is found in countries with low income especially in Asia, Africa and South America (Morand-Ferh *et al*., 2004). In Nigeria, goats are the predominant ruminant biomass (Mainna, 2002; FAO, 2013). Besides their meat and milk production potential (Egwu *et al.*, 1995), they also serve as source of income to rural dwellers (Ikwuebu *et al.*, 1994). Since the Red Sokoto (Maradi) goat is the most widely distributed and the predominant goat breed in Nigeria with an estimated population of 70% (Osuhor *et al.*, 1998), enhancing the productivity of these goats is expected to improve the economy of rural farmers (Dubeuf, 2011).

Thyroid hormones play an important role in seasonality of reproduction among many animal species including birds, rodents and mammals (Moenter *et al*.,1991; Dahl *et al*., 1995). Temperature control of neonates at birth is dependent mainly on heat production by oxidation of fat from brown adipose tissue (BAT) by a process under the control of T_3 (Dauncey, 1990). Breeds of sheep with higher concentrations of plasma T_3 and T_4 had been shown to have a more active thyroid and BAT than those with low T_3 and T_4; thus, cold thermogenesis is more efficient in the breed with higher concentrations of T_3 and T_4 (Symonds*et al*., 1989;Dwyer and Morgan, 2006). Similarly, breeds of sheep with higher concentrations of plasma T_3 and T_4 had higher rectal temperature and were quicker to stand and suckle from their dams (Dwyer and Morgan, 2006). Thus, the ability of animals to maintain homoeothermy is influenced by their serum TH concentration which may affect the behavior to stand and suckle after birth. Collectively, these factors may affect neonatal mortality. Thyroid hormones have been implicated in the negative energy balance during the course of some diseases and in the process of resumption of cyclic ovarian function in

ruminants(Huszenicza *et al*., 2002). Therefore, an understanding of the effect of endogenous factors such as breed, age and sex, and environmental conditions such as season on serum TH profiles, could allow the monitoring and manipulation of thyroid physiology, in a manner to improve animal health, welfare and production (i.e. improved growth rate, milk and hair fibre yield) (Todini, 2007). Thus, the need to generate reference data on TH in our local breeds of goats, for the purpose of research, production, diagnosis and treatment of thyroid abnormalities cannot be over emphasized.

1.3 Aims of the Study

To establish the base line values of serum T_4, $T_3$and TSH and evaluate the effect of breed, sex, age, BMI and season on serum concentrations of these hormones in theRSG and SHG.

1.4 Objectives of the Study

The following were the objectives of the study:

1. To obtain baseline values for serum T_4, T_3,TSH and T_4:T_3 in RSG and SHG.
2. To evaluate the effect of breed, sex, age and BMI on serum T_4, T_3 and TSH in RSG and SHG.
3. To determine the influence of season on serum concentration of T_4, T_3,TSH and T_4:T_3in RSG and SHG.

1.5 Null Hypothesis

Breed, sex, age, BMI andseason do not affect serum concentrations of T_4, T_3,TSH and T_4:T_3in RSG and SHG.

CHAPTER TWO

LITERATURE REVIEW

2.1 Goat Production

As at 2013, the world goat population was approximated to bemore than one billion(FAO, 2013), with 95% of this population being in developing countries (Devendra, 2000). The largest population of goats is in Asia. This is primarily due to a huge population in China. Africa has a goat population of 351.9million; Nigeria with a population of 57.3 million contributes largely to this.The world's goat flock is the third largest after cattle and sheep (FAO, 2013). There has been a regular increase in goat stocks world-wide, and this increase involved particularly the countries with low income (70%), but also in countries with high and intermediate income (20 and 25%, respectively). Goats account for 30% of Africa's ruminant livestock and have an estimatedpopulation of 147 million in sub-Saharan Africa (Lebbie, 2004).

The high protein and low fat content of goat meat, makes it a nutritionally desirable alternative of red meat (Johnson *et al.*, 1995). Over the last 20 years, the world goat meat production hasrisen rapidly from 5-6% to 125%, while theworld goat milk production rose rapidly from2-2.5% to 70%, when compared to all other species(FAO, 2013). In Africa alone, goatmeat and milk productions have risen by 17% and 12%, respectively(Devendra, 2001). Though there is no comprehensiveinformation on goat milk production in Nigeria, meat production is up to 0.29 million metric tons (FAO, 2013).In developing countries, less than 5% of all marketed milk is obtained from goats (Dubeuf *et al*., 2004).China and India produce about 45% of the world's goat skins. Developing countries produce and use about 95% of the goat skin they produce, while some of the better skins are finished in developed countries (Morand-Fehr *et al.*, 2004).

In developing countries, goats play a vital role in the economy of many poor livestock owners who earn their livelihood by rearing these animals throughout the year on different terrains (Sharma *et al*., 2013; Habibu *et al*., 2014). Goats can survive in very harsh environments because of several adaptation mechanisms, which include the capacity of walking distances, the ability to select the most nutritive plants or plant fractions, the efficient digestion of the less nutritive fractions rich in fibre due to a very intensive urea cycle, among others. Rearing goats tend to be easier because of their little demand for feedsince they can graze on bushes, shrubs and range vegetation, which cattle and sheep accept poorly. Also, starting a goat farm requires less investment than cattle or sheep, particularly to buy live animals in order to establish a goat flock. This could be a major reason for recent advancement in goat population and production (Morand-Fehr *et al.,* 2004).

The continuous and rapid increase in goat population and products in developing countries, especially among the poorest of those countries, indicates that goats might serve as a solution to the nutritional challenges accompanying the continuous increase in human populations (Boyazoglu andMorand-Fehr,2001). The use of goats in events of religious and traditional festivals makes the animal a cultural asset, as opposed to one of purelyeconomic interest (Alexandre *et al*., 2002). On the contrary, social disregard for and rejection of goat milk, yoghurt, cheeses or meat in some countries and cultures are factors militating against goat production (Morand-Fehr *et al.,* 2004).

2.2 Breeds of Goats

Worldwide, there are 102 recognised breeds of goats with live weights ranging from 9 to 13kg for small tropical breeds to over 100kg for large improved dairy breeds (Dhanda *et al.*, 2003). The majority of goat breeds in the temperate regionshow seasonality in

reproductiveactivities (Chemineau *et al*., 1992a). Generally, goats may be distributed into those used for meat, dairy, skins, fibre production, and as companion animals.

The West African dwarf, Red Sokoto and the Sahelian (White-Borno) goat breeds are the most common in Western Africa,while the Omani breed is predominant in North Africa. In East Africa, the Kigezi breedis the most common, while in South Africa, the Small East African breedis more predominant. Despite the large genetic resources of the goats in Africa, there has been no deliberate effort to conserve and improve the good genetic traits of these breeds (Otoikhianand Orheruata,2010). Small ruminant breeds in tropical Africa are characterised by small birth weights, low milk production, slow growth rates and small mature weights **(**Mack, 1983**)**.

Substantial number of temperate animals show seasonality in breeding. The temperate breeds of sheep and goatsmeasure the day length (photoperiod) and use these measurements to predict and prepare themselves for annual breeding (Nakao *et al*., 2008).However, the arid, semi-arid tropical and subtropical breeds of goats and sheep are known to breed year-round, with environmental factors such as rainfall and feed availability influencing their reproductive activity (Martins*et al*., 2004).

In Nigeria, there are three distinct breeds of goats; namely Red Sokoto, Sahel and West African Dwarf goat breeds (Egwu et al., 1995). Production characteristicsof the small ruminant showed that breeds of goats in the country had low fertility rate, 40% twins and triplets birth rates, and low mortality rates of 22% for kids and14.4% for adults. The productivity indices for 90 and 180 days weaning age were 0.259 kgand 0.437 kg kid/kg doe respectively. Milk production characteristic of the goats vary frombreed to breed (FAO,

2001; Gall, 1996). The WAD breed produces about 0.4kg milk per day during a lactationperiod of 126 days (Lawal-Adebowale, 2012).

2.2.1 Red Sokoto breed (RSG)

In Nigeria, the RSG are widely distributed and are the predominant breed, constituting 70% of the country's goat population and about 12.5% of total African goat population (Osuhor *et al*., 1998; Habibu *et al*., 2014). Red Sokoto goats are uniformly dark red in colour. Both sexes are horned, with short hair and short horizontal ears (Adu *et al*., 1979). At 1 to 2 years old, the mean body weight, body length and height at withers for males are 16.67 ± 0.56 kg, 78.80 ± 0.82 cm and 56.44 ± 0.72 cm, respectively. The dimensions of the females are 16.16±0.55 kg, 79.49 ± 0.80 cm and58.49 ± 0.70 cm for body weight, body length and height at withers,respectively. At 3 to 4 years old, the weight, meanbody weight, body length and height at wither for males are 21.65 ± 0.68 kg, 85.43 ± 0.91 cm and 61.07±0.49 cm,respectively, while in females, there values are 22.94±0.47 kg, 87.33±0.64 cm and 62.77±0.37 cm,respectively (Hassan and Ciroma, 1992). The RSG produce a daily milk yield of about 0.5 to 1.5kg during a lactation period of 100 days (Lawal-Adebowale, 2012).

2.2.2 Sahel Goat (SG)

The Sahel or Desert breed of goat is foundin West Africa around the Sahel belt, south of theSahara. In Nigeria, these goats are found in the Sahel Savannah zone ofthe north-eastern, especially in Borno State where they are also referred to as Borno White goats (Figure2.1). They have floppy ears, long legs and are medium to large in size. Both sexes have horns (Ngere *et al*., 1984). The breed has a short, fine coat which is white in colour or sometimes mixed with brown or black. It has long pendulous ears, usually longer than the head (Cisse *et al.,* 2002).It has a well-defined body conformation when compared to West Africa Dwarf and

RSG. Its well-developed udder makes it a better dairy breed (Moruppa and Ngere, 1984). It produce between 0.8 and 1.0kg of milk daily over a lactation period of 120days (Lawal-Adebowale, 2012). The mean yearling weight of adult Sahel goats is 24.7 ± 5.3 kg for males, 21.6 ± 5.1 kg for non-pregnant females and 27.7 ± 6.4 kg for those with pregnancy over four months (Mohammed and Amin, 1996). In southern Nigeria, these goats have been used to improve the genetic make-up of West Africa Dwarf breeds of goatsto enhance productivity (Otoikhian and Orheruata, 2010).

2.3 Seasons in Nigeria

There are three seasons in the northern Guinea savannah zone of Nigeria (Figure2.1), namely: cold-dry (harmattan; November–February), hot-dry (March–April) and rainy (May–October) seasons (Igono and Aliu,1982; Dzenda *et al*.,2011). The hot-dry season is characterized by high ambient temperature (AT) and long duration of sunshine (Adenkola *et al.*, 2011; Habibu *et al*., 2014). The harmattan is characterized by relatively higher AT in the afternoon and low AT of about 10 ^{o}C in the evening and early morning hours. During the harmattanseason, the wind is cold-dry and dust laden (Igono and Aliu, 1982).Of all the seasons, the rainy season has the highest annual rainfall andrelative humidity. These seasons are known to influence livestock production in the tropics (Ayo*et al*., 1998).

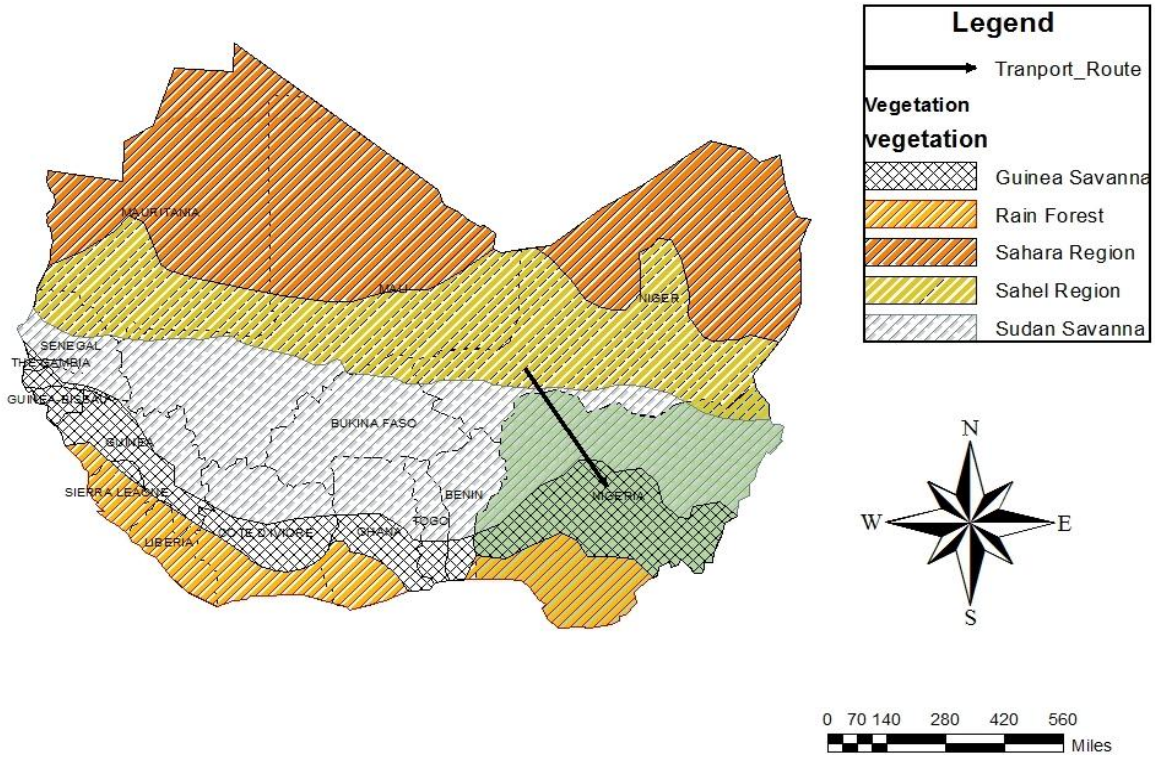


Figure2.1: Map of West Africa indicating the geographical areas and transportation of Sahel goats

2.4 The Thyroid Gland

The thyroid gland and the thyroid system in mammalian species are known to be extremely conserved. This indicates that they are critical for species survival (Choksi *et al*., 2003).Species and breed differences exist in the anatomy of the gland. The isthmus which connects the two lobes of the thyroid is the region that varies markedly between species. Humans and the pig have a large discrete isthmus that forms a pyramidal lobe connecting the two lateral lobes. The cow has a fairly wide band of glandular tissue that forms the connecting isthmus. The isthmus in goats, horses, sheep, cats, and dogs is a narrow remnant of tissue and may be nonexistent. The size of the thyroid relative to body weight is very small in all animals, approximating 0.20% of body weight (Singh and Beigh,2013).

Thyroid gland proliferation is under the control of a number of hormones and growth factors,effected through paracrine and/or autocrine actions (Eggo, 2010). Thyroid-stimulating hormone (TSH) plays a predominant role in regulating thyroid cell function and proliferation (Medina and Santisteban, 2000). However, unlike other growth factor receptors, insulin R (or IGF-IR) activation is obligatory for expression of TSH-mediated function and proliferation (Grozovsky *et al*., 2007).

The continuous synthesis of THs by the thyroid follicular cells require a medium supplying nutrients, iodide, TSH and insulin-like growth factor I (IGF-I) or insulin(Eggo, 2010). Some signalling pathways activated by certain cell receptors interact with TSH to modulate the activities of the thyroid gland. The p42/44 mitogen-activated protein kinase (MAPK) pathway is activated by many growth factors, with some being produced by thyroid cells (Bidey *et al*., 1999).This pathway is generally mitogenic, but also regulates differentiation (Ragno *et al*., 1998). The phosphoinositide 3 kinase (PI3K) pathway is coupled to growth factor receptors and thyroid hormone receptors as well. This pathway is rather prosurvival

than mitogenic and also regulates differentiation. Also, activation of isoenzymes of protein kinase C(PKC) occurs when phospholipases are activated by Gq/11protein-coupled receptors and receptor tyrosine kinases(RTKs). In thyroid cells, PKC activation inhibits iodidemetabolism. Equally, phospholipase action invokescalcium-regulated pathways, which also regulates differentiation. Activation of PKC occurs when phospholipases are activated by Gq/11 protein-coupled receptors and RTKs (Wipff and Hinz, 2008). This pathways and receptors in or on thyroid cellspredispose theiractivities tomodulation by endogenous factors (Eggo, 2010).

2.5 Biosynthesis and Metabolism of Thyroid Hormones

Thyroid hormones [3,5,3'-triiodothyronine (T_3) and 3,5,3',5'-tetraiodothyronine (thyroxine or T_4)], are iodinated derivatives of the amino acid tyrosine. The assembly of thyroid hormones occur within the follicular lumen of the thyroid gland on a protein called the thyroglobulin (Capen and Martin, 2003). Biosynthesis and secretion of thyroid hormones involves several steps, including the following: (i) iodide uptake from the blood stream into the thyroid by the sodium/iodide symporter and its transport into the follicular lumen, which is partly mediated by pendrin; (ii) oxidation of iodide, which involves thyroperoxidase and H_2O_2 generated by dual oxidases; (iii) iodination of thyroglobulin; (iv) storage of thyroid hormones in a form bound tothyroglobulin; and (v) reabsorption and hydrolysis of follicular thyroglobulin and secretion of thyroid hormones (Yoshihara *et al*., 2012).

Thyroid stimulating hormone (TSH), which is secreted by the anterior pituitary gland, regulates the synthesis and the secretion of TH. A functional TSH has two subunits namely: TSHβ subunit and common pituitary glycoprotein α-subunit.TSHβ is responsible for regulating the biological specificity and synthetic rate of TSH (Pierce and Parson, 1981). In the hypothalamus, thyrotropin releasing hormone (TRH) and dopamine can also rapidly

regulate the transcription of TSH subunit genes. With dopamine both subunit genes appear to be suppressed, but with TRH treatment,α-subunit and TSHβ mRNA synthesis were increased (Shupnik *et al*., 1986). Also, plasma TH levelsthrough a negative feedback mechanism, act on the hypothalamus to regulate TSH synthesis by decreasing the rates of transcription of the **α**and TSHβ subunit genes, with the TSHB gene being more severely affected **(**Shupnik *et al*., 1985**).** The plasma levels of TH also exert a negative feedback control on the pituitary. Equally, several factors influence the activity of thyroid and plasma levels of the hormones, acting at the levels of hypothalamus, pituitary and/or thyroid gland, or by peripheral monodeiodination of the hormones (Todini, 2007).The thyroid gland predominantly secretes the inactive prohormone T_4, as well as small amounts of the physiologically active thyroid hormone T_3.

Thyroxinebinding globulin (TBG), transthyretin, albumin, and several lipoproteins function as the transport proteins for T_4 and T_3 in plasma(Williams and Bassett, 2011).Free thyroid hormone levels are thus dependent upon the concentrations and saturations of these proteins. In adult sheep more than 99.9% of T_4 and 99.5% of T_3 circulate in blood bound to plasma proteins (Chopra *et al*., 1975). Thyroxin is exclusively synthesized and secreted by thyroid follicular cells, whereas the majority of circulating T_3 isgenerated in peripheral tissues by enzymatic removal of a 5'-iodine from T_4 (Friesema *et al*., 2005).

2.6 Physiologic Effects of Thyroid Hormones

The main physiologic functions of TH are to increase cellular glucose availability, stimulate protein synthesis, increase lipid metabolism, stimulate cardiac function, increase oxygen utilisation and heat production in all cells of the body (Capen and Martin, 2003). Hence its use as an index of metabolism in several studies (Pereira*et al*., 2008;Haque *et al*.,

2012)Thyroid hormones are critically involved in the development, plasticity, and functioning of the central nervous system (Bernal, 2002). Experimental studies have shown thatunder normal conditions, thyroid hormones may influence the expression or activation of uncoupling protein, β-adrenergic receptor, and peroxisome proliferator-activated receptor-gamma, all of which are involved in regulating insulin sensitivity (Dallongeville *et al*., 2003; Wang *et al*., 2004). Hence, in obese diabetic rodents, treatment with thyroid hormone enhanced insulin sensitivity and reduced hyperglycaemia and hyperinsulinaemia (Koritschoner *et al*., 2001). Thyroid hormone, have been reported to regulate thermogenesis through a mitochondria protein called uncoupling proteins (UCPs)(Gong *et al*., 1997). The UCPs transport fatty acid anions from the inner surface to the outer surface of the inner mitochondrial membrane (Garlid *et al*., 1996). At the outer surface the anions are protonated and the neutral molecules return inside. The net result is the exothermic movement of protons from outside to inside of the inner mitochondrial membrane, down their concentration gradient (Gong *et al*., 1997). This proton dissipates energy as heat instead of being used for adenosine triphosphate production (Nicholls and Locke,1984). In ovine lungs, both maternal cold exposure and maternal nulliparity enhanced UCP2 abundance in the offspring compared to maternal non-cold exposure and maternal multiparityrespectively (Yakubu*et al*., 2007).

2.7Activity of Thyroid Hormone Receptors

Thyroid hormones have three types of receptors. The avb3 integrin receptor is located on the plasma membrane, whereas the classic nuclear receptors TRα1 and TRβ1 may shuttle between the nucleus and the cytosol (Lin *et al*., 2009).While, most of the physiological actions of TH are mediated by binding to nuclear receptors and effected through genomic response, some of the actions are rapid and non-genomic (Davis *et al*., 2005). Thyroid hormone receptors (TRs) are members of the superfamily of nuclear receptors (DeGroot *et*

al., 1989). In the absence of a ligand, these receptors bind to thyroid response elements (TREs) and repress expression of target genes by virtue of interaction with co-repressors (Oetting and Yen, 2007). There are two TR genes, THRA and THRB, each of which produces two mature transcripts. The TRa1 and TRa2 (c-erbAa-2) transcripts and proteins are derived as alternative splice variants of THRA. Although TRa2 binds to TREs, it is unable to bind ligand and therefore represses transcription. TRb1 and TRb2 aretranscript/protein variants of THRB generated by use ofalternative promoters. The TRs bind to TREs as homodimers,or as heterodimers with 9-cis retinoic acid receptors(RXRs). The TR/RXR heterodimers likely play an importantrole in mediating response to thyroid hormones. Although TRs bind to TREs as either homo or heterodimersin absence of bound ligand, the ligand-bound TRs bind toTREs primarily as heterodimers with RXR (Yen, 2001).

2.8Thyroid Hormones Deiodinase Enzymes

Since T4 has a long half-life (1 week in humans and 1 day in rats), the role of hypothalamus–pituitary–thyroid axis in the regulation of T_4 bioavailability is complemented by the expression and activity of iodothyronine deiodinases (Kuiper *et al*., 2005). Iodothyronine deiodinase or deiodinase enzymes are critical regulators of plasma and intracellular action of THs (Salvatore, 2011). They are selenoproteins, with differences in structure and tissue distribution among various species (Chadio *et al*., 2006). The deiodinase type 1 (Dio 1) or type 2 (Dio 2), generally activate the inactive T_4 by deiodinating it to T_3 (Williams and Bassett, 2011). Most of the circulating T_3 is derived from conversion of T_4 to T_3 by the actions of Dio 2. The major role of Dio 2 is to control the intracellular T_3 concentration, its availability to the nucleus, and the saturation of the nuclear T3 receptor in target tissues (Williams and Bassett, 2011). Another deiodinase, deiodinase type III (Dio 3), deiodinate the inner ring of both T_3 and T_4, thereby inactivating and converting them (Dentice and

Salvatore, 2011) to 3,3'- diiodothyronine (T_2) and reverse 3,3',5'-triiodothyronine (rT_3), respectively (Kaiser *et al*., 1986). For this reason, Dio3 is considered to be the major physiological inactivator and terminator of TH actions at peripheral level (Salvatore, 2011). Though reverse T_2 is considered biologically inactive, because it does no bind to nuclear receptors, it is a powerful inhibitor of Dio 2(Kaiser *et al*., 1986).Administration of T_2 to rats resulted in a decrease in serum TSH, T_3, and T_4 in a T_2 dose-dependent manner,whereas oxygen consumption increased in these animals, indicating the direct action ofT_2 on this physiological variable (Padron *et al*., 2014). Dio 3 has also been implicated in the hypothyroid status of critically ill patients (Huang and Bianco, 2008). While T_4 is the most potent post-transcriptional inactivator of Dio 2, T_3 rapidly induces the Dio 3 enzyme at transcriptional level (Salvatore, 2011).

Dio 1 and 2 are outer-ring deiodinase and are referredto as 5'-deiodinase enzymes (5'D), while D_3 is an inner-ring deiodenase and is referred to as 5-deiodinase (5D) enzyme.Both Dio 2 and 3 collectively control cellular T_3 availability by a mechanism that is largely independent of serum TH concentrations (Bianco and Kim, 2006).Through Dio 2 primarily, pituitary and hypothalamic cells can monitor both serum T_3 and T_4 independently and influence TSH release, accordingly (Salvatore, 2011). While the liver and the kidney show the highest deiodinating activity, it occurs in most if not all tissues (Chadio *et al*., 2006).

In the developing foetus, where low plasma T_3 is necessary for the proper development and growth of foetal tissues, Dio 3 is highly expressed in the placenta, the endometrium and other embryonic tissues. Consequently,the free T_3 in the foetus is almost ten-fold lower than that in the maternal plasma, while reverse T_3 is very high (Salvatore, 2011).In the plasma,deiodinases serve as an effective homeostatic mechanism, acting as the first line of

defenceduring iodine deficiency and chronic illness (Wartofsky and Burman, 1982); and thyroid dysfunction in order to maintain plasma T_4 or, at a minimum, plasma T_3 at a constant level (Salvatore, 2011).

2.9Thyroid Hormones Transporters

Specific transport mechanisms involving TH transporter proteinsare required for the transport of TH across cells (Bernal, 2006). The TH transporter proteins include system-L (L-type amino acid transporter 1 and CD98), monocarboxylate transporters (MCTs) 8 and 10, and organic anion-transporting polypeptides 1A2 and 4A1 (Loubière*et al*., 2012). These mechanisms of transportation are critical for TH action, and the existence of these transporter families represents a new mechanism through which TH metabolism and action are regulated (Dentice and Salvatore, 2011).

2.10 Thyroid Hormones Metabolism and Excretion

In mammals, sulfation of TH is catalysed by sulfotransferases, while desulfation is catalysed by arylsulfatases. Generally, sulfation plays a role in detoxification processes in a biological system. It increases the water solubility of hydrophilic substances, such as TH, hence facilitating their urinary and biliary excretion. During TH metabolism, sulfation also allows for the transport and temporary storage of receptor-inactive T_3-sulfate which can be reactivated in the presence of sulfatases (Darras *et al*., 2000). The role of sulfation in TH deiodination has been demonstrated in rats. Sulfated iodothyronines are not substrates for deiodination by Dio 2 and Dio 3. On the other hand, sulfation greatly facilitates the inner ring deiodination of T_4, while the outer ring deiodination of T_4 is completely blocked by sulfation. Inner ring deiodination of T_3-sulfate by Dio 1 is facilitated in a similar way, while outer ring deiodination of rT_3 remains unaffected after sulfation (Visser, 1990). Thyroid hormones can

also be inactivated by glucuronidation in the liver and secretion into bile (Chopra *et al*., 1978).

2.11Role of Thyroid Hormones in Reproduction

2.11.1 Female reproduction

While the temperate breeds of goat and sheep show aperiod of quiescence and renaissance (Nakao *et al*., 2008), those in the tropics display only a period of quiescence. Nevertheless, in both the temperate and tropic environment, offsprings are produced and raisedin seasons in which the climate ismoderate and feedavailability is high(Ikegami and Yoshimura, 2012).The photoneuroendocrine system which consist of the retina, the suprachiatic nucleus (that serves as the circardian clock) and the pineal gland (that secretes melatonin at night), regulate the ambient photoperiod in mammals that show seasonality in reproduction (Reiter, 1987). Melatonin secreted at night act on the mediobasal hypothalamus(MBH) and pars tuberalis to express photoperiodism. The signals are then decoded to control the gonadal axis, through the secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus and a preceding release of gonadotropins (luteinizing hormone [LH]) and follicle-stimulating hormone [FSH]) from the pituitary gland(Nakao *et al*., 2008).Thoughmelatonin is secreted at night in both mammals and birds, it has little or no involvement in thephotoneuroendocrine system in the avian species (Juss *et al*., 1993; Gwinner *et al*., 1997).

In both mammals (Nicholls *et al*., 1988) and bird (Bentley *et al*., 1997), TH have been reported to be involved in seasonality of reproduction in temperate regions. Amongst mammals, sheep, goats and hamsters show seasonality in breeding. Goats and sheep breed during the short days (SD), when the period of melatonin production is prolonged. While melatoninsuppresses gonadotropin release in hamster during SD season, but has a stimulatory effect in sheep (Bittmanand Karsch, 1984) and goat (Delgadillo *et al*., 2001).

Birds experience a wave of gonadotropin hormones secretion only during long days (LD)(Nicholls *et al*., 1983). Of all animal species, birds have the most sophisticated photoperiodic mechanism, with quails being the excellent model for studying photoperiodism (Nakao *et al*., 2008). Thus, quail is the best model for deciphering the effect of TH on animal reproduction. However, it is important to note that while LD activate the breeding season of birds (Nicholls *et al*., 1983), SD activate the period of reproductive recrudescence in sheep (Bittman and Karsch, 1984) and goats (Yasuo *et al.*, 2006).

In quails, exposure tolong days initially induces the expression of the beta-subunit ofthyroid-stimulating hormone (TSHB) in the pituitary gland (Nakao *et al*.,2008), and TSH isformed by heterodimerization of TSHB and the common glycoprotein alpha subunit (CGA). Thyroid-stimulating hormone acts on the TSH receptors (TSHR)inthe ependymal cellslining the ventrolateral walls of the third ventricle (i.e.,the infundibular recess) within the MBH toinduce the expression ofDio 2 (Nakao *et al*., 2008), a thyroid hormone-activating enzyme that converts the prohormone T_4 tobioactive T_3. Although the expression ofathyroid hormone-inactivating enzymeDio 3, inthe ependymal cellis induced under short-day conditions and suppressed under long-day conditions (Yasuo *et al*.,2005), the regulation of Dio3 expression by TSHR activation is yet to be demonstrated (Goto *et al*., 2013).These reciprocal responses of Dio 2 and Dio 3 to photoperiod seem toeffectively regulate the amount ofbioactive T_3 within the MBH. In line with this, Yoshimura *et al*. (2003) demonstrated a ten times higher levels of T_3 in the MBH of quailsduring LD compare to SD, with no difference in plasma levels of T_3 in the plasma and other parts of the brain. Probably through the effects of TH on CNS development and neuronal plasticity (Bernal, 2002), the long day-induced accumulation ofT_3 appears to activate the gonadal axis by causing

morphologic changes that alter the neuro-glial interaction between gonadotropin-releasing hormone terminals and tanycytes inthe median eminence (Yamamura *et al*.,2004;Yamamura *etal*.,2006).Photoperiodic changes in the expression of TSHB, Dio2, and Dio3 have also been shown in several mammalian species, namely; goats (Yasuo *etal*.,2006), sheep (Hanon *et al*.,2008) and hamsters (Barrett *et al*.,2007;Revel *et al*.,2006). Inmammals,the photoperiodic melatonin signal is the primary regulator ofthe TSH-Dio2-T3 cascade (Yasuo *et al.,* 2007; Revel *et al*.,2006), but the exact mode ofaction ofmelatonin on this cascade remains unclear (Goto *et al*., 2013).From the earlier mentioned reports, it is clear that the local activation of the T_3 within the MBH, induced by long-day conditions, plays a key role in photoperiodic regulation of seasonal reproductionin both mammal and birds (Nakao *et al*., 2008;Ikegami and Yoshimura, 2012).

Two groups of Alpine goats (seasonal breeders) exposed to tropical and temperate photoperiod showed seasonality of estrus and ovulatory activities.The seasonal anestrus in both groups occurred during the same period under the temperate (8 to 16 h of light per day) andtropical (11 to 13 h of light per day) photoperiodic cycle (Chemineau*et al*., 1992).

A marked seasonality in the ovulatory activity of tropical Creole goats and Black-Belly ewes was induced when females were exposed to a simulated temperate photoperiod. Unexpectedly, and differing from the results obtained in their original breeding location, Black-Belly ewes and, to a lesser extent, Creole goats exposed to a simulated tropical photoperiod also showed significant seasonality in their ovulatory activity. This unexpected difference suggests that other external factors such as temperature may act in combination with photoperiod to inhibit breeding activity (Chemineau *et al*., 2004).A recent study in goats, demonstrated five mutations in the TSHB gene, of interest is the fact that the genotype distribution of both single locus and haplotype were significantly different between seasonal

and non-seasonal goat breeds. The five closely linked mutations of TSHB may be the casual cause of the diversities of reproductive seasonality and this information could possibly be used to develop techniques aimed at decreasing reproductive seasonality in goat (Huang *et al*., 2013).

It is also noteworthy that in goats, which breedunder short-day conditions, a long-day stimulus suppressedthe expression of Dio 2.This effect was contraryto that observed in species that breed under longdayconditions (Yasuo *et al*., 2006). Thyroidectomy in Cashmere goats in late breeding season advanced the onset of seasonal anoestrus34 days earlier than in control, while anoestrus persisted throughout the course of the experiment (Walkden-Brown *et al*., 1996).More studies have been conducted in thyroidectomised sheep than goats and contrary results were reported (Todini, 2007). Thyroidectomised ewes began their sexual season at the same time as intact animals, but continued to cycle when the intact ewes entered seasonal anoestrus (Nicholls *et al.,* 1988; Maurenbrecher and Barrell, 2003).Hence, the function of the thyroid hormone in influencing seasonal activity is believed to be limited to a specific seasonal window (Thrun *et al*., 1997, Billings *et al*., 2002).Thyroid hormones are necessary during a limited period late in the breeding season to allow transition to seasonal anoestrus (Thrun *et al*., 1996 and 1997a), acting mainily within the brain to promote inhibition of neuroendocrine reproductive function (Viguie´ *et al.,* 1999). Thyroid hormones permit the increase of the responsiveness to the oestradiol negative feeback, but are also required for steroid-independent seasonal cycles in luteinising hormone pulse frequency (Anderson *et al.,* 2002). Since the onset of the subsequent breeding season was not affected by thyroidectomy during anoestrus, the permissive role of TH appeared to be limited to changes related to transition to seasonal anoestrus, (Thrun *et al*., 1997b). Thus, it could be

asserted that TH may be required for the long-term expression and maintenance of the endogenous seasonal reproductive rhythm in animals(Billings *et al*., 2002).

2.11.2Male reproduction

Experimentally induced hypothyroidism in goats resulted in a significant decrease in plasma testosterone levels when compared with the control goats (Gupta *et al*., 1991). In adult rams, thyroidectomy abolished seasonal cycles of gonadotropin secretion and decreased testicular size (Parkinson and Follett, 1994 and 1995).Furthermore, in the goat testis, it has been shown that T_3 induces the synthesis of a soluble protein in the Leydig cells, which stimulates androgen release (Jana and Bhattacharya, 1994; Jana *et al*., 1996).

Sertoli cells (SCs) play important roles in spermatogenesis. They create cytoplasmic crypts around germ cells and providenutrients and growth factors. The number of Sertoli cells determines the efficiency of spermatogenesis,as one Sertoli cell can only support a limited number of germcells (Orth *et al*., 1988).Follicle-stimulating hormone required for prepubertal Sertoli cell proliferation in several species. A number of facts suggest that Sertoli cell proliferation,arrest and differentiation depend mainly on T_3(Jannini *et al*., 1995;Holsberger and Cooke, 2005). In rodents, abnormally high levels of serum T_3 during the neonatal period cause Sertoli cells to exit the cell cycle resulting in fewer adult Sertoli cells and smaller testes(Cooke *et al.,* 1994);while abnormally low levels of T3 prolong the period of Sertoli cell proliferation resulting in an increase in their numbers, testicular size and sperm production in adulthood (Cooke *et al*., 1994; Van Haaster *et al*., 1992).It has also been reported that T_3 limits postnatal Sertoli cellproliferation byactivation of TRalpha1 present in these cells (Fumel *et al*., 2012). Ina recent study involving lamb ram, TH levelswere high as SC exited the cell cycle, and decreaseonly at the end of the first wave of spermatogenesis

whenmost Sertoli cell have stopped dividing and were close tohaving complete germ cell support systems in ram lambs (Oluwole *et al*., 2013).

2.12 Factors Influencing Plasma Concentrations of Thyroid Hormones

Differences in thyroid function are caused by a combination of genetic factors (such as breed and sex) and environmental factors (such as season and nutrition)(Hansen *et al*., 2004). Several studies have demonstrated marked seasonal variation in thyroid activity and in blood thyroid hormones concentration. These hormonal variations are particularly important in the free-ranging and grazing animals,such as goats(Todini *et al*., 1992) and sheep (Souza *et al*.,2002). Such variations in hormone concentration, allow the animals to adjust their metabolic balance to different environmental conditions, nutrients requirements and availability, and to homeoretic changes during different physiological stages (Todini *et al*., 2007).

2.12.1Ambient temperature

The major exogenous regulator of thyroid gland activity and plasma thyroid hormones concentrations is ambient temperature. Low temperature stimulates,while high temperature inhibits thyroid activity in sheep (Valtorta *et al*., 1982) and goats (Todini *et al*., 1992; Ribeiro et al., 2015). Heat stress is known to decrease; blood T_3 and T_4 concentrations (Sharma *et al*., 2013), metabolic rate, feed intake, growth and milk production(Valtorta *et al*., 1982; Silanikove,2000). While cold stress in sheep (Hocquette*et al*., 1992;Ekpe and Christopherson, 2000;Doubek *et al*., 2003) induces increased blood THlevels. Breed differences in T_3response to thermal stress have been reported in cattle. Compared with the thermoneutral condition, thermal stress caused a decrease in blood levels of T_3,with the exotic cattle breed being more severely affected than the local breed (Pereira*et al*., 2008).The

decrease in thyroid hormone levels during heat stress is an adaptive response whichmight be an attempt to reduce metabolic rate and heat production (West, 2003).The seasonal pattern of blood TH levels oftenshowed maximal values during winter (cold months) andminimal values during summer (hotter months)(Salem *et al*., 1991;Webster *et al*., 1991; Okab *et al*., 1993; Menegatos *et al*.,2006).

Rearing animals in environments with low ambient temperature stimulates the hypothalamic-thyroid axis which increases the hypothalamic release of TRH, resulting in enhanced TH production (Symonds *et al*., 1996). On exposure to cold, lambs with low plasma T_3 concentrations relied more on shivering thermogenesis, while those with greater concentrations of T_3, depended more on nonshivering thermogenesis (Symonds *et al*., 1989).The increase in thyroid hormone production and semen quality of rams in the colder season of the year (Griffin *et al*., 1962) indicate an intimate link between thyroid function and pituitary gonadotropin secretions which control the reproductive system (Souza *et al*., 2002). However, in instances where temperature ranges are not extreme (mild climate, indoor housing, shelter in the night time), the effect of photoperiodic seasonality on TH profiles prevail over ambient temperature (Todini, 2007).Response of animals to changes in factors that influences serum TH are not immediate or sudden, but rather delayed. Changes caused byphotoperiod (Todini *et al*., 2006) have been reported to be characterised by such response.

2.12.2 Photoperiod

While local availability of thyroid hormone within the MBH, induced by long-day conditions, plays a key role in photoperiodic regulation of seasonal reproduction (Nakao *et al*., 2008)in the plasma, spring (increasing daylength) is characterised by high TH values, but autumn (decreasing daylength) by low TH concentrations (Menegatos *et al*., 2006; Todini *et al*.,

2006).Menegatos *et al*. (2006) reported that serum thyroxine levels in ewe showed a typical photoperiodic seasonal pattern, regardless of the reproductive status,displaying the dominance of photoperiodic seasonality in this species.

In ewes(Menegatos *et al*., 2006) and goats (Błaszczyk *et al*., 2004) that breed naturally in the spring and autumn respectively, oestrus cycle is characterised by higher serum T_4 profilein the spring than in the autumn.In a related study, oestrus cycle in cold-dry season in the tropics was characterized by higher serum T_4 thanthe hot-dry season cycles (Kawu*et al*., 2013).This suggests the dominance of ambient temperature in influencing serum concentration of T_4 in the tropics. Notwithstanding, the small amplitude of photoperiodicity changes in the tropics (Chemineau *et al*., 2004) may also contribute to changes in serum TH profiles in the animals.

Photoperiodic changes in TH have a close link with melatonin. In goats (Błaszczyk *et al*., 2004), rats (Rom Bugoslavskaia and Shcherbakova, 1986) and Syrian hamsters (Vaughan *etal*., 1984) melatonin seem to increase serum T_4concentration in the long-day, but decrease it in the SD. Since nocturnal melatonin secretion is higher than diurnal secretion (Reiter, 1991) and higher melatonin secretion occurs in short-day (antumn) than in long-day(spring) (Błaszczyk *et al*., 2004), the increase and decrease in serum T_4 concentration caused by melatonin in spring and autumn, respectively,could explain why long-day is characterized by higher serum TH levels than short-day.

Exposure of Alpine and Saanen bucks to artificial photoperiodic cycles resulted in plasma T_3 levels rapidly following the photoperiodic changes, increasing during long-day and decreasing during short-day. The effects of day-length changes, on plasma T_4 concentrations

were seen after a delay of several weeks and the T_3:T_4 ratio showed very marked variations, increasing during long-day and decreasing during short-day (Todini *et al*., 2006).

2.12.3 Effect of breed on serum TH concentration

There is littleinformation on influence of goat breeds on TH profiles (Todini, 2007). Dairy goat breed have been shown to have higher T_3, but lower T_4 compared to meat breed.The management practices associated with differences in types of goats (meat and dairy) may be responsible for this (Kouakou *et al*., 2012). At birth, Blackface lambs had higher $T_3$and T_4 levels than Suffolk lambs and this was correlatedwith higher body temperature and better thermoregulatoryability. However, the ratio of $T_3$to T_4 was equal in both breeds immediately after birth (Dwyer and Morgan, 2006). Lamb breeds that were usually reared underextensive conditions (hilly regions) have an improved thermoregulationthan those reared intensively in lowlands. This beingpartly related to birthcoat characteristics, accompanied byhigher TH concentrations (important for endogenous heatproduction and hair growth) in hilly than lowland lambs(Dwyer and Lawrence, 2005). The role ofmaternal cold exposure in enhancing UCP2 abundance in the offspring (Yakubu*et al*., 2007) mayalso play a role in thermoregulatory adaptation of the offspring.In general, larger body size, enhanced growth potential (Williams *et al*., 2004), and higher prolificacy (Fallah-Rad and Connor, 1999) are important factors associated with breed difference in serum TH concentrations in sheep. However,Gündoğan (2007)did not observe any breed difference in serum T_3 concentration of rams.

2.12.4 Influence of age on thyroid activity

In the pregnant animals, a pre-partum increase in foetal T_3 profiles is accompanied by a rise in cortisol level (Sensky *et al*., 1994). Subsequently, the postpartum surge in thyroid hormone

production plays a critical role in thermoregulatory adaptation after birth (Heasman *et al*., 2000). Plasma T_3 concentration in vaginally delivered lambs increase rapidly from fetal values of <2 nmol/L to 6 nmol/L within 0.5 hour after birthand then gradually decline during the first 1 to 2 months of postnatal life but remain above adult values of 1 nmol/L (Symonds *et al*., 1989; 1994). Lambs delivered pre-term or at term that exhibit low plasma thyroid hormone concentrations are at much greater risk of hypothermia (Heasman *et al*., 2000).This is also the case for near-term lambs delivered by the caesarean route, which are characterized by lower plasma thyroid hormone concentrations than those born vaginally (Clarke *et al*., 1997)

Rise inneonatal plasma T_3 and fT_4followed that of TSH concentration, lasting for 24 h after birth, while T_4 levels declined whenTSH levels were still elevated (Cabello and Wrutniak, 1990). This means that the thyroid gland seemed unable to respond, in terms of T_4secretion, to a prolonged stimulation by TSH,probably because of depletion of hormonal stores in the gland which occur during the first minutes of life (Slebodzinski, 1972). Due to the expression of Dio 3 in the placenta, the endometrium and other embryonic tissues, foetal levels of rT_3 is very high (Savatore, 2011).Plasma rT_3 levels during the first 48 h of life progressively decreased in suckling lambs, while an opposite trend was observed in bottle-fed lambs (Cabello and Wrutniak, 1986 and 1990).

Blood TH were lower in lambs separated from their mothers just after parturition than in those maintained with their mothers (Firat *et al*., 2005). Neonatal lambs had higher levels of T_3 and T_4 compared with growing lambs and ewes (Peeters *et al*., 1992). In another study, lambs had significantly higher concentration of T_4 when compared to the 1 and 3-year old sheep,suggesting higher metabolic activity in the lambs (Novoselec *et al*., 2009).Similarly,

Kouakou *et al*. (2012) reported higher T_3 and T_4in matured goats than kids.In another study, however, neither age nor breed seemed to influence serum TH patterns(Peeters *et al*., 1989).

2.10.5 Influence of sex on thyroid activity

In young animals, there is no sex-dependent differences in blood TH concentrations, whereas in adult goats mean plasma TH levels were higher in does than in bucks (Todini *et al*., 1992). In young cashmere goats, T_3 levels were lower in males than in females after 8 months of age, while T_4 was not affected bysex (Celi *et al*., 2003). Sex-related differences in circulating TH have been reported in other mammals and were attributed to the activity of sex steroid hormones with differences in total T_4 levels being linked to oestrogen-reduced catabolism of thyroxinebinding globulin (TBG)(Ain *et al*., 1987); or androgen inhibition of the synthesis of TBG by the liver (Federman *et al*., 1958; Todini, 2007). Furthermore, androgens are known to inhibit TSH secretion by the pituitary (Christianson *et al*., 1981).

2.12.6 Relationships between circulating thyroid hormones and nutrition, feed in-take and weight gain

Nutrition

Nutrition is an important factor regulating reproductive function in domestic animals. Experimental evidence from cattle, sheep and laboratory rodents indicates that energy deficiency can inhibit reproductive function at various stages of the reproductive cycle (Schillo, 1992; Wade *et al*., 1996). Reproductive performance is commonly correlated with body weight changes. The onset of puberty in heifers depends on the body weight rather than the age (Tanaka *et al*., 2002). Plasma thyroid hormones levels correlated with feed intake in many ruminant species, including those which exhibit very marked seasonal cyclicity in feed intake, body weight and reproductive activity, such as deers (Chao and Brown, 1984) and

reindeers (Timisjarvi *et al*., 1994). Triiodothyronine directly stimulates feed intake at the hypothalamic level independent of changes in energy expenditure (Kong *et al*., 2004). Equally, type of diet may also influence the plasma thyroid hormone levels. Under different feeding conditions such as diet restriction, as observed in sheep (Rhind *et al*., 2000), or energy supplementation in lambs (Alshaikh *et al*., 1997), ewe (Shetaewi and Ross, 1991), and ram (Zhang *etal*., 2004), blood thyroid hormones levels served as good indicators of the nutritional status of animals (Riis and Madsen, 1985).In another study, T_3 had positively correlated with mean corpuscular haemoglobin concentration, serum glutamate, oxaloacetate transaminase, serum glutamate pyruvate transaminase, amylase, total proteins, total globulin, cholesterol and estrogen (Bhooshan*et al*., 2010).

Higher plasma TH concentrations were observed in lactating Angora does and their kids supplemented with energy and protein (horse bean) compared to control (Todini *et al*., 2005). Goats with a slightly higher energy intake showed higher plasma TH concentrations during the second half of gestation, and the associated mid- and late gestation decrease in plasma TH (Menegatos *et al*., 2006) was attenuated and delayed. These effects suggested that energy balance could play a major role in affecting the decline in plasma TH levels usually observed at the end of gestation in small ruminants (Todini *et al*., 2007). On the other hand, ewes fed low energy diet experienced a decrease in serum T3 (Rae *et al*., 2002). In contrast to the above findings, no significant difference in blood TH concentrations and in the rates of type II and type III deiodinase activity in the skin was found between cashmere goats maintained at high and low planes of nutrition (Rhind *et al*., 2006). Goats are traditionally reared in region where major fluctuations in feed availability occur through-out the year (Silanikove, 2000).This may result in variation in quality and quantity of feed in-take, and therefore affecting body condition (Schillo, 1992). Such fluctuations in feed availability influenced by

season may affect thyroid activity with higher profile during the seasonwith abundant feedand lower profile during the season with scanty feed (Todini, 2007).

Foetal metabolic programming is a phenomenon that links adverse exposures to certain factors during foetal life to altered body functions and health outcomes later in life. Such outcomes may include development of obesity, type 2 diabetes and cardiovascular disease (Johnsen *et al*., 2013). Some studies have reported the involvement of the hypothalamic–pituitary–thyroid axis in this phenomenon (Zahediasl, 2010). Both nutrient restriction in suckling rats (Bonomo *et al*., 2008; Lisboa *et al*., 2010) and foetal growth restriction in lambs (Rae *et al*., 2002) downregulated thyroid gland metabolism. In the study of Lisboa *et al*. (2010) involving rats, the thyroid gland metabolism remained downregulated into adulthood. In a recent study, late gestation under nutrition (LG-UN) unmistakably programmed the thyroid hormones axis resulting in adult hyperthyroidism associated with increased thyroid expression of genes regulating TH synthesis and deiodination. Also, LG-UN increased THR and deiodinase expression in some target tissues such as liver, cardiac muscle, and longissimus dorsi muscle but decreased THR and deiodinase expression in adipose tissues. Thus, LG-UN appears to program for differentiated thyroid hormones response or sensitivity in major target tissues. The programming effects mediated by LG-UN on TH signalling in target tissues were evident early in life, before LG-UN effects could be detected in circulating levels of T3 and T4 in serum. The effects of LG-UN were permanent and even more strongly expressed in adulthood. This could predispose to the development of obesity when nutrition is abundant (Johnsen *et al*., 2013).

Feed in-take

The involvement of hypothalamic-pituitary-thyroid (HPT) axis in regulation of body weight has been well established. Thyroid dysfunction usually have grievous consequences on appetite and weight (Wolf *et al*., 1996). Similarly, the direct role of the HPT axis in regulation of appetite, independent of energy expenditure has been reported. So also, the direct influence of TRH, TSH (Lin *et al*., 1983) and T_3 (Kong *et al*., 2004) on feed in-take has been documented. In addition to the direct stimulation of feed intake by T_3 at the hypothalamic level (Kong *et al*., 2004), T_3 is also involved in the seasonal regulation of appetite and body weight in hamsters which naturally shows seasonality in appetite, weight gain and reproduction (Murphy *et al.,* 2012). Centrally administrated TRH and TSH reduced food intake in rodents (Lin *et al*., 1983; Vijayan and McCann, 1877). A similar effect on food intake has been reported following peripheral administration of TRH (Choi *et al*., 2002).

Weight Gain and Growth

Blood levels of TH are regarded as good indicator of nutritional status of animals (Riis and Madsen, 1985). Nutritional status of goats can be calculated using the goat body mass index (Tanaka *et al*., 2002). In euthyroid humans, a positive correlation between BMI and serum TSHhas been reported (Iacobellis *et al*., 2005). However, the correlation between BMI and FT_4 was negative, while the correlation was positive with FT_3(Marwaha *et al*., 2013). Similarly, a slight elevation in serum TSH level was associated with an increase in the occurrence of obesity. In contrast, however,another study demonstrated no association between BMI and serum free T_3 levels (Knudsen *et al*., 2005).

Plasma TH levels positively correlated with lambs' birth-weight (Dwyer and Morgan, 2006), while T_4 correlated negatively with litter size in sheep (Stafford *et al*., 2007). Within breed,

heavy lambs had greater plasma T_3 and T_4 immediately after birth than light lambs (Dwyer and Morgan, 2006). Administration of prophyl thiouracil to pregnant ewes resulted in a severe decline in serum T_4 concentration. However, weight gain in the control compared with the prophyl thiouracil-treated pregnant ewes was not significant. Likewise, there was no significant difference in body weight between lambs of control and prophyl thiouracil-treated ewes (Gifford *et al*., 2007).

Growth

Early studies in goats demonstrated that thyroidectomy in kids caused a gradual cessation of growth. The injection of thyroxine or the feeding of thyroid caused a restoration of the growth (Reineke*et al*., 1941). Similarly, yearling rams with retarded growth had lower serum T_3 when compared to yearling rams without retarded growth. However, the latter study reported no difference in T_4 and TSH between the two ram groups (Kozat *et al*., 2007). Through the activation of PI3 K/Akt/mTOR pathway, T_3 have been reported to induce physiologic growth. Triiodothyronine regulates this pathway by the interaction of the cytosol-localized TRα1 with the p85α subunit of PI3 K (Hiroi *et al*., 2006; Kenessey and Ojamaa, 2006).

2.12.7 Influence of minerals and vitamins on serum thyroid hormone concentration

Selenium

Selenium is present in deiodinase enzymes, while other selenoproteins play a protective role for the thyrocytes against damage by hydrogen peroxide produced during TH biosynthesis (Kohrle *et al*., 2005). Selenium deficiency is associated with impaired growth, fertility and overall health of livestock (Weiss *et al*., 1990). Oral iodine and selenium supplements increased blood concentrations of TH in sheep, and selenium supplementation alone

increased plasma T_3, but decreased T_4 concentrations (Bik, 2003). Following selenium supplementation, type I deiodinase activity decreased in the liver and increased in the pituitary, while pituitary type II deiodinase was unaffected; indicating that enzyme activity is homeostatically controlled when a sufficient amount of selenium is present, in order to ensure TH homeostasis (Chadio *et al*., 2006). In another study, however, supplementation of Cashmere goats with seleniumdid not affect circulating TH levels, but improved the mRNA expression levels of skin type III deiodinase (Qin *et al*., 2013).

Iodine

In ruminants, iodine deficiency has been associated with late fetal development, early embryonic mortality, abortions, stillbirths, births of weak newborn, prolonged gestation, placental retention e.t.c. (Hetzel and Mano, 1989; Ferri *et al*., 2003). Iodine supplementation can modify the function of the thyroid gland through the secretion of TH (Randhawa and Randhawa, 2001; Qin *et al*., 2011).Supplemental iodine increased levels of TH and improved the mRNA expression levels of skin Dio 2 (Qin *et al*., 2013). Also, it increased FT3 concentration and FT3/FT4 ratio in dairy goats (Nudda *et al*., 2013). Dietary iodine requirements are increased in pregnancy due to increased thyroid hormone production, increased renal iodine losses, and foetal iodine requirements. Adverse effects of iodine deficiency in pregnancy include maternal and foetal goiter, cretinism, intellectual impairments, neonatal hypothyroidism, and increased pregnancy loss and infant mortality. Iodine deficiency during pregnancy, even when considered to be mild, resulted in enhanced or excessive thyroidal stimulation, leading to goitrogenesis in both the pregnant female and the foetus (Glinoer *et al*., 1990). Thus, pregnancy should be viewed as an "environmental" factor that could trigger the thyroid machinery and induce thyroid pathology in areas with a marginally reduced iodine intake (Glinoer, 2004). Dietary iodine requirement is high in

lactation due to the concentration of iodine in milk (Pearce, 2012), with the requirement being higher in goats compared with other ruminants (Meschy, 2000).

Cobalt

Ruminants require cobalt for ruminal microorganisms to synthesize vitamin B12. In mammals, vitamin B12 is an important cofactor for the enzymes -Co A mutase and methionine synthase, which are important for gluconeogenesis and methionine synthesis (Matthews, 1999). The major physiological effect of a Co-induced vitamin B12 deficiency is a progressive loss of appetite, which results in decreased weight gain, and in severe cases, weight loss (Underwood and Suttle, 2001). The element stimulates the growth of the thyroid gland. Importantly, cobalt deficiency is associated with a reduction in type I monodeiodinase activity and T_3 level (Stangl *et al*., 1999), while excess of cobalt may result in goitre and decreased production of thyroid hormone (Barceloux, 1999). Kozat *et al.* (2007) reported lower amounts of T_3, cobalt, and other minerals in yearling rams with retarded growth when compared with yearling rams without retarded growth.A significantly positive correlation was reported between FT_3 and zinc, FT_3 and manganese and copper, but a significantly negative correlation between manganese and T_3 (Nazifi *et al*., 2008)

Vitamin E

Vitamin E (α-tocopherol) and selenium (Se) have complementary role, as antioxidants, in the protection of cells against the damaging effects of lipid peroxides and free radicals produced during normal metabolism (Rooke *et al.*, 2004).Frequent administration of Vitamin E and selenium to pregnant ewes was characterised by higher serum T_3 concentration (Pavlata *et al*., 2004). Plasma level of T_3 was higher in lambs born from ewe treated with vitamin E than those born from control ewes (Soliman *et al*., 2012). A significant elevation in serum

concentration of T_4has been reported in ewes supplemented with Vitamin E2, Se + Vitamin E1 and Se + Vitamin E2 groups than in control and Se only groups (Shahat and Abdel Monem, 2011).

Vitamin A

Vitamin A, retinoids, and thyroid hormone are known to suppress serum TSH levels and decrease TSH-β subunit gene promoter activity (Wood *et al*., 1989). Through the retinoid X receptor (RXR)-γ isotype (Brown *et al*., 2000), vitamin A and its retinoid derivatives influence the function of the pituitary-thyroid axis (Morley *et al*., 1978), by suppressing serum TSH levels and TSH-β subunit gene expression (Sherman *et al*., 1999). Vitamin A deficient rats (Morley *et al*., 1978) and RXR-deficient mice (Brown *et al*., 2000) had significantly high TSH, T4 and T3 serum concentration compared to control. Since the RXR-γ isotype has limited tissue distribution including the anterior pituitary and hypothalamus (Krezel *et al*., 1999), as well as thyrotropes within the anterior pituitary (Haugen *et al*., 1997). Brown *et al*. (2000) hypothesized that the RXR-γ isotype is most likely involved in the regulation of the pituitary-thyroid axis.

2.12.8 Effect of stress on serum TH concentration

Stress in livestock could be physical or psychological. Physical stress include: extreme temperature, feed and/or water deprivation, pain and diseases.While, psychological stress include: fear, restraint and isolation (Grandin, 1998). Stress stimuli are known to cause activated T-cells to produce cytokines (Early *et al*., 2010). Cytokines such as certain members of the interleukin (IL) family and tumor necrosis factor-α (TNFα) are reported to decrease 5'-deiodinase enzymes (Dio 1 and 2) activity in peripheral tissues during stressful conditions such as starvation,resultingin a condition called low T_3syndrome (Pang *et al*.,

1989).Low T_3syndrome or euthyroid sick syndrome is observed during systemic non-thyroidal illness, and involves a decrease in plasma concentration of T_3, an increase in rT_3level and, in severe cases, a decrease in $T_4$and TSH concentrations. Most of these changes are caused by a lower T_3production rate and a decreased rT_3clearance rate due to the diminished extrathyroidal 5'-deiodinase enzymes activity (Wartofsky and Burman, 1982).

Physiological or metabolic (abnormal metabolism) stressors generate highly reactive oxygen species that release free radicals and simultaneously increase lipid peroxidation in the cells (Halliwell and Gutteridge, 1990; Samson andNelson,2000).Acceleration of the basal metabolic rate and the energy metabolism of tissues in several mammalian species is one of the major functions of thyroid hormones (Schwartz and Oppenheimer, 1978). Also, thyroid hormones maintain the oxidant/antioxidant equilibrium to protect the cell (Asayama *et al*., 1987). Accumulating evidence has suggested that in over secretion of thyroid hormones, metabolic reactions are accelerated, oxygen consumption increases, and, owing to oxidative reactions, free radical production is increased as well. This activates the antioxidant enzymes system. Thus, as energy need increases in hyperthyroidism, oxidants accumulate in the cell (Seymen *etal*., 1999). This means that thyroid hormones could constitute an oxidant stress risk to cells,whereas in hypothyroidism, oxidative stress and the antioxidant status present variable results (Venditti *et al*., 1997). The hypometabolic state induced by hypothyroidism is associated with a decrease in free radical production and lipid peroxidation products. However, just as TH in euthyroidism are known to modulate the free radical induced oxidative damage of lipids, hypothyroidismalso have similar effects(Paller, 1986). Hypothyroidism also confers some protection against lipid peroxidation (Devasena *et al*., 2001). However,oxidative stress and membrane damage due to hypothyroidism have also been reported (Dariyerli *et al*., 2004).

Tissue difference in lipid peroxidation has been reported. Tissues of hypothyroid rats showed no alteration in the lipid peroxidation, whereas in hyperthyroid rats, lipid peroxidation increased in liver and heart but not in skeletal muscle (Venditti *et al*., 1997).The antioxidant effect of melatonin in heat stressed animals has been suggested to probably be through interaction of TH with other hormones viamodification of adrenal function (Sejian and Srivastava, 2009).

2.12.9 Influence of thyroid hormones on body temperature

The ability of newborn animals to survive is crucially dependent on their response to the environmental condition into which they are born. Small ruminants are born, often into cold or wet environments, with low fat cover and have a high surface area to body weight ratio, which exacerbates heat loss (Stephenson *et al*., 2001; Dwyer and Morgan , 2006). There is a high energy demand to maintain body temperature, and this must be supplied by efficient metabolism of brown adipose tissue (BAT). Temperature control at birth is dependent mainly on heat production by oxidation of fat from BAT by a process under the control of triiodothyronine (Dauncey, 1990). Symonds *et al*. (1989) showed that lambs with low plasma T_3 concentrations (below 1.73 nmol/L) relied more on shivering thermogenesis in response to cold exposure than lambs with greater concentrations of T3 (>2.06 nmol/L), that relied more on non-shivering thermogenesis.

The postpartum surge in thyroid hormone production is known to play a critical role in thermoregulatory adaptation after birth (Heasman *et al*., 2000). Lambs delivered pre-term or at term that exhibit low plasma thyroid hormone concentrations are at much greater risk for hypothermia, in part because of lower abundance and thermogenic activity of the brown

adipose tissue–specific uncoupling protein 1 (UCP-1; Heasman *et al*., 2000). This is also the case for near-term lambs delivered by the cesarean route, which are characterized by lower plasma thyroid hormone concentrations and brown adipose tissue function than those born vaginally (Clarke *et al*., 1997).

Ambient temperature influences both rectal temperature(Kabuga, 1992) and TH activities (Todini,2007). High ambient temperature increase rectal temperature (Montsma*et al*., 1985; Ayo *etal*., 1999), but decrease serum concentration of TH and vice versa.In a study to demonstrate if neonatal lambs showing slow behavioural progress to standing and sucking also have an impaired ability to maintain body temperature,lower TH were observed in lamb breeds which had lower rectal temperature and are slower to stand and suck from their mothers (Dwyer and Morgan, 2006). Decrease in serum TH in the afternoon coincided with an increase in rectal temperature in goats. This could be a physiological response to cope with rise in ambient temperature in the noon (Dutta *et al*., 2002).Experimentally induced hypothermia in rats resulted in a significant decrease in fT_3, fT_4 and T_4, but a significant increase in $T_3$and no effect on TSH level (Shirpour *et al*., 2003). The latter study suggested thatexcessive conversion of T_4 to T_3 under stressful conditions resulting from hypothermia could probably be responsible for the fluctuations in TH levels. Although, T_3 alters body temperature, it could not account for the magnitude of the rise in temperature during exercise. The effects of T_3 on body temperature at rest and during exercise are mediated through mechanisms other than alterations in metabolic rate(Stager, 1983).

2.12.10 Effect of reproductive status on serum TH concentration

Pregnancy

The main change in thyroid function associated with the pregnancy is the requirement of an increased production of thyroid hormone that depends directly upon the adequate availability of dietary iodine and integrity of the glandular machinery (Glinoer, 2004). Both thyroid activity and levels of blood THhave been reported to increase during gestation in all mammalian species investigated. Some mechanisms have been suggested to be responsible for these observations. They include increased binding protein concentrations in plasma, secretion of thyrotropic factors by the placenta, enhanced responsiveness of pituitary TSH secretion to hypothalamic TRH and changes in maternal TH catabolism (De Leo *et al*., 1998; Glinoer, 2001). Usually, there is no significant correlation between maternal and foetal T_4 levels, except towards the end of pregnancy, when the foetus(es) plays a competitive role (higher thyroid activity, iodine affinity and uptake than maternal ones), such that a decrease in maternal plasma fT4 concentrations has been observed in goats (McDonald *et al*., 1988), and in single and twin pregnancies in ewe (Abdollahi *et al*., 2013).

Hypothyroidism during pregnancy has been shown to cause prolong gestation (Lucas *et al*., 1958) and reduced litter size and, foetal weight (Stempak, 1962). In ewe, twin pregnancy had lowerTH than single pregnancy at the end of gestation period (Abdollahi *et al*., 2013). The decrease in T_3 and T_4 concentrations during this period in twin bearing ewes maybe due to increased metabolism resulting from stress and cortisol secretion around parturition in twin compared with single pregnancies (Khan and Ludri, 2001).Serum concentration of T_3 has been shown to be higher in pregnant sheep in comparison to lactating sheep, whereas there was no significant difference inlevel of T_3 and T_4between non-pregnant and pregnant sheep (Novoselec *et al*., 2009).

After an initial transient phase with low serum TSH (due to high hCGlevels) near the end of the first trimester, serum TSH levels tended to increase progressively until term, where they could reach levels that were twice (or even higher) the preconception serum TSH levels (Glinoer, 2004).

Lactation

The onset of lactation is marked by a decrease in serum TH levels, followed by a gradual increase, which was maintained until the goats became pregnant again (Riis and Madsen, 1985). Though TH administration is known to stimulate lactation in many species (Tucker, 1994; 2000), an inverse relationship between blood hormone concentration and milk yield has been reported in goats (Riis and Madsen, 1985), at least during the first phases of lactation. In ewes, during late lactation, the increase in T4 concentration in blood seems related to the decrease of milk production (Bass, 1989). Though, T3 has been shown to be higher in pregnant sheep in comparison to lactating sheep (Novoselec *et al*., 2009), higher TSH in lactating ewe in comparison to pregnant ewe have been reported (Peeters *et al*., 1992).However, in another study, the pattern of TH during lactation indicated no significant difference in serum TH concentration during this period (Antunović *et al*.,2011).

In vivo studies indicated thatTH administration can increase milk productionin dairy cows. Also, *invitro* studies have shown thatT3 potentiates the activity of otherlactogenic and galactopoietic hormones (Bhattacharjee and Vonderhaar, 1984). Tissuesensitivity to thyroid hormones can be altered by iodothyroninedeiodination and changes in expression of TH nuclearreceptors.Increased expression of mammary TRβ1 and DIO2, and decreased RXRα, provide a mechanism that increase TH activity within the mammary gland during lactation (Capuco *et al*., 2008).

During the transition from pregnancy to lactation, adjustments in TH physiology becomes necessary to create a conducive metabolic state for lactation. It has been shown in rats (Aceves and Valverde, 1989; Jack *et al*., 1994) and cows (Pezzi *et al*., 2005) that 5'-deiodinase activity decreased in the liver and kidney (primary contributors of plasma T3) during the transition from pregnancy to lactation, while 5'-deiodinase activity in mammary tissue increased. Furthermore, the magnitude of these changes in rats was proportional to lactation intensity, which was manipulated by adjusting litter size (Aceves and Valverde, 1989; Jack *et al*., 1994). Similarly, increasing lactational intensity in dairy cows by GH administration alters 5'D activity in extrathyroidal tissues. During late lactation, GH increased 5'D activity in mammary tissue concurrent with increased milk production (Tucker, 1979). This means that the extent of conversion of T_4 to T_3 by liver and mammary gland tissues appear to be related to establishment of lactation.

Effect of oestrus cycle on serum TH concentrations

During induced or spontaneous oestrus in goats, a rise in plasma total fT4 levels has been observed(Blaszczyk *et al*., 2004). In ewes, plasma T_4 levels were higher during oestrus and lower during the luteal phase. Likewise T_3concentrations and T_3/T_4 ratios werehigher during the luteal phase, while the concentrations of rT_3 were not associated with the oestrous cycle phases. A significant negative correlation between TSHand progesterone level has been reported during the oestrous cycle in cows (Peeters *et al*., 1989). However, in goats (Zarei *et al*., 2009) and mares (Johnson, 1986), non-significant fluctuations in TSH, T_4 and T_3were observed during the oestrus cycle. Many factors known to decrease the circulating level of $T_4$and/or T_3have been associated with reduced reproductive efficiency (Huszenicza *et al*., 2002). Reduced plasma TH (hypothyroidism) caused by thiourea treatmentresulted in lengthening of oestrus cycle and weak oestrus behaviour in does (Reddy *et al*., 1996). In

Savanna Brown goats, cold-dry season oestrus cycle was characterized by higher serum T_4 and longer cycle length and oestrus duration when compared with early and late rainy season cycles (Kawu, 2011).In cattle, Spicer *et al*. (2001) reported a direct stimulatory effect of $T_3$and T_4on thecal cell steroidogenesis. The stimulatory effect of $T_3$and T_4on androstenedione production (i.e. two- to fourfold increases) was similar to the influence of LH on androstenedione production (i.e. four- to ninefold increases). However, in the latter study, $T_4$was a much weaker (i.e. 1.3-fold increase) inducer of thecal cell progesteroneproduction than was LH.

2.13Disorders ofThyroid Function in Ruminants

Abnormalities of the thyroid gland are well known in companion animals but less so in livestock. In livestock, nutritional iodine deficiencies are of greater importance than thyroid-gland diseases, particularly in the iodine-deficient areas(Singh and Beigh,2013).

2.13.1 Hypothyroidism

Hypothyroidism is a thyroid disorder characterised by low serum TH concentrations, but high TSH. It is the most prevalent thyroid disturbance in small ruminants and causes disorders that reduce the animals' ability to defend itself against infections, and also render them vulnerable to ketosis (Gupta *et al*., 2010). Diverse factors such as, iodine deficiency and chronic disease can induce hypothyroidism (Todini, 2007). Some conditions can cause asymptomatic hypothyroidism, as is typical of secondary euthyroid conditions.They include:hypothalamic-pituitary-thyroid axis disorders; withpossible effects on serum hormone-binding proteins, disturbances in hormone metabolism, disorders in the peripheral distribution of hormones, inhibition of hormone synthesis and an increase in the release of cytokines (Kumar *et al*., 2006). Enlarged hyperplastic thyroid and colloid goiters have been reported in fishes, reptiles, birds and mammals (Schlumberger, 1955). Goitre in goats could be hyperplastic (Capen and

Martin, 2003), congenital dyshormonogenetic (de Vijlder *et al*., 1981) or colloidal, with enlargement of the cranio-ventral neck region (Cheema *et al*., 2010). Abortion, delivery of still born or weak kids, myxedema and hair loss are common signs of goitre in goats. Also, surviving kids lagged behind in their growth and often suffered from bronchopneumonia as an additional disease (Bires *et al*., 1996).

Experimentally,hypothyroidism is commonly induced in ruminantsthrough the use of methimazole and prophyl-thiouracil. Unlike methimazole, prophyl-thiouracildoes not only blocks thyroid hormone synthesis, butalso inhibits type I iodothyronine deiodinase in liver and kidney (Leonard and Visser, 1986).Defects in thyroglobulin (TG) synthesis have been reported to cause congenital hypothyroidism in goats, sheep and cattle (de Vijlder, 2003). On the TG molecule, the sites where iodothyronine residues are formed are the so called hormonogenic sites. An important hormonogenic site is the N-terminal tyrosine residue (tyr 5; acceptor) that most likely couples with iodotyrosine 130 as donor. Any mutation that could causeslight alteration on the TG moleculemay influence coupling efficiency and consequently, thyroid hormone synthesis and release (Hishinuma *et al*., 1999).Decreased circulating levels of TSH and TH as well as impaired iodine uptake are indicative of defect in TG synthesis. However, one of the parameters important for the diagnosis is the presence of relatively low plasma TG concentration in relation to the plasma TSH level. In practice, the definition ‘TG synthesis defect’ is a clinical-physiological one. It does not cover defects in the gene coding for TG, but includes defects in the whole process of TG synthesis (Van de Graaf *et al*., 1999). In goats reports on defect in TG synthesis implicated the Dutch goats, a mixed strain of Saanen and Dwarf goats. The defect is inherited in an autosomal recessive way (Kok *et al*., 1987).

2.13.2 Hyperthyroidism

Among domestic animal species, disturbances of growth resulting from the production of excess TH is mainly observed in in adult cats and often related to adenomas compared to hyperactive follicular cells. In affected cats, the neoplastic cells release both T_4 and T_3 at an uncontrolled rate causing a marked increase in blood levels of both hormones(Nelson, 1998). In hyperthyroid cats the total levels of T_4 in the serum range from 5.0 to over 50 µg/dl and total levels of T_3 in the serum range from 100 to 1,000 ng/dl, while innormal cat, serum levels of T_4 in cats, as measure by radioimmunoassay, were approximately 1.5 to 4.5 µg/dl and serum T_3 levels are 60 to 100 ng/dl. Hyperthyroidism is associated with weight loss in spite of a normal or increased appetite and with restlessness and increased activity(Singh and Beigh,2013).

Due to the efficient enteroheptic excretory mechanism ofTH in dogs, it is difficult for hyperthyroidism to occur, either as a result of endogenous production by a tumor or through exogenous administration of TH. Hence, thyroid tumors in the dog only occasionally produce sufficient amount of thyroid hormone to overload the extremely efficient enterohepatic excretory pathways and produce clinical signs of hyperthyroidism (Singh and Beigh,2013). The clinical signs associated with hyperthyroidism in dogs that have functional thyroid tumors include polyuria and polydipsia and weight loss, despite increased appetite and polyphagia, leading to muscle atrophy and weakness(Capen and Martin, 2003;Singh and Beigh,2013).

2.13.3 Other diseases that affect thyroid hormone

Hemo-parasitic diseases

Issi *et al*. (2011)reported low levels of FT_3, FT_4, total T_3 and total T_4 in the pre-treatment of cattle naturally infected with *Theileria annulata*. A similar study performed by Badiei *et al*. (2010)in crossbred Holstein cattle naturally infected with *Theileria annulata* revealed low levels of T_3, T_4, FT_3 and FT_4. The authors postulated a paramount effect of anorexia.Similarly, Azimzadeh *et al*. (2013) concluded that hypothyroidism with concurrent oxidative stress are significant signs of ovine babesiosis.

Endocrine dysfunctions have been observed in both human and animal trypanosome Infections resulting in polyglandular endocrine failure in animals due to local inflammation of the pituitary, thyroid, adrenal and gonadal glands (Reincke*et al*., 1998).Chronictrypanosome infection in goats causes considerable decrease inplasmathyroxine level(Mutayoba *et al*., 1988). *Trypanosoma evansi* infection incamels causes hypothyroidism with a decrease inblood T_3 and T_4(Lomo *et al*., 1995).Trypanosomoses may also be accompanied by paralleldecrease in the level of blood TSH as reported by Al-Garawi *et al*. (2001).It has been suggested that thethyroid dysfunction observed in trypanosomoses may at least contribute to the lethargy seen in affected animals (Fatihu *et al*., 2009).

Endotoxin-mediated diseases

In commercial large-scale dairy herds certain endotoxin-mediated disorders (acute putrid endometritis, endotoxin mastitis) are known to occur frequently in postpartum dairy cows (Huszenicza *et al*., 1999). Endotoxin exposition is a strong stimulus for cytokine release, reducing the production and circulating level of $T_4$and inhibiting the T_4deiodination to T_3in

many species, including lab rodents (Bartalena *et al*., 1998; Bertók, 1998), humans (Berczi, 1993) and also ruminants (Lohuis *et al*., 1988; Jánosi *et al*., 1998; Kahl *et al*., 2000). Almost all steps of thyroid hormone synthesis, secretion and peripheral metabolism may be negatively influenced by this endotoxin-induced cytokine release (Bartalena *et al*., 1998).During the inflammatory process some of the cytokines (TNFα, IL-1) are important mediators of changes in thyroid status (e.g. inhibition of TSH release from pituitary cells and decreased activity of type-I 5'D in thyroid and liver tissue) (Pang *et al*., 1989;Hashimoto *et al*., 1995; Jánosi *et al*., 1998).

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Experimental Location

The study was carried out in the National Animal Production Research Institution (NAPRI), Ahmadu Bello University, Shika, Zaria, Nigeria (latitudes 11 and 12^{o} N and longitudes 7 and 8^{o} E).Rainfall in Shika occurs mainly between the months of April and October and an average annual rainfall of approximately 1100 mm has been reported. The maximum ambient temperature range in Shika is 27 – 35 °C depending on season (Taiwo *et al*., 2005).

3.1.1 Breed identification, animal feeding, housing and health status

Breed identification of the experimental goats was done based on phenotypic characteristics as described by Adu *et al*. (1979) and Ngere *et al*. (1984). The animals were managed semi-intensively. They were housed in concrete floor and half-walled pens. They were allowed to graze in natural pasture during the day and supplemented with *Digitaria smutsi* hay and concentrate ration (ground maize: 20%; cotton seed cake; 30%; wheat offal: 40%; bone meal: 5% and salt: 5%) at 3% body weight per day. Water was provided *ad libitum*. The kids were allowed to suckle their mothers directly.Pregnant and lactating does were sampled during the study.Health status of the goats was evaluated based on behaviour, rectal temperature, heart rate, respiratory profile, appetite and faecal consistency. Animals on the farm were routinely screened for haemoparasites and helminths, and only clinically healthy animals were used.

3.2 Experimental Animals Grouping

A total of 240 animals were used during the three seasons of the study. Eighty goats (n=80) were sampled per season and a total of 240 blood samples were collected and assayed. The 80 goats per season were split into two groups of 40 RS and SH goats each. The 40 RS goats were designated as Group I and the 40 SH goats as Group II. Group I and II were further subdivided in 20 males and 20 females. The 20 males and 20 females in Group I and II were again subdivided based on age into 10 kids and 10 adult goats, respectively. The various groups and subdivisions of the Group I and II had 20 goats each. Every group had equal number of males and females (i.e. 20 males and 20 females). Similarly, each of the male and female groups had equal number of kids and adult goats as shown in the scheme presented in figure 3.1 below**.**

3.3 Body mass index

Morphometric dimensions for determination of BMI were obtained using a measuring tape. Body length was measured as the length from the external occipital protuberance to the base of the tail, while withers height was measured as the length from the surface of a platform to the withers as described by Hassan and Ciroma (1992).Body mass index was then determined using the following mathematical formula as described by Tanaka *et al.* (2003):

$$\textbf{gBMI = body weight (kg)/\{withers height (m)/body length (m) × 10\}}$$

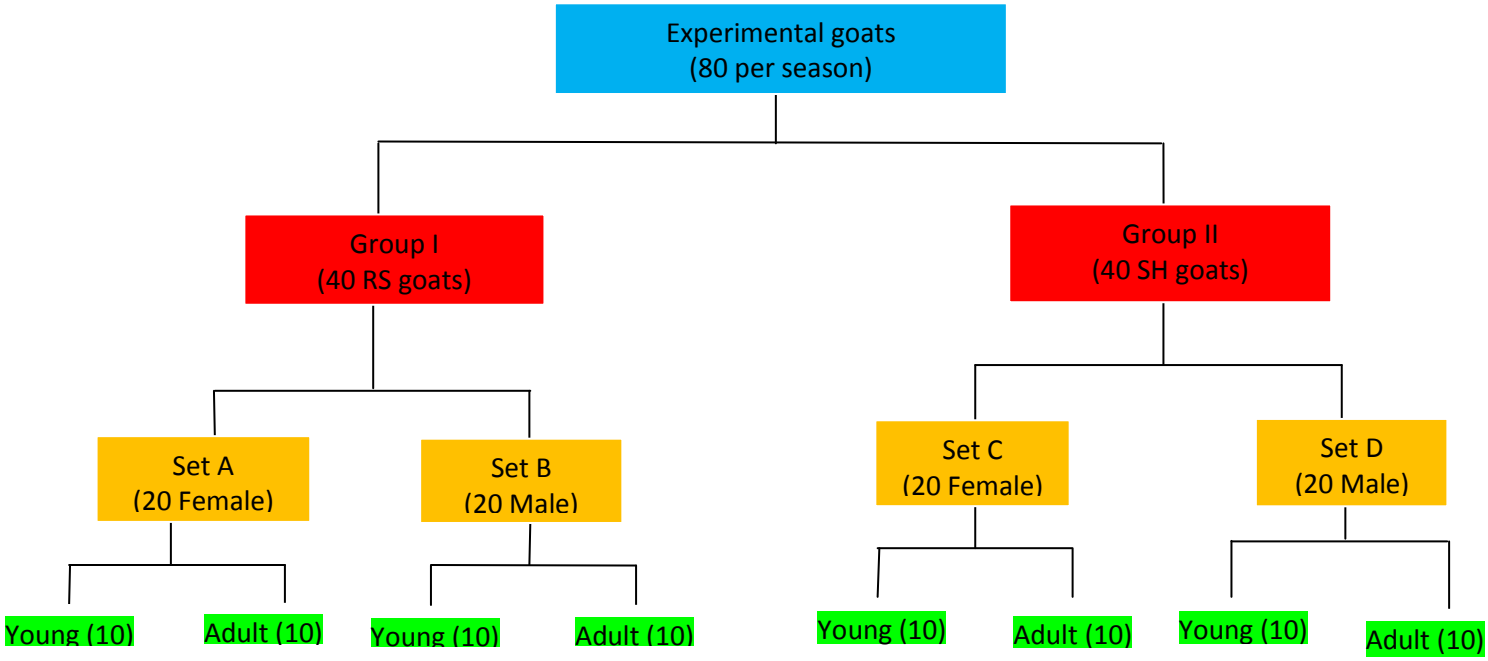


Figure 3.1: Animal grouping and subgrouping of RS (Red Sokoto)and SH (Sahel) goats sampled during the cold-dry seasons (CDS), hot-dry seasons(HDS) and rainy seasons (RAS) (n = 80 per season).

3.4 Ageing of animals

The farm records and dental eruption pattern (McNitt, 1983) was used to age the animals. Goats that were between 0 – 5 months of age were considered to be young, while goats that were between 1 – 4 years of age were considered to be adults (Bekele *et al*., 2011).

3.5 Seasons of the Study

Three seasons wereadopted for this work, as described by Igono and Aliu(1982) and Dzenda *et al*.(2011)are:

- Cold dry season (December / January)
- Hot dry season (March / April)
- Rainy season (July / August)

3.6 Meteorological Parameters

Parameters such as ambient temperature, relative humidity, sunshine hours and rainfall were obtained from the MeteorologicalUnit, Institute of Agricultural Research, Ahmadu Bello University, Zaria, located about 5 km away from the experimental site. The temperature humidity index (THI) was used to evaluate the level of heat stress imposed by the environment on the goats and was calculated using the equation reported by Ravagnolo *et al*. (2000):

THI = (1.8 x T + 32) – {(0.55 – 0.0055 x RH) x (1.8 x T – 26)}

Where *T* = ambient temperature (^{o}C) and RH = relative humidity (%).

3.7 Blood Sample Collection

Two millilitres of blood were collected from every animal through the jugular vein using 5ml syringe. The blood was immediately, but gently transferred into a non-heparinized test tube and allowed to stand for 1 hour. Subsequently the blood samples were centrifuged at 3,000 gyrations for 10 minutes. The serum was then decanted into serum sample bottles, capped and stored at -20^{o}C until analysed for, T_4,$T_3$and TSH.

3.8 Analysis of Serum Total Thyroxine, Total Triiodothyronine and Throid Stimulating Hormones

Commercial enzyme-linked immunoassay kit(AccuBind ELISA Microwells;Monobind Inc® USA) was used for the analysis of serum T_4,T_3andTSH.Assay sensitivitiesfor total T_4, total T_3, and TSH were 3.2 ng/well,0.04 ng/well and 0.078µIU/mL, respectively. The intra-assay coefficients of variation for normal levels of T_4, T_3 and TSH were 1.6, 6.4 and 5.4%, respectively.While, the inter-assay coefficients of variation for normal levels of T_4, T_3 and TSH were 6.1, 6.7 and 7.9%, respectively.

3.8.1 Principles of total triiodothyronine assay

To quantitatively determine serum total T_3, a commercially prepared microwell competitive enzyme- linked immunosorbent assay (ELISA) kit (Monobind Inc® USA) for T_3 (Total triiodothyronine ELISA Microwells) was used. Being competitive ELISAs, the same principle underlies the function of both T_4 and T_3. The principle underlying the function is that certain amount of anti-T_3 antibodies were coated on microtitre wells of the T_3plates. A measured amount of the serum sample and a constant amount of T_3conjugated with

horseradish peroxidase was added to the microtitre wells. An incubation period of 60 minutes at room temperature was allowed. During this period, the T_3 in the test samples and the conjugated T_3 competed for the limited binding on the anti-T_3 antibodies, respectively. The wells were then washed with water 5 times to remove unbound T_3 conjugates. A solution of 3,3',5,5'-Tetramethylbenzidine (TMB) was then added and incubated for 10 minutes at room temperature, resulting in the development of blue colour. The colour development was stopped by the addition of 2N HCL and the absorbance taken with a spectrophotometer at 450nm. The intensity of the colour formed was proportional to the amount of enzyme present, but inversely related to the amount of unlabelled T_3 in the sample. By making reference to the series of T_3 standards assayed in the same way, the concentration of T_3 in the unknown samples was determined.

Test procedure for triiodothyronine

i. The microplate's wells were formatted for each serum reference, control and patient specimen to be assayed.

ii. 0.025 ml (25µl) of the appropriate serum reference, control or specimen was pipetted and poured into the assigned wells.

iii. 0.100 ml (100µl) of Working T_4 Enzyme Reagent was added to all wells.

iv. The microplate was gently swirled for 20 – 30 seconds to mix and was then covered. It was then incubated for 60 minutes at room temperature.

v. The content of the microplate was discarded by decantation and the plate blotted with an absorbent paper.

vi. 350µl of wash buffer was added, decanted and blot blotted with an absorbent paper. This was repeated two additional times for a total of three (3) washes.

vii. 0.100 ml (100µl) of working substrate solution was then added to all wells. The reagent was always added in the same order to minimize reaction time differences between wells. It was then incubated at room temperature for fifteen (15) minutes.

viii. 0.050ml (50µl) of stop solution was then added to each well and gently mixed for 15 – 20 seconds. The reagent was always added in the same order to minimize reaction time differences between wells.

ix. The absorbance in each well was read at 450nm (using a reference wavelength of 620 – 630nm to minimize well imperfections) in a microplate reader. The result was read within thirty (30) minutes of adding the stop solution.

3.8.2 Principles of total thyroxin assay

To quantitatively determine serum total T_4 a commercially prepared microwell competitive enzyme- linked immunosorbent assay (ELISA) kit (Monobind Inc® USA) for T_4 (Total Thyroxine ELISA Microwells) was used. The principle underlying the function is that certain amount of anti-T_4 antibodies were coated on microtitre wells of the T_4 plates. A measured amount of the sample serum and a constant amount of T_4 conjugated with horseradish peroxidase was added to the microtitre wells. An incubation period of 60 minutes at room temperature was allowed. During this period, the T_4 in the test samples and the conjugated T_4 and T_3, competed for the limited binding on the anti-T_4 antibodies, respectively.The wells were then washed with water 5 times to remove unbound T_4 conjugates. A solution of TMBwas then added and incubated for 10 minutes at room temperature, resulting in the development of blue colour. The colour development was stopped by the addition of 2N HCL and the absorbance taken with a spectrophotometer at 450nm. The intensity of the colour formed was proportional to the amount of enzyme present, but inversely related to the

amount of unlabelled T_4 in the sample. By making reference to the series of T_4 standards assayed in the same way, the concentration of T_4 in the unknown samples was determined.

Test procedure for T_4

i. The microplate's wells were formatted for each serum reference, control and patient specimen to be assayed.

ii. 0.050 ml (50µl) of the appropriate serum reference, control or specimen was pipetted and poured into the assigned wells.

iii. 0.100 ml (100µl) of Working T3 Enzyme Reagent was added to all wells.

iv. The microplate was gently swirled for 20 – 30 seconds to mix and was then covered. It was then incubated for 60 minutes at room temperature.

v. The content of the microplate was discarded by decantation and the plate blotted with an absorbent paper.

vi. 350µl of wash buffer was added, decanted and blot blotted with an absorbent paper. This was repeated two additional times for a total of three (3) washes.

vii. 0.100 ml (100µl) of working substrate solution was then added to all wells. The reagent was always added in the same order to minimize reaction time differences between wells. It was then incubated at room temperature for fifteen (15) minutes.

viii. 0.050ml (50µl) of stop solution was then added to each well and gently mixed for 15 – 20 seconds. The reagent was always added in the same order to minimize reaction time differences between wells.

ix. The absorbance in each well was read at 450nm (using a reference wavelength of 620 – 630nm to minimize well imperfections) in a microplate reader. The result was read within thirty (30) minutes of adding the stop solution.

3.8.3 Principles of thyroid stimulating hormone assay

The TSH ELISA (Monobind Inc® USA)was used for the assay. It is based on the principle of a solid phase enzyme-linked immunosorbent assay. The assay system utilizes a unique monoclonal antibody directed against a distinct antigenic determinant on the intact TSH molecule. Mouse monoclonal anti-TSH antibody was used for solid phase immobilization (microtiter wells), and goat anti-TSH antibody was in the antibody-enzyme (horseradish peroxidase) conjugate solution. The test sample was allowed to react simultaneously with the two antibodies, resulting in the TSH molecules being sandwiched between the solid phase and enzyme-linked antibodies. After a 60-minute or overnight incubation at room temperature, the solid phase was washed with water to remove unbound labelled antibodies. A solution of TMB was added and incubated for 20 minutes, resulting in the development of a blue colour. The colour development was stopped with the addition of 3N HCl, and the resulting yellow colour was measured spectrophotometrically at 450 nm. The concentration of TSH was directly proportional to the colour intensity of the test sample.

Test procedure for TSH

i. The microplate's wells were formatted for each serum reference, control and patient specimen to be assayed.

ii. 0.050 ml (50µl) of the appropriate serum reference, control or specimen was pipetted and poured into the assigned wells.

iii. 0.100 ml (100µl) of Working TSH Enzyme Reagent was added to all wells.

iv. The microplate was gently swirled for 20 – 30 seconds to mix and was then covered. It was then incubated for 60 minutes at room temperature.

v. The content of the microplate was discarded by decantation and the plate blotted with an absorbent paper.

vi. 350µl of wash buffer was added, decanted and blotted with an absorbent paper. This was repeated two additional times for a total of three (3) washes.

vii. 0.100 ml (100µl) of working substrate solution was then added to all wells. The reagent was always added in the same order to minimize reaction time differences between wells. It was then incubated at room temperature for fifteen (15) minutes.

viii. 0.050ml (50µl) of stop solution was then added to each well and gently mixed for 15 – 20 seconds. The reagent was always added in the same order to minimize reaction time differences between wells.

ix. The absorbance in each well was read at 450nm (using a reference wavelength of 620 – 630nm to minimize well imperfections) in a microplate reader. The result was read within thirty (30) minutes of adding the stop solution.

3.9Statistical Analysis

The data collected were expressed as mean and standard error of the mean (±SEM). Comparisons between breeds, sexes and age groups were done using Student's *t*-test. One-way analysis of variance, followed by Tukey's post-hoc test was used to compare values among the three seasons. Pearson's correlation test was used to determine the relationship between variable. The statistical package used was Graphpad Prism for windows (2003). Values of $P<0.05$ were considered significant.

CHAPTER FOUR

RESULTS

4.1 **Meteorological Parameters during the Study Period**

Mean values of meteorological parameters recorded during the study period are shown in Table 4.1. The values of ambient temperature were significantly ($P<0.05$) higher during afternoon hours compared to the morning hours. The HDS had a significantly higher ambient temperature both during the morning and afternoon hours compared to the other seasons. The RH was higher in the morning compared to the afternoon hours. The RH of the morning and afternoon periods were highest during the RAS and lowest during CDS. The difference in RH was significantly different between groups. On the other hands, the wind speed was significantly ($P < 0.05$) lower in the HDS compared to other seasons. The Sunshine hours was significantly higher ($P < 0.05$) in the CDS than other seasons. The RAS had a higher ($P<0.05$) amount of rainfall compared to HDS. The photoperiod was longer during the RAS and shorter during the CDS. The increase ($P<0.05$) in photoperiod across the seasons, from the CDS to the RAS was significant.

Parameters	CDS	HDS	RAS
Relative Humidity % (Morning)	20.26 ± 0.64[a] (14.00 – 27.00)	52.93 ± 2.27[b] (20.00 – 87.00)	78.03 ± 1.24[c] (60.00 – 90.00)
Relative Humidity % (Afternoon)	15.66 ± 0.71[a] (7.00 – 22.00)	24.77 ± 0.26[b] (22.00 – 28.00)	70.48 ± 1.41[c] (57.00 – 93.00)
Ambient Temperature ^{o}C (Morning)	16.42 ±0.54[a] (12.00 – 23.00)	24.77± 0.26[b] (22.00 – 28.00)	22.84 ± 0.25[c] (20.00 – 24.00)

Table 4.1: Mean (±SEM) values of meteorological parameters in the months of December (CDS), April (HDS) and August (RAS) during the period of the study

Ambient Temperature ^{o}C (Afternoon)	30.61 ± 0.59^{b} (28.00 – 39.00)	38.88 ± 0.38^{a} (25.00 – 41.00)	31.0 ±0.30^{b} (27.00 – 34.00)
Temperature-humidity Index (Morning)	57.81 ± 1.72^{a} (51.92– 62.03)	72.28 ± 2.44^{b} (65.61– 80.66)	71.43 ± 1.77^{b} (65.88– 76.27)
Temperature-humidity Index (Afternoon)	74.45 ± 2.37^{b} (69.92 – 83.24)	84.62 ± 0.88^{a} (82.68– 86.85)	79.63 ± 2.27 (75.25– 82.81)
Wind Speed (km/day)	163.90 ± 6.47^{b} (212.20 – 215.20)	138.50 ± 0.03^{a} (102.50 – 199.40)	158.5 ±5.91^{b} (104.30 – 251.20)
Sunshine Hours	8.58. ±0.15^{a} (6.40 – 9.80)	7.09. ± 0.35^{b} (16.00 – 9.70)	6.3 ± 0.37^{b} (1.30 – 9.60)
Rainfall (mm)	0.0	4.93 ± 2.00^{a} (1.70 – 8.60)	13.53 ± 2.03^{b} (4.8 – 21.40)
Photoperiod (hours)	11.60 ± 0.00^{a} (11.60 – 11.62)	12.23 ±0.01^{b} (12.22 – 12.27)	12.49 ± 0 .01^{c} (12.47 – 12.52)

CDS - cold-dry season, HDS – hot-dry season and RAS – rainy season. Values with different superscript ($^{a, b, c}$) are significantly different($P < 0.05$).
Source: Meteorological Unit, Institute of Agricultural Research, Ahmadu Bello University, Zaria

4.2Serum Concentrations of T_3 and T_4 in Red Sokoto and Sahel Goats

Specific and overall mean values (± SEM) of serumT_3 and T_4 in RS and SH are presented in Table 4.2. Irrespective of season, RSG kids had significantly higher ($P < 0.05$) serum $T_3$and T_4 concentrations than the adult goats. Mean values of serum T_3 and T_4 of RSG and SHG, respectively were as follows: T_3: 2.19 $\pm$ 0.083 vs 1.96 $\pm$ 0.09, T_4: 47.40 $\pm$ 0.17 vs

44.30±0.20. Irrespective of season, RSG had significantly higher ($P < 0.05$) values of circulating $T_3$and T_4 than the SHG.

Table 4.2: Mean (±SEM) values of serum concentration ofT_3, and T_4 in Red Sokoto and Sahel goats

	RSG	SHG
T_3 (ng/ml)		
Young	2.41 ± 0.08^{x}	2.10 ± 08
	(1.08 – 3.40)	(0.940 – 3.20)
Adult	1.96 ± 0.09^{y}	1.91 ± 0.1
	(0.92 – 3.20)	(0.90 – 3.65)
Mean	2.19 ± 0.08^{a}	1.96 ± 0.09^{b}

T_4 (ng/ml)		
Young	51.90 ± 2.00 [x]	46.70 ± 2.00
	(37.50 – 91.90)	(22.50 – 78.50)
Adult	42.82 ± 1.40 [y]	4.19 ± 1.90
	(25.00 – 75.07)	(15.00 – 67.50)
Mean	47.40 ± 9.20[a]	44.30 ± 2.00[b]

CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Valueswith different superscript are statistically significant ($P < 0.05$). x,y:between age groups;a,b:between breeds

4.3 Meanof Serum Concentration of TSH and T_3:T_4 in Red Sokoto and Sahel Goats

Specific and overall mean values (± SEM) of serumTSH and T_3:T_4 in RSG and SHG are presented in Table 4.3. Red Sokoto goat kids had significantly higher ($P < 0.05$) serum TSH concentrations than the adult goats. Mean values of serum TSH and T_3:T_4in RSG and SHG,

respectively were as follows: TSH: 0.76 ± 0.03 vs 0.82 ± 0.04, T_3:T_4: 0.05 ± 0.00 vs 0.05 ± 0.00.

Table 4.3: Mean (± SEM) of serum concentration of TSH and T_3:T_4 in Red Sokoto and Sahel goats

	RSG	SHG
TSH (µIU/ml)		
Young	0.81 ± 0.02 [x]	0.81 ± 0.04
	(0.50 – 1.20)	(0.508 – 1.90)
Adult	0.82 ± 0.04 [y]	0.82 ± 0.04
	(0.17 – 1.61)	(0.50 – 1.50)

Mean	0.76 ± 0.03	0.82 ± 0.04
T_3:T_4		
Young	0.051 ± 0.0028	0.046 ± 0.0029
	(1.08 – 3.4)	(0.012 – 0.13)
Adult	0.05 ± 0.00	0.0461 ± 0.00
	0.92 – 3.20	(0.03 – 0.08)
Mean	0.05 ± 0.00	0.05 ± 0.00

CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RSG – Red Sokoto goats and SHG – Sahel goats. Valueswith different superscript are statistically significant ($P < 0.05$). x,y:between age groups.

4.4Percentages of Serum Thyroid Hormones that are in Form of$T_3$and T_4 in Red Sokoto and Sahel Goats

Table 4.3 showsthe percentages of serum TH that are in form of T_3 and T_4 in Red Sokoto and Sahel goats. The percentage of TH that was in form of T_3 was higher in RSG than SHG, while the TH that was in form of T_4 was lower in RSG than SHG.

Table 4.4:Percentages of serum triiodothyronine and thyroxin in Red Sokoto and Sahel goats

	RSG	SHG	Overall

T_3 (%)	4.62	4.22	4.42
T_4 (%)	95.38	95.78	95.58

4.5 Effect of Sex onSerum T_3 and T_4 ConcentrationsinRed SokotoAnd Sahel Goats during the Cold-dry, Hot-dry and Rainy Seasons

Effect of sex on serum concentrations of T_3 and T_4 in male and female RSG and SHGduring the CDS, HDS and RAS are presented in Table 4.4. In RSG, females had higher ($P < 0.05$) concentration of circulating T_3 than males in the RAS. Similarly, the female goats had significantlyhigher ($P < 0.05$)concentration of circulating T_4 than male RSGduring the RAS. Similarly, in the SH goats, the female goats also had higherT_3 concentration than male in the CDS and also significantly higher ($P < 0.05$) circulating T_3 in female thanmale goats in the RAS.There was no significant breed difference in the values of circulating T_4 in SHG.

Table 4.5: Effect ofsexonserum T_3 and T_4 concentrations(Mean ± SEM)in Red Sokoto and Sahel goats during the cold-dry, hot-dry and rainy seasons

	RSG		SHG	
	Male	Female	Male	Female
T_3 (ng/ml)				
CDS	2.22 ± 0.10	2.37 ± 0.13	1.88 ± 0.12[a]	2.35 ±0.13[b]
HDS	1.63 ± 0.15	1.56 ± 0.13	1.84 ± 0.25	1.53 ± 0.18
RAS	2.31 ± 0.12[a]	2.67 ± 0.09[b]	2.15 ±0 .01	1.98 ± 0.09
T_4 (ng/ml)				
CDS	40.15 ± 1.95[a]	53.05 ± 4.01[b]	43.00 ± 1.93	46.73 ± 2.32
HDS	46.77 ± 2.44	46.53 ± 3.07	44.91 ± 5.45	45.85 ± 0.13
RAS	43.28 ±3.40	49.05 ± 2.91	41.50 ± 2.06	44.85 ± 3.20

CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RSG – Red Sokoto goats and SHG – Sahel goats. Values of the same parameters with different superscript (a,b)are statistically significant ($P < 0.05$).

4.6 Effect of Sex on Serum TSH and T_3:T_4Values in Red Sokotoand SahelGoats during the Cold-dry, Hot-dry and Rainy Seasons

Effect of sex on serum concentrations of TSH and T_3:T_4in male and female RSG and SHG during the CDS, HDS and RAS are presented in Table 4.5. In RSG, serum TSH concentration was significantly higher ($P < 0.05$) in males than in females during the HDS. Similarly, T_3:T_4 was significantly higher ($P < 0.05$) in male than female goats during the CDS.

In SH goats, females had significantly higher ($P < 0.05$) T_3:T_4than males during the HDS. However,there was no significant difference between sexes in the values of circulating TSH in SHG.

Table 4.6: Effect ofsexon values (mean ± SEM)of serum TSH and T_3:T_4in Red Sokoto

and Sahel goats during the cold-dry, hot-dry and rainy seasons

	RSG		SHG	
	Male	Female	Male	Female
TSH (µIU/ml)				
CDS	0.76 ± 0.02	0.75 ± 0.02	0.89 ± 0.06	0.85 ± 0.08
HDS	0.77 ± 0.03[a]	0.70 ± 0.02[b]	0.77 ± 0.05	0.71 ± 0.04
RAS	0.80 ± 0.06	0.81 ± 0.09	0.78 ± 0.09	0.93 ± 0.08
T_3:T_4				
CDS	0.057 ± 0.00[a]	0.048 ± 0.00[b]	0.045 ± 0.00	0.052 ± 0.00
HDS	0.032 ± 0.00	0.034 ± 0.00	0.031 ± 0.00[a]	0.045 ± 0.00[b]
RAS	0.054 ± 0.00	0.063 ± 0.01	0.048 ± 0.00[a]	0.053 ± 0.01[b]

CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RSG – Red Sokoto goats and SHG – Sahel goats. Values of the same parameters with different superscript (a,b)are statistically significant ($P < 0.05$).

4.7 Effect of Age on Serum Concentration of $T_3$and T_4in Red Sokoto and SahelGoats during the Cold-dry, Hot-dry and Rainy Seasons

Effect of age on serum concentrations of T_3andT_4in RSG and SHGduring the CDS, HDS and RAS are presented in Table 4.6. In RSG, kids had significantly higher ($P < 0.05$) serum T_3 concentration than adult goats in all the seasons. Similarly, the kids of RSG had significantly higher ($P < 0.05$) serum T_4 concentration than adult goats during the CDS and RAS.

In SHG, the kids had significantly higher ($P < 0.05$) serum T_3 concentration than adult goats during the HDS. However, serum concentration of T_4 was significantly lower ($P < 0.05$) in kids than adult SHG during the HDS.

Table 4.7: Effect of ageonserum T_3 and T_4 concentrations (mean ± SEM)in Red Sokoto and Sahel goats during the cold-dry, hot-dry and rainy seasons

	RSG		SHG	
	Young	Adult	Young	Adult
T_3 (ng/ml)				
CDS	2.51 ± 0.11[a]	2.14 ± 0.11[b]	2.12 ± 0.11	2.11 ± 0.16
HDS	1.95 ± 0.15[a]	1.29 ± 0.07[b]	1.96 ± 0.20[a]	1.30 ± 0.196[b]
RAS	2.70± 0.09[a]	2.31 ± 0.11[b]	1.98 ± 0.09	0.15 ± 0.09
T_4 (ng/ml)				
CDS	51.54 ± 3.61[a]	39.47 ± 2.46[b]	46.75 ± 2.42	42.69 ± 1.68
HDS	50.15 ± 2.78	46.68 ± 1.65	51.96 ± 4.04[a]	34.82 ± 4.64[b]
RAS	53.27 ± 3.66[a]	40.09 ± 2.00[b]	40.72 ± 2.13	54.48 ± 2.98

CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RSG – Red Sokoto goats and SHG – Sahel goats. Values of the same parameters with different superscript (a,b)are statistically significant ($P < 0.05$).

4.8Effect of Age on Serum Concentration of TSH and T_3:T_4in Red Sokoto and Sahel

Goatsduring the Cold-dry, Hot-dry and Rainy Seasons

Effect of age on serum concentrations of TSH and T_3:T_4in RSG and SHG during the CDS, HDS and RAS are presented in Table 4.7. In RSG, significantly higher ($P < 0.05$) value of circulating TSH was observed in adultscompared withkids during the RAS. The value of T_3:$T_4$was significantly higher ($P < 0.05$) in kids than adult RSG.

Table 4.8: Effect ofage onserum concentration (mean ± SEM)ofTSH and T_3:T_4in Red Sokoto and Sahel goats during the cold-dry, hot-dry and rainy seasons

	RSG		SHG	
	Young	Adult	Young	Adult
TSH (µIU/ml)				
CDS	0.73 ± 0.02	0.77 ± 0.02	0.98± 0.01	0.75 ± 0.02
HDS	0.74 ± 0.02	0.73 ± 0.03	0.76 ± 0.04	0.72 ± 0.04
RAS	0.69 ± 0.05^{a}	0.93 ± 0.10^{b}	0.81 ± 0.09	0.92 ± 0.09
T_3:T_4				
CDS	0.05± 0.00	0.053 ± 0.00	0.047 ± 0.00	0.05 ± 0.00
HDS	0.04 ± 0.00^{a}	0.027 ± 0.00^{b}	0.037 ± 0.00	0.039 ± 0.01
RAS	0.06± 0.01	0.05 ± 0.00	0.056 ± 0.00	0.043 ± 0.00

CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RSG – Red Sokoto goats and SHG – Sahel goats. Values of the same parameters with different superscript (a,b) are statistically significant ($P < 0.05$).

4.9Effects of Breed and Season onSerum T_3in Buck-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed on serum T_3 concentration in buck-kids ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.1. Serum concentration of $T_3$was significantly higher ($P<0.05$) in RSGthanSHG buck-kids, during the CDS and RAS. In RSG, circulating T_3 level was significantly lower ($P < 0.05$) during the HDS than the CDS and RAS. There was no significant difference between seasons in circulating T_3in SHG.

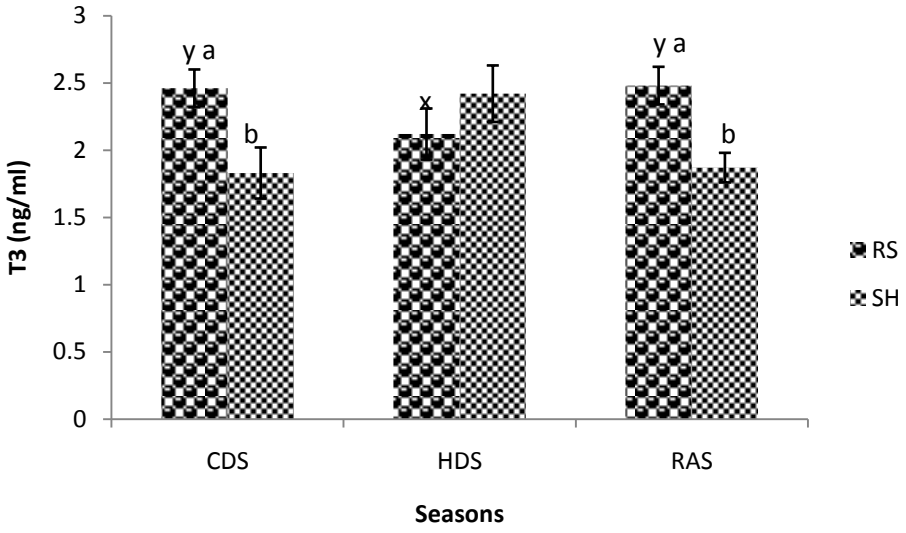


Figure 4.1: **Mean (±SEM)serum concentrations of T_3 in buck-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats.Bars with different alphabets are statistically significant (P <0.05). x,y: between seasons, a,b: between breeds.

4.10Effects of Breed and Season onSerum T_3 in Adult Bucks of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed on serum T_3 concentration in adult bucks ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.2. Serum concentrations of T_3 was significantly lower ($P<0.05$) in RSG than SHGduring the HDS as compared with the CDS and RAS.

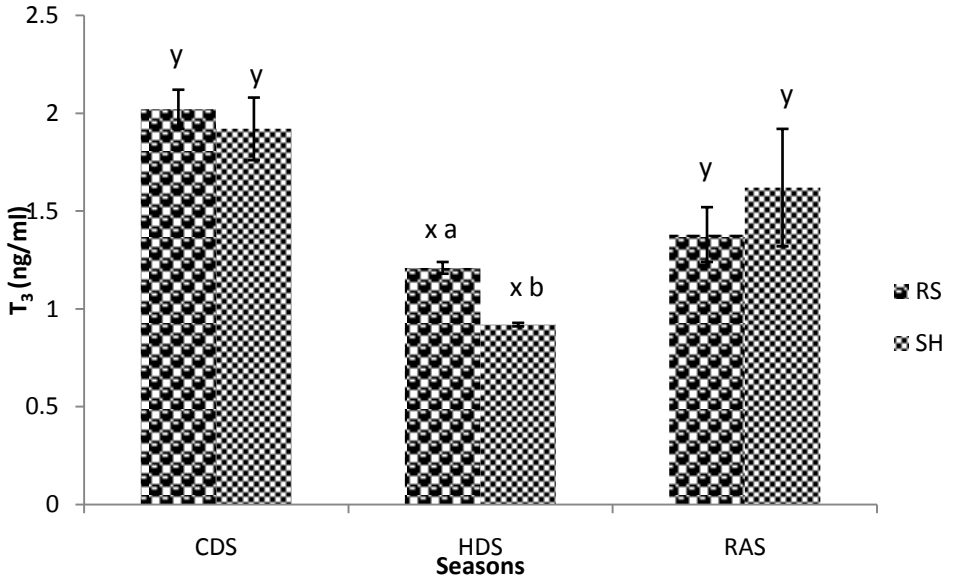


Figure 4.2: **Mean (±SEM)serum concentration of T_3 in adult bucks of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and Sahel goats. Bars with different alphabets are statistically significant ($P < 0.05$). x,y: between seasons, a,b: between breeds.

4.11Effects of Breed and Season on Serum T_3 in Doe-Kids of RSG and SHG during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed on serum T_3 concentration in doe-kids ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.3.In both breeds, circulating $T_3$was significantly lower ($P < 0.05$) during the HDS compared with the CDS and RAS. However, there was no significant difference within season in serum concentration of T_3between RSG and SHG.

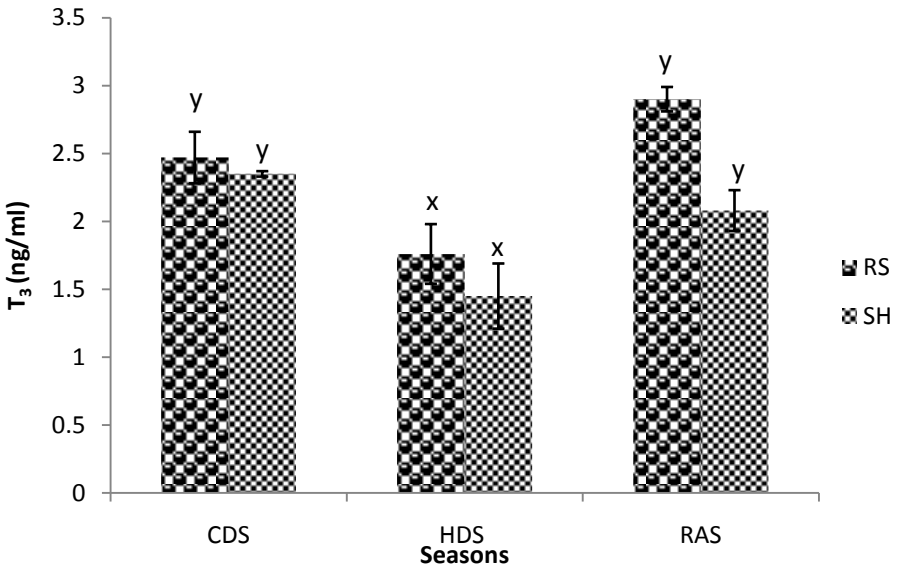


Figure 4.3: **Mean (±SEM)serum concentrations of T_3 in doe-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Bars with different alphabets are statistically significant ($P < 0.05$). x,y: between seasons.

4.12Effects of Breed and Season on Serum T_3 in Adult Does of RSG and SHG during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed on serum T_3 concentration in adult does ofRS and SH goats during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.4. In RSG, circulating $T_3$was significantly lower ($P < 0.05$) during the HDS compared with the CDS and RAS. While in SH goats, circulating $T_3$was significantly lower ($P < 0.05$) during the HDS compared with the CDS. However, there was no significant difference within season in serum concentration of T_3between RSG and SHG.

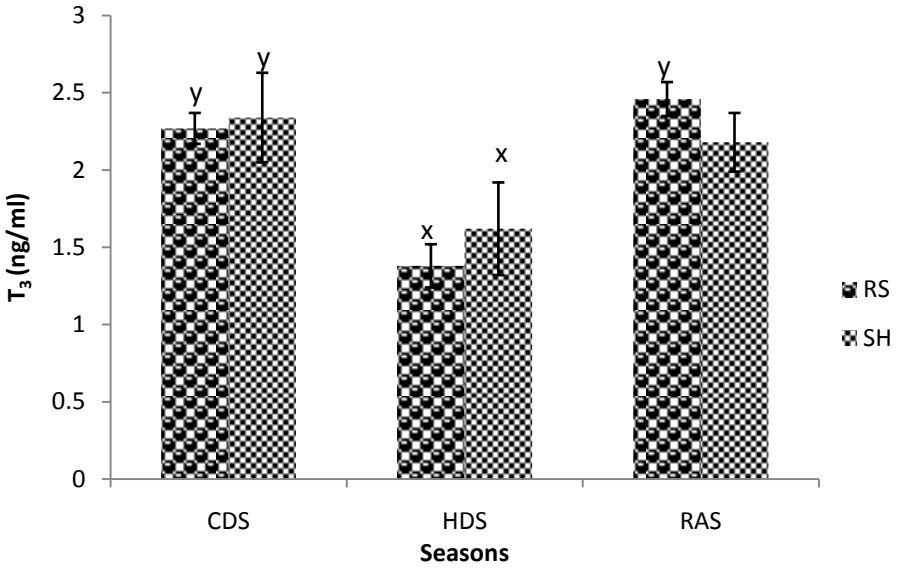


Figure 4.4: **Mean (±SEM)serum concentrations of T_3 in adult does of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Barswith different alphabets are statistically significant (P < 0.05). x,y: between seasons.

4.13Effects of Breed and Season on Serum T_4 in Buck-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed on serum T_4 concentration in buck-kids ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.5. Serum concentration of $T_4$was significantly higher ($P<0.05$) in RSG than SHGduring the RAS.Circulating $T_4$was significantly higher ($P < 0.05$) during the HDS compared with the RAS in SHG.

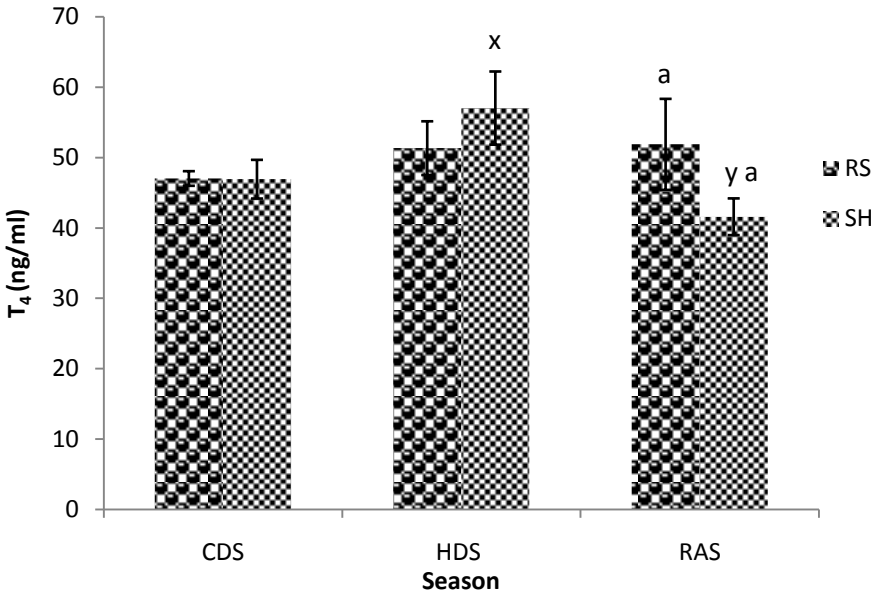


Figure 4.5: **Mean (±SEM)serum concentrations of T_4 in buck-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Barswith different alphabets are statistically significant (P < 0.05). x,y: between seasons, a,b between breeds

4.14Effects of Breed and Season on Serum T_4 in Adult Bucks of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed on serum T_4 concentration in adult bucks ofRS and SH goats during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.6. Serum T_4 was significantly higher ($P<0.05$) in RSGthan SHGin the HDS, but lower ($P< 0.05$) in RSG than SHG in the CDS.Circulating $T_4$was significantly higher ($P < 0.05$) in the HDS compared with the CDS in RSG. However, circulating $T_4$was significantly lower ($P < 0.05$) during the HDS compared with the RAS in SHG.

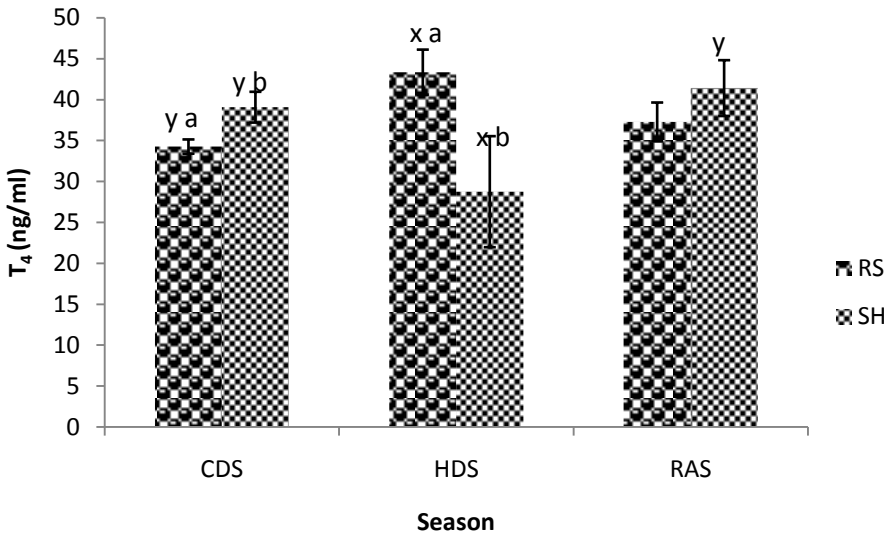


Figure 4.6: **Mean (±SEM) serum concentrations of T_4 in adult bucks of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Bars with different alphabets are statistically significant ($P < 0.05$). x,y: between seasons, a,b between breeds

4.15Effects of Breed and Season on Serum T_4 in Doe-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed on serum T_4 concentration in doe-kids ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.7. Serum concentration of $T_4$was significantly higher ($P<0.05$) in RSG than SHGduring the RAS.In both breeds of goats, there was no significant difference between seasons in serum concentrations of T_4.

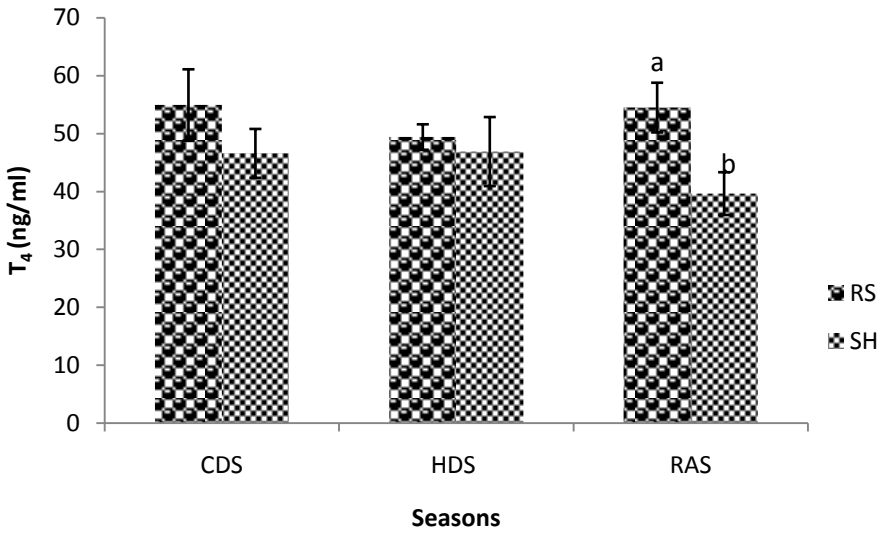


Figure 4.7: **Mean (±SEM)serum concentrations of T_4 in doe-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Bars with different alphabets are statistically significant (P < 0.05).a,b: between breeds.

4.16Effects of Breed and Season on Serum T_4 in Adult Does of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed on serum T_4 concentration in adultdoes ofRS and SH goats during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.8. Serum concentration of $T_4$was significantly higher ($P<0.05$) in RSG than SHGduring the HDS.In both breeds of goats, there was no significant difference between seasons in serum concentrations of T_4.

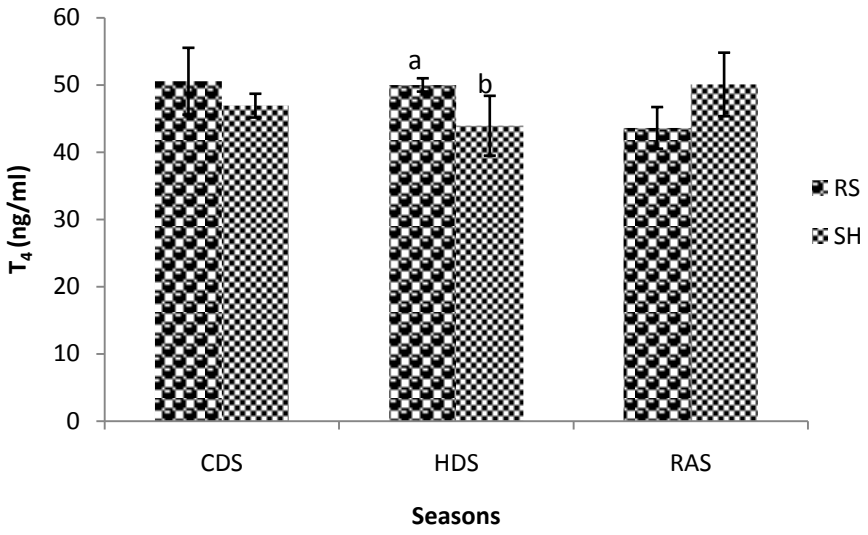


Figure 4.8: **Mean (±SEM)serum concentrations of T_4 in adult does of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats.Barswith different alphabets are statistically significant ($P < 0.05$). a,b: between breeds.

4.17Effects of Breed and Season onSerum TSHin Buck-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed and season on serum TSHconcentration in buck-kids ofRS and SH goats during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.9.Serum concentration of TSHwas significantly lower ($P<0.05$) in RS than SH goats during the HDS.In SHG, serum concentration of TSHwas significantly lower ($P<0.05$) in the RAS compared with the CDS and HDS.

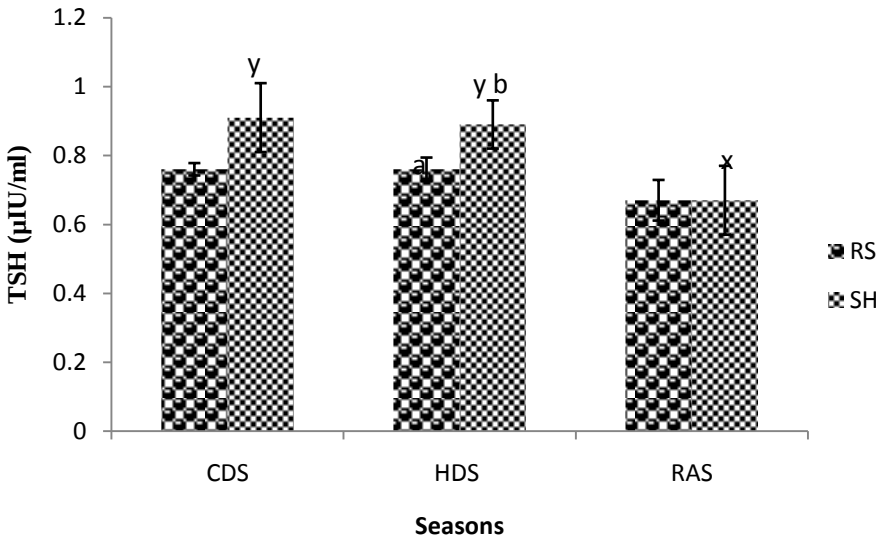


Figure 4.9: **Mean (±SEM)serum concentrations of TSH in buck-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Bars with different alphabets are statistically significant (P < 0.05). x,y: between seasons, a,b: between breeds.

4.18Effects of Breed and Season onSerum TSHin Adult Bucks of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed and season on serum TSHconcentration in adult bucks ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.10.Red Sokoto goats had significantly higher ($P<0.05$) serum concentration of TSHthan SHGduring the HDS.In SHG, serum concentration of TSHwas significantly lower ($P<0.05$) during the HDS compared with the RAS.

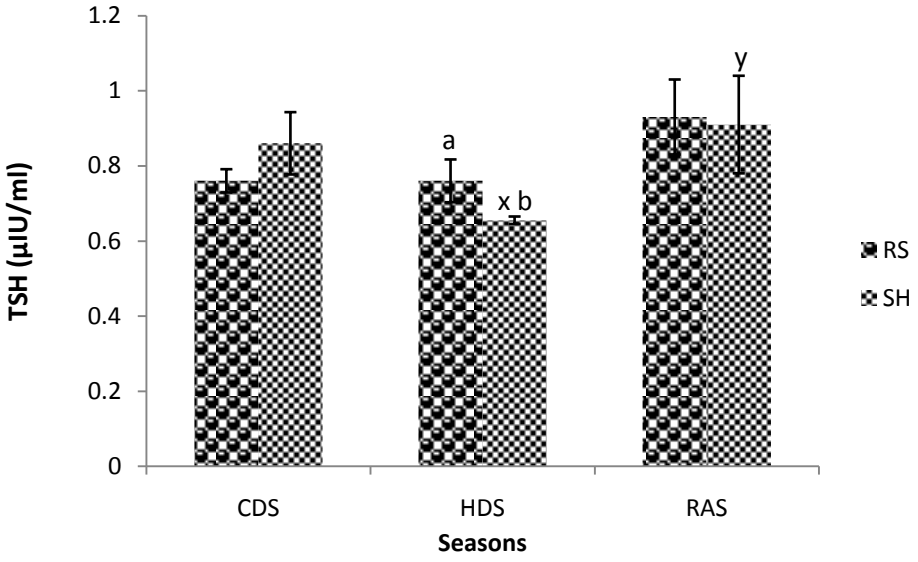


Figure 4.10: **Mean (±SEM)serum concentrations of TSH in adultbucks of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Bars with different alphabets are statistically significant (P< 0.05). x,y: between seasons, a,b: between breeds.

4.19Effects of Breed and Season onSerum TSHin Doe-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed and season on serum TSHconcentration in doe-kids ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.11.Serum concentration of TSHwas significantly higher ($P<0.05$) in RSG than SHGduring the HDS.However, in both breeds, there was no significant differencebetween seasonsinserum concentrations of TSH.

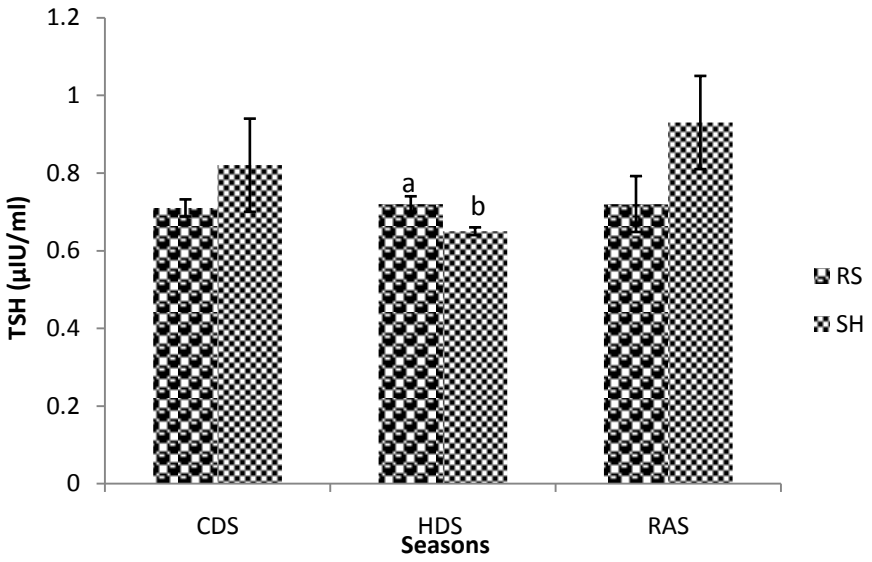


Figure 4.11: **Mean (±SEM)serum concentrations of TSH in doe-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Barswith different alphabets are statistically significant (P < 0.05). x,y: between seasons, a,b: between breeds.

4.20Effects of Breed and Season onSerum TSHin Adult Does of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed and season on serum TSHconcentration in adult doe ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.12.Red Sokoto goats had significantly lower ($P<0.05$) serum concentration of TSHthan SHG goats during the HDS. In both, however, there was no significant difference between seasonsinserum concentrations of TSH.

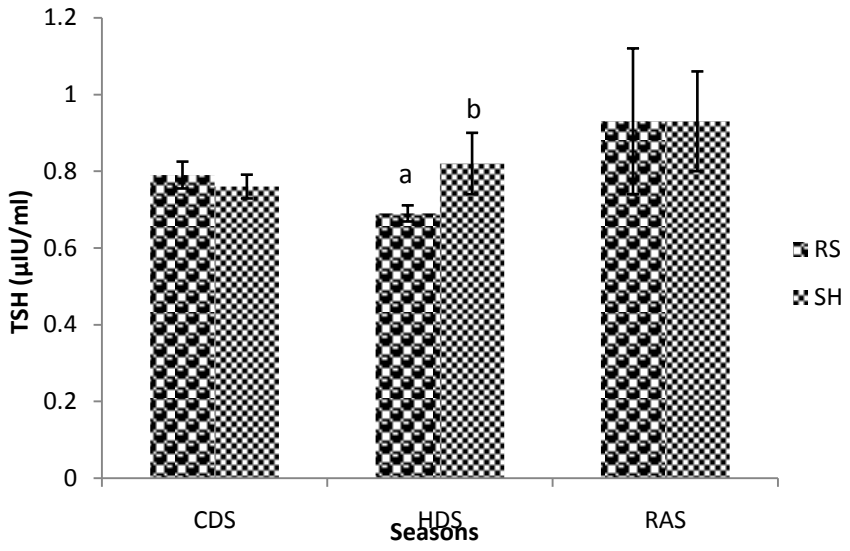


Figure 4.12: **Mean (±SEM)serum concentrations of TSH in adult does of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Bars with different alphabets are statistically significant (P < 0.05). a,b: between breeds.

4.21Effects of Breed and Season on T_3:T_4in Buck-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed on T_3:T_4 in buck-kids ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.13. There was no significant difference invalues of T_3:T_4between breeds and seasons.

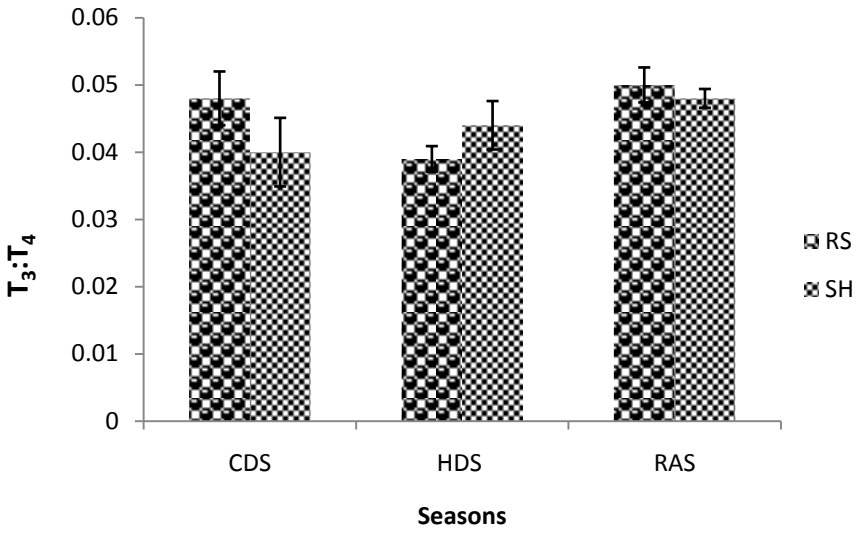


Figure 4.13: **Mean (±SEM) valuesof T_3:T_4 in buck-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats.

.

4.22Effects of Breed and Season onT_3:T_4 in Adult Bucks of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed onT_3:T_4in adult bucks ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.14. In RSG, value ofT_3:$T_4$was significantly lower ($P<0.05$) in the HDS compared with the RAS. However, there was no significant breed difference ($P>0.05$) within season invalues of T_3:T_4in both breeds.

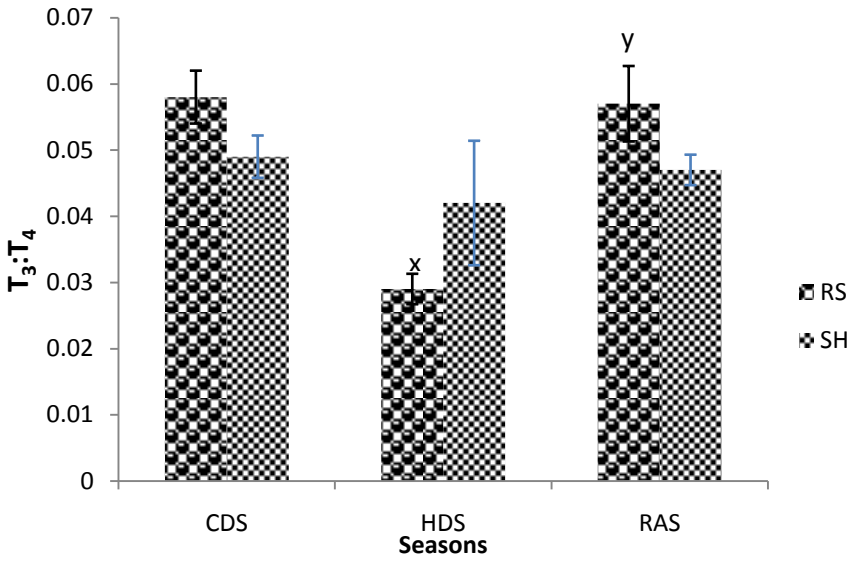


Figure 4.14: **Mean (±SEM) valuesof T_3:T_4inadult buck of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Bars with different alphabets are statistically significant ($P < 0.05$). x,y: between seasons.

4.23Effects of Breed and Season on T_3:T_4in Doe-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed onT_3:T_4in doe-kids ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.15. In RSG, value ofT_3:$T_4$was significantly lower ($P<0.05$) in the HDS compared with the CDS and RAS.Similarly, values of T_3:$T_4$was significantly lower ($P<0.05$) in the HDS compared with RAS in SH goats. There was no significant breed difference ($P>0.05$)within season values of T_3:T_4.

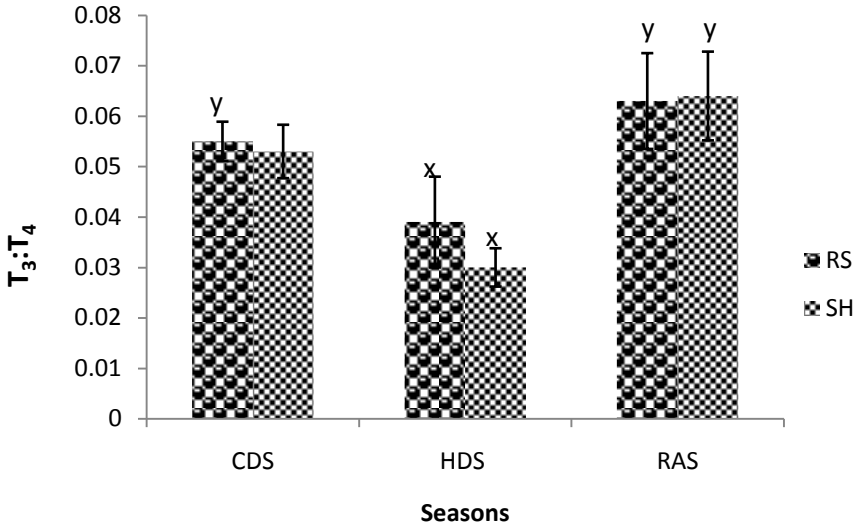


Figure 4.15: **Mean (±SEM) values of T_3:T_4 in doe-kids of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Bars with different alphabets are statistically significant (P <0.05). x,y: between seasons, a,b between breeds

4.24Effects of Breed and Season onT_3:T_4in Buck-Kids of RS and SH Goats during the Cold-dry, Hot-dry and Rainy Seasons

Results of the effect of breed on T_3:T_4 in buck-kids ofRSG and SHG during the cold-dry, hot-dry and rainy seasons are shown in Figure 4.16. Value of T_3:$T_4$was significantly higher ($P<0.05$) in RSG than SHGduring the RAS.

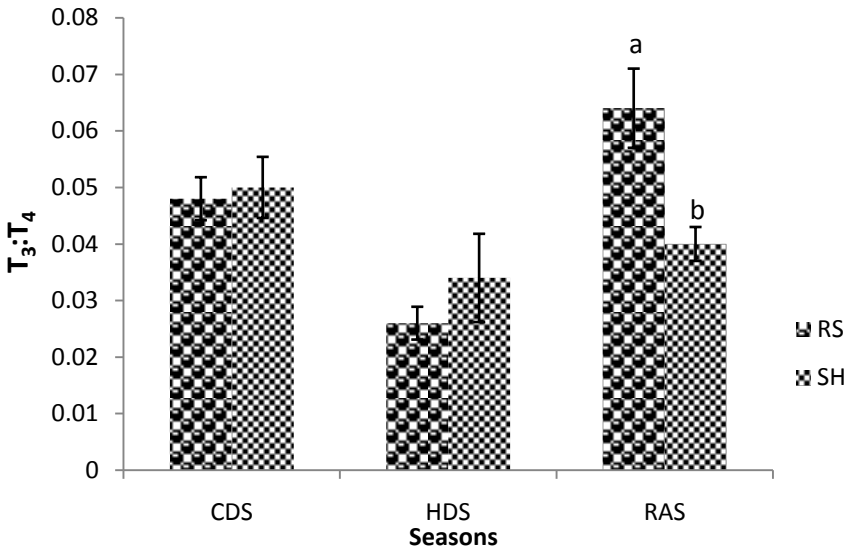


Figure 4.16: **Mean (±SEM) values of T_3:T_4 in adult does of RS and SH goats during the cold-dry, hot-dry and rainy seasons (*n*=10).**CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats. Bars with different alphabets are statistically significant ($P < 0.05$). x,y: between seasons, a,b between breeds

4.25 Effect of Breed on Body Mass Index Red Sokoto and Sahel goats

Effect of breed on BMI of RSG and SHG in kids and adult goats is shown in Table 4.8. In the goat kids, BMI was significantly higher ($P < 0.05$) in RS than SH goats. However, no significantdifference was observed in BMI between adult RSG and SHG.

Table 4.9: Mean (±SEM) values of body mass index in young and adult RS and SH goats

	Young	Adult
Red Sokoto	0.84 ± 0.05^{x}	2.54 ± 0.01
Sahel	0.69 ± 0.05^{y}	2.50 ± 0.09

Values with different superscript ($^{x, y}$) within column and ($^{a, b}$) within season are significantly different, $P < 0.05$

4.26 Coefficient of Correlation between BMI and Serum Concentrations of T_3, T_4, TSH and T_3:T_4 in YoungRed Sokoto and SahelGoats during the Cold-dry, Hot-dry and Rainy Seasons

The relationship between BMI and circulating concentrations of T_3,T_4, TSH and T_3:T_4in young RSG and SHGduring the cold-dry, hot-dry and rainy seasonsare presented in Table 4.9. In young goats, a significantly positive correlation ($r = 0.781$; $P<0.05$) was observed between circulating$T_3$and BMI in male RSG, while the relationship wasnegative ($P < 0.05$)in SHGduring the HDS. Similarly, a significantly negative correlation ($r = -0.776$; $P < 0.05$) was observedbetween circulatingT_4 and BMI during the HDS in RSG buck.A significantly positive correlation ($r = 0.619$; $P < 0.05$) was observed between TSH and BMI in SH goats during the HDS, while the correlation wasnegative ($r = -0.575$; $P < 0.05$) in RSG during the RAS. Similarly, the correlationbetween T_3:T_4 and BMI was positive ($r = 0.900$; $P < 0.05$) in RSG during the CDS. However, the correlation between T_3:T_4 and BMI was negative ($r = -0.749$; $P < 0.05$) in SHG during the HDS.

Table 4.10: Pearson's correlation coefficient between BMI and circulating concentrations of T_3,T_4, TSH and values of T_3:T_4 for young goats

	BODY MASS INDEX					
	CDS		HDS		RAS	
	RSG	SHG	RSG	SHG	RSG	SHG
T3						
Male (M)	0.462	-0.474	0.781*	0.254	0.141	0.287
Female (F)	0.574	0.400	-0.519	-0.908*	-0.079	-0.145
M+F	0.428	0.165	0.534	-0.776*	0.028	-0.201
T4						
Male (M)	-0.094	-0.413	0.659	0.344	-0.044	-0.126
Female (F)	-0.377	-0.031	-0.285	-0.837*	-0.552	0.0165
M+F	0.009	-0.314	0.306	-0.257	-0.279	0.146
TSH						
Male (M)	-0.055	0.094	-0.630	0.496	-0.821*	0.416
Female (F)	-0.485	0.305	-0.033	0.318	-0.462	0.111
M+F	-0.272	0.241	-0.406	0.619*	-0.575*	0.193
T_3:T_4						
Male (M)	0.336	-0.187	0.136	0.053	-0.018	0.389
Female (F)	0.900*	0.511	-0.256	-0.694	0.412	0.278
M+F	0.272	0.448	-0.0125	-0.749*	0.296	0.246

CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RS – Red Sokoto goats and SH – Sahel goats, M+F – correlation of male and female goats. Valueswith asterisk (*) are statistically significant. $P < 0.05$ (*)

4.27Coefficient of Correlation between BMI and Serum Concentrations of T_3, T_4, TSH and T_3:T_4in AdultRed Sokoto and Sahel Goats during the Cold-dry, Hot-dry and Rainy Seasons

The relationship between BMI and circulating concentrations of T_3,T_4, TSH and T_3:T_4 in adult RSG and SHGduring the cold-dry, hot-dry and rainy seasons are presented in Table 4.10. The correlationbetween T_3 and BMI was significantly positive ($r = 0.611$; $P < 0.05$) in RS goats during the CDS. Similarly, significantly positive correlation ($r = 0.620$; $P < 0.05$) was observed between BMI and T_4 during the CDS in RSG, while in the HDS and RAS, the correlation was negative ($r = -0.545$; $P < 0.05$). The correlation between TSH and BMI was significantly negative ($r = -0.862$; $P < 0.05$), in the HDS in female RSG.

Table 4.11: Pearson's correlation coefficient between BMI and circulating concentrations of T_3,T_4, TSH and values of T_3:T_4 for adult goats

	BODY MASS INDEX					
	CDS		HDS		RAS	
	RSG	SHG	RSG	SHG	RSG	SHG
T3						
Male (M)	0.443	-0.341	-0.461	-0.099	-0.136	-0.484
Female (F)	0.278	-0.545	0.065	0.467	-0.090	0.176
M+F	0.611*	-0.015	-0.152	-0.335	-0.142	0.130
T4						
Male (M)	0.052	0.064	-0.481	-0.376	0.034	-0.795*
Female (F)	-0.019	0.518	-0.439	-0.213	-0.428	-0.411
M+F	0.620*	-0.446	-0.545*	-0.542	0.073	-0.178
TSH						
Male (M)	0.215	-0.113	-0.277	0.551	0.640	-0.163
Female (F)	0.385	-0.023	-0.141	-0.862*	0.023	0.630
M+F	-0.076	0.348	-0.172	-0.359	0.318	0.364
T3:T4						
Male (M)	0.428	-0.471	0.309	0.171	0.538	-0.333
Female (F)	0.374	-0.744	0.179	-0.318	0.127	0.162
M+F	-0.049	0.043	0.249	0.052	0.315	0.384

CDS - cold-dry season, HDS – hot-dry season, RAS – rainy season, RSG – Red Sokoto goats and SHG – Sahel goats,M+F – correlation of male and female goats.Valueswith asterisk (*) are statistically significant. $P < 0.05$ (*)

CHAPTER FIVE

DISCUSSION

The values of T_3 and T_4 in RS and SH in all the seasons are within the range reported in other tropical breeds of goats such as the Balady and Damascus goats of Egypt (Abdel-Fattah, 2014) and Barbari goats of India (Sharma *et al*., 2013). On the average, circulating concentration of total T_3 and T_4 in goats according to the present study were mostly in the form of T_4 (95.5%) compared with T_3 (4.5%). These values agree with the findings of other studies and are close to that reported by Todini (2007) who reported approximately 98 and 2% for T_3 and T_4, respectively. There was paucity of information on serum concentration of TSH in goats. However, values of circulating TSH reported in the present study in RS (0.76 ± 0.03 µIU/ml) and SH (0.82 ± 0.04 µIU/ml) goats are lower compared to values reported in Noemi (1.39 ± 0.07 µIU/ml) and Najdi (1.54 ± 0.10 µIU/ml) sheep of Saudi Arabia using ELISA(Al-Damegh, 2012). This may be due to species difference.

The main sources of circulating T_3 was either the thyroid gland itself (which include that liberated by thyroglobulin during TH synthesis and those produced through the action of Dio1 and 2 on T_4 in the gland) or as a result of the action of Dio 1 and 2 on the plasma T_4(Dunn and Dunn, 2001; Kohrle,2007). Thus, the ratio of T_3 and T_4 gives an indirect measure of the amount of T_4 converted to T_3 according to the body demand for the bioactive TH (T_3). Hence, high T_3:T_4 may suggest increaesd body demand for the physiological effect of TH and vice versa.

The present study reported high concentration of circulating T_3 and T_4 in females compared to males, irrespective of age. This agrees with the findings of other studies in goats (Todini *et al*., 1992; Celi *et al*., 2003; Vijay *et al*., 2014). However, the finding of the present study is contrary to that of Celi *et al*.(2003) who reported that sex does not affect circulating

T_4concentrations and that of Todini *et al*.(1992)whoreported that the influence of sex on TH concentrations was noticed only in adult goats.

With respect to season, sex-dependent influence was noticed in circulating T_4 during all the seasons and in T_3 only during the CDS and RAS. Sex-related difference in TH has been demonstrated in mammals and is reported to be due to the effect of sex hormones. The higher TH levels in females maybe due to estrogen-reduced catabolism of TBG (Ain *et al*., 1987), while the lower TH levels in males maybe attributed to androgen inhibition of the synthesis of TBG by the liver (Christianson *et al*., 1981; Todini, 2007).

The current study demonstrated a lower TSH concentration in females compared to males during the HDS. This may indicate a sex difference in the response of goat to the effect of heat stress. Also, since T_4 was higher in females compared to males, it is possible that the negative feedback inhibition of TSH secretion from the pituitary may be responsible for the low TSH in females. However, in agreement with the finding of the current study during the CDS and RAS, Khan and Akhter (2001) reported no significant difference in TSH between males and females.

The conversion of T_4 to T_3 is important in thermoregulation during the CDS and the HDS as this may regulate body metabolism in order to increase and decrease basal metabolic rate during the CDS and HDS, respectively (Ribeiro *et al*., 2015). The ability of goats to adjust the conversion pattern may influence their adaptation to a given season. Thus, the higher T_3:T_4 in doe-kids of SH compared to their male counterparts may indicate a better adaptation in the doe-kids. Since the higher metabolic rate induced by T_3 may enhance the adaptation and survival of the doe-kids, while the reduction may affect the adaptation of buck-kids during the CDS. Similarly, the lower T_3:T_4 in SH doe-kids compared to buck-kids during the HDS may suggest a better adaptive mechanism in the former, since lower conversion of

T_3will reduce metabolic rate during heat stress. The reason for the generally high T_3:T_4 in females is probably due to the high circulating T_4 in females which may provoke the action of D1 and 2 to convert T_4 to T_3 (Salvatore, 2011).

In the current study, higher values of T_3 and T_4in young compared to adult goats. This finding agrees with that of Vijay *et al*. (2014) who reported higher values of T_3 and T_4 in young Marwari goats compared to adults. Similar findings have been reported in several mammalian species (West *et al*., 2014) and maybe due to the important role TH play in the development and maturation of the young mammals,through its role in stimulating protein synthesis (Corcoran *et al*., 1977; Todini, 2007). This is further supported by the high T_3:T_4 in young compared to adult, indicating an increase in conversion of T_4 to T_3so as to ensure high circulating concentration of the bioactive T_3.

The RS goats of Nigeria are indigenous to the Northern Guinea Savannah zone,while the SH goats are indigenous to the Sahel zone of Nigeria. Recently the introduction of SH into the Northern Guinea Savannah and other zones of Nigeria, mainly by commercial and institutional farms have been observed. The concentration of circulating T_3 and T_4 were higher in RS than SH goats during the CDS and RAS. This indicate that RS goats are better adapted to the Northern Guinea Savannah zone than the SH goats. The higher circulating T_3 and T_4 concentrations during the CDS may aid the RS goats to survive better through increased thermogenesisin response to low ambient temperature.This may also help to improve thermogenesis during the RAS since high rainfall is associated with low ambient temperature in the semiarid environment. This is particularly beneficial to the kids born during the CDS since the newborn usually have poor homeostatic mechanism and require high TH to prevent hypothermia (Dwyer and Morgan, 2006). The high TH in the RS goats may be responsible for the high BMI observed in the current study in RS compared to SH goats. However, the high circulating T_3 in adultRS bucks in the HDS may affect

thermoregulation during this season. This is because the high circulating T_3 during the HDSmay increase heat load in the adultRS bucksdue to the concomitant effect of high ambient temperature and high metabolic rate. On the other hand, other groups of RS goats (kids and does) tend to decrease circulating T_3 during the HDS to prevent an increase in body heat load.

In concordance with the result of the present study, several studies have reported breed difference in TH activities in goats (Abdel-Fattah, 2014) and sheep (Dwyer and Lawrence 2005). Circulating concentrations of THis influenced by factors such as management system, prolificacy, body size andbody coat characteristicsof the breed (Todini, 2007). Also, by influencing the circulating concentration of TH,these factors play a vital role in thermoregulation. In the current study, it is conceivable that the high TH levels in RSG as compared to SHG could be due to differencein geographical location of the goats.The RSG goats are indigenous to the Northern Guinea Savannah, which is associated with lower ambient temperature compared with Sahel region, while SHGare indigenous to the Sahel zone but only adaptedto this region.Also, lower ambient temperature is one of the most important stimuli of TH secretion (Ribeiro*et al*., 2015). Furthermore, the high T_3:T_4 observed in RSG than SHGin this study, suggested higher rate of conversion of T_4 to the bioactive T_3in RSG. This indicated higher activity of deiodinase enzyme (Dio 1 and 2) andphysiological effectsof TH in RSG than SHG. It has been reported that female sheep with high TH produced lambs with high circulating T_3 (Hefnawy *et al*., 2014), this may explain why RSG kids hadhigher TH than SHG kids, since circulating TH was higher in their parents.

Upon comparing the results of circulating TH and the meteorologicalparametersin the three seasons, the CDS with the lowest ambient temperature recorded the highest values of TH and T_3:T_4as compared to the HDS. Conversely, the HDS which had the highest ambient temperaturerecordedthe lowestvalues of circulating TH and T_3:T_4 as compared to the CDS.

This finding agrees with other studies in goats (Al-Samawi *et al*., 2014, da Silva *et, al*., 2014;Banerjee*et al*., 2014). Ambient temperature is one of the main stimuli of TH secretion (Ribeiro *et al*., 2015) in most mammals.Generally, as a thermoregulatory response, an increase in TH is known to occur in cold season due to the need to increase heat production and enhance survival (Abdul Fattah, 2014). Conversely, high ambient temperature during summer causes a decrease in circulating TH levels which is a thermoregulatory response to prevent additional heat load that may arise due to an increase in metabolic rate (Omran *et al*., 2013; Sejian *et al*., 2014).

Seasons with longer day length (longer photoperiod) are associated with higher TH activities compared to seasons with shorter day length (shorter photoperiod)(Menegatos *et al*., 2006;Ikegani and Yoshemura, 2012). In the current study the RAS had the highest photoperiod and higher T_3 and T_3:T_4 compared to the HDS. However, due to the short difference (approximately one hour) in the tropical photoperiod between the RAS (12.49 h), and theCDS (11.6 h) and HDS (12.23 h), photoperiod alone may not account for the high T_3in the RAS compared to the HDS. The role of nutrition and favourableambient temperature may also be involved, since the nutritional status of animal feeds usually improve during the RAS (Lanyasunya *et al*., 2006) and the ambient temperature is relatively low. The result of the present study indicates that in the tropics ambient temperature has a greater influence on TH production than photoperiod.

The current study showedthat circulatingT_3levels were generally lowerin male and female goats during the HDS, but levels of T_4did notdecreasein comparison with other seasons, except in male SH goats.In consonance with this finding, Stockman(2006)also reported lower values of circulating T_3 and T_4 in rams during summer, but only theT_3 level was lower in ewes. This may aid the female animals to maintain a high T_4 (TH reservoir) irrespective of season, thus, ensuring that significantseasonal changein TH production does not occur.

However, the conversion of T_4 to T_3 will be done according to basic physiological needs of the body probably, in order to prevent excess heat production during the hot season in the current study.Similar pattern of thermoregulation was also observed in the goat kids of both breeds.The low serum level ofT_4 in male SHGwas probably due to reduced production by the thyroid gland as a result of the low circulating TSH levels recorded in the goats. On the other hand, high serum $T_4$was observed in the buck-kids of SHG during the HDS compared to other seasons. This may be due to increased production by the thyroid gland, as a result of the high circulating TSH levels recorded in the goats (Capen and Martins, 2003).

In Sahel buck-kids and adult bucks of RSG,a different pattern of TH profile was observed, where highercirculating T_4,but non-significant change in T_3levels was observed during the HDS compared to other seasons. This finding agrees with the observations in buffalo bulls, where T_4 was higher during summer compared to winter, while there was no significant change in serum T_3 (Mayahi *et al*., 2014). The high circulating T_4 during the hot season may be due to a reduction in the conversion of T_4 to T_3 by the Dio 1 and 2.

The current study showed no significantchange in circulating TSH between seasonsin RS goats and female SH goats,and this agrees with the finding of Mayahi *et al*. (2014) in buffalos,who demonstrated no significant difference in TSH in buffalos between summer and winter. This may indicate a relatively more efficient adaptation to seasonal changes in this group of animals and also explains why circulating T_4did not decrease in the female goats.

The generalized decrease in circulating T_3 during the HDS compared to the other seasons as observed in the current study may be due to the reduction in the conversion of T_4 to T_3 indicated by a lower T_3:T_4 observed during this season. This is an attempt to decrease the availability of the bioactive T_3 in circulation. Also, the study of Mayahi *et al*.(2014) reported a decrease in theuptake ofT_3 during summer. In contrast to the findings of this study, El-

Nouty *et al*. (1990) reported lower concentration of serum T_4 and higher rate of conversion of T_4 toT_3, but no significant change in T_3 during summer compared to the winter in cows. However, in other studies, no significant difference in T_3:T_4 was observed between cows exposed to a thermoneutral environment and those exposed to prolonged cold (Bernier *et al*., 2012).

Body mass index(Estrade-Cortes *et al*., 2009) and circulating TH (Riis and Madsen, 1985) are good indicatorsof the nutritional status or body energy reserve of animals. In the current study,consistency was not observed in the correlation between BMI and serum concentrations of T_3, T_4, TSH andT_3:T_4in different seasons of the year. Generally, a positive correlation was observed between BMI and serum concentration of $T_3$and T_4 during the CDS, while the correlation was negative during the HDS. The positive correlation between BMI and TH during the CDS in RS goats agrees with the study of Milionis and Milionis(2013)in which total T_3 and T_4 had a positive association with BMI in women.

In the present study, a negative association was observed between BMI and TSH in adult RS goats, while a positive correlation was observed in adult SH goats all the seasons. In a similar trend, Solanki *et al*.(2013) reported a positive correlation, while Milionis and Milionis (2013) reported a negative correlation between BMI and TSH in humans. Although the negative association between BMI and T_3:T_4 in SH goats during the HDScontradictsthe finding of Milionis and Milionis (2013), the positive association in female RS goats during the CDS agrees with the latter's study. Thus, indicating that the relationship between BMI and T_3:$T_4$is influenced by season.

The positive correlation between BMI and TSH is probably due to the role of TSH in stimulating preadipocyte differentiation which results in adipogenesis (Bell *et al*., 2000; Valyasevi *et al*., 2002; Schäffler *et al*., 2005; Feldt-Rasmussen, 2007). Although TH have a lypolytic effect which may reduce body energy stores, the anabolic effect of TH in protein

synthesis (Capen and Martin, 2003) may be responsible for the positive association between BMI and circulating TH in some seasons. The findings of the current study suggest that circulating TH and TSH concentrations may affect BMIand the relationship may be influenced by season, breed, sex and age.

CHAPTER SIX

CONCLUSION AND RECOMMENDATION

6.1 Conclusion

i. Baseline values of serum concentration of T_3, $T_4$and TSH have been obtained in RS and SHgoats in the Northern Guinea Savannah zone of Nigeria.

ii. Serum concentration of T_3, T_4, TSH and T_4:T_3 were affected by breed,sex, age, BMIand season in RS and SH goats.

6.2 Recommendations

i. Clinicians and researcher should take into cognizance breed, sex, age, BMI and season when interpreting serum values of T_3, T_4, TSH and T_4:T_3 in RS and SH goats in the Northern Guinea Savannah zone of Nigeria.

ii. Small ruminant producers should consider the relatively less efficient thermoregulatory adaptation of SH goats during the CDS of the Northern Guinea Savannah zone of Nigeria in the provision of housing, feeding and management practice.

iii. The impact of the decrease in TH during the HDS on other physiologic activities that are dependent on TH needs to be investigated.

REFERENCES

Abdel-Fattah, M.S. (2014). Effect of summer shearing on some blood constituents, thyroid gland andcortisol responses of Balady and Damascus Goats in desert of Sinai, Egypt. *World Applied Sciences Journal*, 30(5): 543-555.

Abdollahi, E., Kohram H. and Shahir M.H. (2013). Plasma concentrations of essential trace microminerals and thyroid hormones during single or twin pregnancies in fat-tailed ewes. *Small Ruminant Research*, 113: 360–364.

Aceves, C. and Valverde, R.C. (1989). Type I, 5‘-monodeiodinase activity in the lactating mammary gland. *Endocrinology*, 124: 2818-2820.

Adenkola, A.Y., Ayo, J.O. and Asala, O.O. (2011). Variations in Haematological Parameters and Erythrocyte Osmotic Fragility of Pigs during Hot-dry and harmattan season in northern guinea Savanna zone of Nigeria. *Nigeria Journal of Physiological Sciences*, 26: 113 – 118.

Adu, I.F., Buvanendran, V. and Lakpini, C.A.M. (1979). The reproductive performance of Red Sokoto in Nigeria. *Journal of Agricultural Science*, 93: 563-566.

Ain, K.B., Mori, Y. and Refetoff, S. (1987). Reduced clearance rate of thyroxine- binding globulin (TBG) with increased sialylation: a mechanism for estrogen-induced elevation of serum TBG concentration. *Journal of Clinical Endocrinology and Metabolism*, 65: 689–696.

Al-Ani, F.K., Khamas, W.A., Al-Qudah, K.M. and Al-Rawashdeh,O. (1998). Occurrence of congenital anomalies in Shami breed goats: 211cases investigated in 19 herds. *Small Ruminant Research*, 28: 225–232.

Al-Damegh, M.A. (2012). Sheep breed type effects on plasma thyrotropin, thyroxine and testosterone in growing ram lambs under hot climate. *Journal of Food, Agriculture and Environment*,10(1): 530-533.

Al-Garawi, A.A., Abdel-Rahman, H. and Elmougy, S.A. (2001). Impairment in the pituitary-thyroid axis of *Camelus dromedarius* infected with *T.evansi*. *Deutsche Tierärztliche Wochenschrift*, 108(4): 172-174.

Al-Samawi, K.A., Al-Hassan, M.J. and Swelun, A.A. (2014).Thermoregulation of female Aardi Goats exposed to environmental heat stress in Saudi Arabia. *Indian Journal of Animal Research*, 48(4): 344 – 349.

Alexandre, G., Beauville, S., Asselin de Bienville, Y. and Shitalou, E. (2002). La ch`evre multifonctionnelle dans la soci´et´e antillaise. *Ethnozootechnie*, 70: 35–52.

Alshaikh, M.A., Salah, M.S., Kraidees, M.S., AlSaiady, M.Y., Abouheif, M.A. and Aldabeeb, S.N. (1997). Plasma concentration of thyroid hormones in lambs fed poultry offal meal in replacement of soybean meal at two different energy levels. *Deutsche Tierärztliche Wochenschrift*, 104: 213–215.

Anderson, G.M., Connors, J.M., Hardy, S.L., Valent, M. and Goodman, R.L. (2002). Thyroid hormones mediate steroid-independent seasonal changes in luteinizing hormone pulsatility in the ewe. *Biology of Reproduction*, 66: 701–706.

Antunović, Z., Novoselec, J., šperanda1, M., Vegara, M., Pavić, V., Mioč, B. and Djidara, M. (2011). Changes in biochemical and haematological parameters and metabolic hormones in Tsigai ewes blood in the first third of lactation. *Archiv Tierzucht*, 54(5): 535-545.

Asayama, K., Dobashi, K., Hayashibe, H., Megata, Y. and Kato, K. (1987). Lipid peroxidation and free radical scavengers in thyroid dysfunction in the rat: a possible mechanism of injury to heart and skeletal muscle in hyperthyroidism. *Endocrinology*, 121: 2112–2118.

Ayo, J.O., Oladele, S.B., Fayomi, A., Jumbo, S.D. and Hambolu, J.O. (1998). Body temperature, respiratory and heart rate in the Red Sokoto goat during the harmattan season," *Bulletin of Animal Health and Production in Africa*,46(2): 161–166.

Ayo, J.O., Oladele, S.B., Ngam, S., Fayomi, A. and Afolayan, S.B. (1999). Diurnal fluctuations in rectal temperature of the Red Sokoto goat during the harmattan season.*Research in Veterinary Science*, 66(1): 7-9.

Azimzadeh, K., Nouri, K., Farooghi, H., Rasouli, S. and Zamani, N. (2013). Plasma malondialdehyde, thyroidhormones and some blood profiles in ovine babesiosis. *Kafkas Universitesi Veteriner Fakultesi Dergisi*, 19(3): 489-493.

Badiei, K., Mostaghni, K,, Pourjafar, M., Ghane, M. and Mohammadi, E. (2010). Serum thyroid hormones and trace element concentrations in crossbred Holstein cattle naturally infected with *Theileria annulata. Comparative Clinical Pathology*, DOI 10.1007/s00580-010-0962-0, 2010.

Banerjee, D., Upadhyay, R.C., Chaudhary, U.B., Kumar, R., Singh, S., Ashutosh, Das, T.K. and De, S.(2014). Seasonal variations in physio-biochemical profiles of Indian goats in the paradigm of hot and cold climate. *Biological Rhythm Research*, DOI:10.1080/09291016.2014.984999.

Barceloux, D.G. (1999). Cobalt. *Journal of Toxicology, Clinical Toxicology*, 37: 201-206.

Barrett, P., Ebling, F.J., Schuhler, S., Wilson, D., Ross, A.W., Warner, A., Jethwa, P., Boelen, A., Visser, T.J., Ozanne, D.M., Archer, Z.A., Mercer, J.G., Morgan, P.J. (2007). Hypothalamic thyroid hormone catabolism acts as a gatekeeper for the seasonal control of body weight and reproduction. *Endocrinology*, 148: 3608–3617.

Bartalena L.F., Bogazzi F., Brogioni S., Grasso L. and Martino, E. (1998). Role of cytokines in the pathogenesis of the euthyroid sick syndrome. *European Journal of Endocrinology*, 138: 603–614.

Bartalena, L. (1990). Recent achievements in studies on thyroid hormone-binding proteins. *Endocrine Reviews*, 11: 47–64.

Bass, J. (1989). Effect of litter size, dietary protein content, ewe genotype and season on milk production and associated endocrine and blood metabolite status of ewes. *Animal Breeding Abstracts*, 58: 275.

Bekele, T., Asfaw, Y., Gebre-Egziabeher, B. and Abebe, G. (2011). Seroprevalence of contagious caprine pleuropneumonia in Borana and Guji lowlands, Southern Ethiopia. *Ethiopian Veterinary Journal*, 15: 69-76.

Bell, A., Gagnon, A., Grunder, L., Parikh, S.J., Smith, T.J. and Sorisky, A. (2000). Functional TSH receptor in human abdominal preadipocytes and orbital fibroblasts. *American Journal of Physiology: Cell Physiology*, 279(2): C335–C340.

Bentley, G.E., Goldsmith, A.R., Dawson, A., Glennie, L.M., Talbot, R.T. and Sharp, P.J. (1997). Photorefractoriness in European starlings (*Sturnus vulgaris*) is not dependent upon the long-day-induced rise in plasma thyroxine. *General and Comparative Endocrinology*, 107: 428–438.

Berczi I. (1993). Neuroendocrine defense in endotoxin shock. *Acta Microbiologica et Immunologica Hungarica*, 40: 265–302.

Bernal, J. (2002). Action of thyroid hormone in brain. *Journal of Endocrinological Investigation*, 25 268–288.

Bernal, J. (2006). Role of monocarboxylate anion transporter 8 (MCT8) in thyroid hormone transport: answers from mice. *Endocrinology*, 147: 4034-4035.

Bernier, J.N., Undi, M., Plaizier, J.C., Wittenberg, K.M., Donohoe, G.R. and Ominski, K.H. (2012). Impact of prolonged cold exposure on dry matter intake and enteric methane emissions of beef cows overwintered on low-quality forage diets with and without supplemented wheat and corn dried distillers' grain with solubles. *Canadian Journal of Animal Science*, 92: 493-500.

Bertók L. (1998). Endotoxins and endocrine system. *Domestic Animals Endocrinology*, 15: 305–308.

Bhardwaj, R.L., Rajput, R., Pathak, V. and Thakur, K. (2006). Comparative anatomy of the thyroid gland of small ruminants. *Indian Journal of Animal Science*, 76: 46-47.

Bhattacharjee, M. and Vonderhaar B.K. (1984). Thyroid hormones enhance the synthesis and secretion of alpha lactalbumin by mouse mammary tissue in vitro. *Endocrinology*, 115:1070–1077.

Bhooshan, N., Kumar, P., Singh, S.K. and Yadav, M.C. (2010). Status of thyroid hormones in blood plasma of goats at different ages and their correlation with other biochemical parameters. *The Indian Journal of Animal Sciences*, 80(4): 39-43.

Bidey, S.P., Hill, D.J. and Eggo, M.C. (1999). Growth factors and goitrogenesis. *Journal of Endocrinology*, 160: 321–332.

Bik, D.E. 92003). Influence of selenium and iodine supplementation on thyroid hormone concentrations in the blood serum of sheep. *Medycyna Weterynaryjna*, 59: 1126–1129.

Billings, H.J., Viguie, C., Karsch, F.J., Goodman, R.L., Connors, J.M. and Anderson, G.M. (2002). Temporal requirements of thyroid hormones for seasonal changes in LH secretion. *Endocrinology*, 143: 2618–2625.

Bíres, J., Bartko, P., Weissová, T., Michna, A. and Matisák, T. (1996). Iodine deficiency in goats as a cause of congenital goiter in kids. *Veterinarni Medicina*, 41: 133-138.

Bittman, E.L. and Karsch, F.J. (1984). Nightly duration of pineal melatonin secretion determines the reproductive response to inhibitory day length in the ewe. *Biology of Reproduction*, 30: 585–593.

Błaszczyk, B., Udała, J. and Gaczarzewicz, D. (2004). Changes in estradiol, progesterone, melatonin, prolactin andthyroxine concentrations in blood plasma of goats followinginduced estrus in and outside the natural breeding season.*Small Ruminant Research*, 51: 209–219.

Bonomo, I.T., Lisboa, P.C., Passos, M.C.F., Alves, B.A., Reis, A.M. and deMoura, E.G. (2008). Prolactin inhibition at the end of lactation programs for hypothyroidism in adult rat. *Journal of Endocrinology*, 198: 331–337.

Boyazoglu, J. and Morand-Fehr, P. (2001). Mediterranean dairy sheep and goat products and their quality. A critical review. *Small Ruminant Reseach*, 40: 1–11.

Brown, N.S., Smart, A., Sharma, V., Brinkmeier, M.L., Greenlee, L., Camper, S.A., Jensen, D.R., Eckel, R.H., Krezel, W., Chambon, P. and Haugen, B.R. (2000). Thyroid hormone resistance and increased metabolic ratein the RXR-g deficient mouse.*The Journal of Clinical Investigation*, 106(1): 73-79.

Cabello, G. and Wrutniak, C. (1986). Plasma free and total iodothyronine levels in the newborn lamb. Physiological consideration. *Reproduction, Nutrition, Development*, 26: 1281–1288.

Cabello, G. and Wrutniak, C. (1990). Thyroid function in the newborn lamb. Physiological approach of the mechanisms inducing the changes in plasma thyroxine, free thyroxine and triiodothyronine concentrations. *Journal of Developmental Physiology*, 13: 25–32.

Capen, C.C. and Martin, S.L. (2003). The thyroid gland. In: Maricio H. P. and Michael P. D. (Ed.) *McDonald's veterinary endocrinology and reproduction*. Blackwell publishing professionals, Iowa, USA. pp. 35-70.

Capuco, A.V., Connor, E.E., and Wood, D.L. (2008). Regulation of mammary gland sensitivity to thyroid hormones during the transition from pregnancy to lactation. *Experimental Biology and Medicine,* 233:1309–1314.

Celi, P., Seren, E., Celi, R., Parmeggiani, A. and Di Trana, A. (2003). Relationships between blood hormonal concentrations and secondary fibre shedding in young cashmere-bearing goats at their first moult. *Animal Science*, 77: 371–381.

Chadio, S.E., Kotsampasi, B.M., Menegatos, J.G., Zervas, G.P. and Kalogiannis, D.G. (2006). Effect of selenium supplementation on thyroid hormone levels and selenoenzyme activities in growing lambs. *Biological Trace Element Research,* 109: 145–154.

Chao, C.C. and Brown, R.D. (1984). Seasonal relationships of thyroid, sexual and adrenocortical hormones to nutritional parameters and climatic factors in white-tailed deer (Odocoileus virginianus) of South Texas.*Comparative Biochemistry and Physiology A,* 77: 299–306.

Cheema, A.H., Shakoor, A. and Shahzad, A.H. (2010). Congenital goitre in goats. *Pakistan Veterinary Journal,* 30(1): 58-60.

Chemineau, P. Daveau, A., Maurice, F. and Delgadillo,J.A. (1992a). Seasonality of estrus and ovulation is not modified by subjecting female Alpine goats to a tropical photoperiod. *Small Ruminant Research*, 8(4): 299–312.

Chemineau, P., Malpaux, B., Delgadillo, J.A., Guerin, Y., Ravault, J.P., Thimonier, J. and Pelletier, J. (1992b). Control of sheep and goat reproduction: use of light and melatonin. *Animal Reproduction Science*, 30: 157–184.

Chemineau, P., Daveau, A., Cognié, Y., Aumont, G. and Chesneau, D. (2004). Seasonal ovulatory activity exists in tropical Creole female goatsand Black Belly ewes subjected to a temperate photoperiod. *BMC Physiology,* doi:10.1186/1472-6793-4-12.

Choi, Y.H., Hartzell, D., Azain, M.J. and Baile, C.A. (2002). TRH decreases food intake and increases water intake and body temperature in rats. *Physiology and Behavior*, 77(1): 1–4.

Choksi, N.Y.,Jahnke, G.D.,Hilaire, C.S. and Shelby, M. (2003). Role of thyroid hormones in human and laboratory animal reproductive health. *Birth Defects Research (Part B,)* 68:479–491.

Chopra, I.J., Sack, J. and Fisher, D.A. (1975). 3,30,50-Triiodothyronine (Reverse T3) and 3,3,50-Triiodothyronine (T3) in fetal and adult sheep: studies on metabolic clearance rates, production rates, serum binding, and thyroidal content relative to thyroxine. *Endocrinology*, 97: 1080–1088.

Chopra, I.J., Solomon, D.H., Chopra, U., Wu, S.Y., Fisher, D.A. and Nakamura, Y. (1978). Pathways of metabolism of thyroid hormones. *Recent Progress in Hormone Research*, 34: 521–567.

Christianson, D., Roti, E., Vagenakis, A.G. and Braverman, L.E. (1981). The sex related difference in serum thyrotropin concentration is androgen mediated. *Endocrinology*, 108: 529–535.

Cisse, M., Ly, I., Nianogo, A.J., Sane, I., Sawadogo, J.G., N'Diaye, M., Awad, C. and Fall, Y. (2002). Grazing behaviour and milk yield of Senegalese Sahel goat. *Small Ruminant Research,* 43(1): 85-95.

Clarke, L., Heasman, L., Firth, K. and Symonds, M.E. (1997). Influence of route of delivery and ambient temperature on thermoregulation in newborn lambs. *American Journal of Physiology*, 272(6 Pt 2): R1931-1939.

Colavita, G.P., Debenedetti, A., Ferri, C., Lisi, C. and Lucaroni, A. (1983). Blood thyroid hormone concentrations by the domestic goat: seasonal and age-related variations.*Bollettino della Societa` Italiana di Biologia Sperimentale,* 49, 779–785.

Cooke, P.S., Zhao, Y.D. and Bunick, D. (1994). Triiodothyronine inhibits proliferation and stimulates differentiation of cultured neonatal Sertoli cells: possible mechanism for increased adult testis weight and sperm production induced by neonatal goitrogen treatment. *Biology of Reproduction*, 51: 1000–1005.

Corcoran, J.M., Eastman, C.J., Carter, J.N. and Lazarus, L. (1977). Circulating thyroid hormone levels in children. *Archive of Diseases in Children*, 52: 716–720.

Dahl, G.E., Evans, N.P., Thrun, L.A. and Karsch, F.J. (1995). Thyroxine is permissive to seasonal transition in reproductive neuroendocrine activity in ewes. *Biology of Reproduction*, 52: 209-219.

Dallongeville, J., Helbecque, N., Cottel, D., Amouyel, P. and Meirhaeghe, A. (2003). The Gly16–.Arg16 and Gln27–.Glu27 polymorphisms of beta2-adrenergic receptor are associated with metabolic syndrome in men. *Journal of Clinical Endocrinology and Metabolism*, 88: 4862–4866.

Dariyerli, N., Toplan, S., Akyolcu, M.C., Hatemi, H. and Yigit, G. (2004). Erythrocyte osmotic fragility and oxidative stress in experimental hypothyroidism. *Endocrine*, 25(1): 1–5.

Darras, V.M., der Geyten, S.V. and Kühn, E.R. (2000). Thyroid hormone metabolism in poultry. *Biotechnology, Agronomy, Society and Environment*,4 (1): 13–20.

Dauncey, M.J. (1990). Thyroid hormones and thermogenesis. In: *Proceeding of the Nutrition Society*, 49: 203–215.

Davis, P.J., Davis, F.B. and Cody, V. (2005). Membrane receptors mediating thyroid hormone action. *Trends in Endocrinology and Metabolism*, 16: 429–435.

da Silva, J.A.R., de Araujo, A.A., Junior, J.B.L., dos Santos, N.F.A., Viana, R.B., Garcia, A.R., Rondina, D. and Grise, M.M. (2014). Hormonal changes in female buffaloes under shading in tropical climate of Eastern Amazon, Brazil. *Revista Brasileira de Zootecnia*, 43(1): 44 – 48.

De Leo, V., la Marca, A., Lanzetta, D. and Morgante, G. (1998). Thyroid function in early pregnancy I: Thyroid-stimulating hormone response to thyrotropinreleasing hormone. *Gynecological Endocrinology*, 12: 191–196.

de Vijlder, I.J.M. (2003). Primary congenital hypothyroidism: defects in iodine pathways. *European Journal of Endocrinology*, 149: 247–256.

de Vijlder, J.J., van Ommen, G.J., Van Voorthuizen, W.F., Koch, C.A., Arnberg, A.C., Vassart, G., Dinsart, C. and Flavell, R.A. (1981). Nonfunctional thyroglobulin messenger RNA in goats with hereditary congenital goiter.*Journal of Molecular and Applied Genetics*, 1: 51-59.

DeGroot, L.J., Nakai, A., Sakurai, A. and Macchia, E. (1989). The molecular basis of thyroid hormone action. *Journal of Endocrinological Investigation*, 12:843–861, 1989.

Delgadillo, J.A., Corillo, E., Moran, J., Duarte, G., Chemnieau, P. and Malpaux, B. (2001). Introduction of sexual activity of male creole goats in subtropical Northern Mexico using long days. *Journal of Animal Science*, 79: 2245-2252.

Dentice, M. and Salvatore, D. (2011). Local impact of thyroid hormone inactivation. Deiodinases: the balance of thyroid hormone. *Journal of Endocrinology*, 209: 273-282.

Devasena, T., Lalitha, S. and Padma, K. (2001). Lipid peroxidation, osmotic fragility and antioxidant status in children with acute post-streptococcal glomerulonephritis. *Clinica Chimica Acta*, 308: 155 161.

Devendra, C. (2000). Animal production and rain fed agriculture in Asia: Potential opportunities for productivity enhancement. *Outlook on Agriculture*, 29(3):161-175.

Devendra, C. (2001). Small holder dairy production systems in developing countries, characteristics, potential and opportunities for improvement, a review. *Asian-Australian Journal of Animal Science*, 14(1): 104–113.

Dhanda, J.S., Taylor, D.G., Murray, P.J., Pegg, R.B. and Shand, P.J. (2003). Goat meat production: Presents status and future possibilities. *Asian-Australian Journal of Animal Science*, 16 (12): 1842-1852.

Doubek, J., Slosarkova, S., Fleischer, P., Mala, G. and Skrivanek, M. (2003). Metabolic and hormonal profiles of potentiated cold stress in lambs during early postnatal period. *Czech Journal of Animal Science*, 48: 403–411.

Doutressoulle, G. (1947). L'élevage en Afrique Occidentale Française. Larousse, Paris.

Dubeuf, J. (2011). The social and environmental challenges faced by goat and small livestock local activities: Present contribution of research-development and stakes for the future. *Small Ruminant Research,* 98: 3-8.

Dumitrescu, A.M., Liao, X., Weiss, R.E., Millen, K. and Refetoff, S. (2006). Tissue-specific thyroid hormone deprivation and excess in monocarboxylate transporter (mct) 8-deficient mice. *Endocrinology,* 147: 4036-4043.

Dunn, J.T. and Dunn, A.D. (2001). Update on intrathyroidal iodine metabolism. *Thyroid,* 11: 407–414.

Dutta, D.J., Sarmah, B.K., Bhattacharyya, B.N., Baruah, K.K, Sarmah, B.C. and Gaswami, J. (2002). Serum thyroid hormone concentration in relation to some physiologic parameters in goats. *Journal of Nuclear Agriculture and Biology,* 31(3-4): 209-212.

Dwyer, C.M. and Lawrence, A.B. (2005). A review of the behavioural and physiological adaptations of hill and lowland breeds of sheep that favour lamb survival. *Applied Animal Behaviour Science,* 92: 235–260.

Dwyer, C.M. and Morgan, A. (2006). Maintenance of body temperature in the neonatal lamb: Effects of breed, birth weight, and litter size. *Journal of Animal Science,* 84: 1093–1101.

Dzenda, T., Ayo, J.O., Lakpini, C.A.M. and Adelaiye, A.B. (2011). Diurnal, seasonal, and sex variations in rectal temperature of African Giant rats (*Cricetomys gambianus,*Waterhouse) . *Journal of Thermal Biology,* 36, 255-263.

Early, B., BuckhamiSporer, K., Gupta, S., Pang, W. and Ting, S. (2010). Biologic response of animals to husbandry stress with implications for biomedical models. *Open Access Animal Physiology,* 2: 25-42.

Eggo, M.C. (2010). Molecular regulation of thyroid gland function. *Current Opinion in Endocrinology, Diabetes and Obesity,* 17: 396–401.

Egwu, G.O., Onyeyili, P.A. Chibuzo, G.A. and Ameh A.J. (1995). Improved productivity of goats and utilisation of goat milk in Nigeria. *Small Ruminant Research,* 16(3): 195–201.

Ekpe, E.D. and Christopherson, R.J. (2000). Metabolic and endocrine responses to cold and feed restriction in ruminants. *Canadian Journal of Animal Science,* 80: 87_95.

Estrada-Cortes, E., Vera-Avila, H.R., Urrutia-Morales, J., Villagomez-Amezcua, E., Jimenez-Severiano., H., Mejia-Guadarrama, C.A., Rivera-Lazano, M.T., Gamez-Vazquez, G. (2009). Nutritional status influences reproductive seasonality in Creole Goat:1 Ovarian activity during seanal reproduction transitions. *Animal Reproduction Science,* 116: 282 – 290.

El-Nouty, F.D., Al-Haidary, A. A. and Salah, M. S. (1990). Seasonal effects on body temperature, thyroid function, blood glucose and milk production in lactating and dry Holstein cows in semi-arid environment. *Arab Gulf Journal of Scientific Research*, 8: 89-103.

Fallah-Rad. A.H. and Connor, M.L. (1999). Relationships of thyroid hormones, IGF-I and testosterone in breeds of ram lambs with low and high prolificacies. *Canadian Journal of Animal Science*, 79: 441–448.

FAO (2001). Pastoralism in the new millennium. Animal Production and Health, Paper150. Food and Agriculture Organisation, Rome. Retrieved December 10, 2011 from http://www.fao.org/DOCREP/005/Y2647E/y2647e00.htm

FAOSTAT (2011): Retrieved December 10, 2013 fromhttp://faostat.fao.org/default.aspx

FAOSTAT (2013): Retrieved June 2, 2015 from http://faostat.fao.org/default.aspx

Fatihu, M.Y., Adamu, S., Ibrahim, N.D., Eduvi, L.O. and Esuivo, K.A.N. (2009). The effect of Experimental Trypanosoma vivax infection on the thyroid gland of Zebu bulls. *Veterinarski Arhiv*, 79 (5): 429-437.

Federman, D.D., Robbins, J. and Rall, J.E. (1958). Effects of methyl testosterone on thyroid function, thyroxine metabolism and thyroxine-binding protein. *Journal of Clinical Investigations*, 37: 1024–1030.

Feldt-Rasmussen, U. (2007). Thyroid and leptin. *Thyroid*, 17: 413-419.

Fernandez, V., Barrientos, X., Kipreos, K., Valenzuela, A. and Videla, L.A. (1985). Superoxide radical generation, NADPH oxidase activity, and cytochrome P-450 content of rat liver microsomal fractions in an experimental hyperthyroid state: Relation to lipid peroxidation. *Endocrinology*, 117: 496–501.

Ferri, N., Ulisse, S., Aghini-Lombardi, F., Graziano, F.M., Di Mattia, T., Russo, F.P., Arizzi, M., Baldini, E., Trimboli, P., Attanasio, D., Fumarola, A., Pinchera, A. and D'Armiento, M. (2003). Iodine supplementation restores fertility of sheep exposed to iodine deficiency. *Journal of Endocrinological Investigation*, 26: 1081–1087.

Firat, A., Ozpinar, A., Serpek, B. and Haliloglu, S. (2005). Comparisons of serum somatotropin, 3,5,3'-triiodothyronine, thyroxine, total protein and free fatty acid levels in newborn Sakiz lambs separated from or suckling their dams. *Annals of Nutrition and Metabolism*, 49: 88–94.

Fraser, M. and Liggins, G.C. (1988). Thyroid hormone kinetics during pregnancy in late pregnancy in the ovine fetus. *Journal of Developmental Physiology*, 10: 208-212.

Friesema, E.C., Jansen, J., Milici, C. and Visser,T.J. (2005). Thyroid hormone transporters. *Vitamins and Hormones*, 70: 137–167.

Fumel, B., Guerquin, M., Livera, G., Staub, C., Magistrini, M., Gauthier, C., Flamant, F., Guillou, F. and Fouchecourt, S. (2012). Thyroid hormone limits postnatal sertoli cell proliferation in vivo by activation of its alpha1 isoform receptor (tralpha1) present in these cells and by regulation of Cdk4/JunD/c-myc mRNA levels in mice. *Biology of Reproduction*, 87(1): 1–9.

Gall, C. (1996). Goat breeds of the world. Margraf Publishing, Weikersheim, Germany.

Garlid, K. D., Orosz, D. E., Modriansky, M., Vassanelli, S. and Jezek, P. (1996). On the mechanism of fatty acid-induced proton transport by mitochondrial uncoupling protein.*Journal of Biological Chemistry*, 271, 2615–2620.

Gifford, C.A., Duffey, J.L., Knight, R.L. and Hallford, D.M. (2007). Serum thyroid hormones and performance of offspring in ewes receiving prophylthiouracil with or without melatonin. *Animal Reproduction Science*, 100: 32-43.

Glinoer, D.(2001). Pregnancy and iodine. *Thyroid*, 11: 471–481.

Glinoer, D., De Nayer, 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.

Glinoer, D. (2004). The regulation of thyroid function during normal pregnancy: importance of the iodine nutrition status. *Best Practice and Research in Clinical Endocrinology & Metabolism*, 18(2): 133–152.

Gong, D., He, Y., Karas, M. and Reitman, M. (1997). Uncoupling protein-3 is a mediator of thermogenesis regulated by thyroid hormone, b3-adrenergic agonists, and leptin. *Journal of Biological Chemistry*, 272: 24129-24132.

Goto, M., Matsuo, H., Iigo, M., Furuse, M., Korf, H. and Yasuo, S. (2013). Melatonin-induced changes in the expression ofthyroid hormone-converting enzymes in hypothalamus depend onthe timing ofmelatonin injections and genetic background in mice. *General and Comparative Endocrinology*, 186: 33–40.

Grandin, T. (1998). Reducing handling stress improves both productivity and welfare. *Professional Animal Scientist*,14: 1-10.

Griffin, S.A., Henneman, H.A. and Reineke, E.P. (1962). Thyroid secretion rate and semen quality. *American Journal of Veterinary Research*, 23: 109–114.

Grozovsky, R., Morales, M.M. and Carvalho, D.P. (2007). Biphasic modulation of insulin receptor substrate-1 during goitrogenesis. *Brazilian Journal of Medical and Biological Research*, 40: 679-686.

Gündoğan, M. (2007). Seasonal variation in serum testosterone, T_3 and andrological parameters of two Turkish sheep breed. *Small Ruminant Research*, 67(2–3): 312–316.

Gupta, B., Moolchandani, A. and Sareen, M. (2010). Effect of induced Hypothyroidism on plasma cholesterol and bilirubin in Marwari Sheep. *Veterinary World*, 3: 323-325.

Gupta, P.S.P., Sanwal, P.C. and Varshney, V.P. (1991). Peripheral plasma testosterone levels in hypothyroid-induced male goats. *Small Ruminant Research*, 6: 185–192.

Gwinner, E., Hau, H. and Heigl, S. (1997). Melatonin: generaion and modification of avian circadian rhythms. *Brain Research Bulleitin*, 44, 439–444.

Habibu, B., Kawu, M.U., Makun, H.J., Aluwong, T., Yaqub, L.S., Ahmad, M.S., Tauheed, M. and Buhari H.U. (2014). Influence of sex, reproductive status and foetal number on erythrocyte osmotic fragility, haematological and physiologic parameters in goats during the hot-dry season. *Veterinarni Medicina*,59(10): 479–490.

Habibu, B.,Kawu, M.U., Makun, H.J., Ibrahim, F., Yaqub, L.S. and Abdullahi, A. (2015). Effect of seasonal changes on haematologic parameters and erythrocyte osmotic fragility of sahel bucks in a tropical savannah. In: *Proceedings of the 40th Annual Conference of Nigerian Society for Animal Production, Zaria*, 2015. pp 156-159.

Hadj-Sahraoui, N., Seugnet, I., Ghorbel, M.T. and Demeneix, B. (2000). Hypothyroidism prolongs mitotic activity in the post-natal mouse brain. *Neuroscience Letters*, 280: 79–82.

Halliwell, B. and Gutteridge, J.M.C. (1990). Role of free radical and catalytic metal ion in human disease: an overview. *Methods Enzymology*, 186: 1-85.

Hamzaoui, S., Salama, A.A.K., Albanell, E., Such, X. and Caja, G. (2013). Physiological responses and lactational performances of late-lactation dairy goats under heat stress conditions. *Journal of Dairy Science*, 96: 6355–6365.

Hanon, E.A., Lincoln, G.A., Fustin, J.M., Dardente, H., Masson-Pevet, M., Morgan, P.J. and Hazlerigg, D.G. (2008). Ancestral TSH mechanism signals summer in a photoperiodic mammal. *Current Biology*, 18: 1147–1152.

Hansen, P.S., Brix, T.H., Sorensen, T.I., Kyvik, K.O. and Hegedus, L. (2004). Major genetic influence on the regulation of the pituitary-thyroid axis: a study of healthy Danish twins. *Journal of Clinical Endocrinology and Metabolism*, 89: 1181–1187.

Haque, N., Ludri1 A., Hossain, S.A. and Ashutosh, M. (2012). Alteration of metabolic profiles in young and adult Murrah buffaloes exposed to acute heat stress. *International Journal of Applied Animal Science*, 1: 23-29.

Hassan, A. and Ciroma, A. (1992). Bodyweight measurements relationship in Nigerian Red Sokoto goats. In: *Proceedings of the First Biennial Conference, African Small Ruminant Research Network*.http://www.fao.org/wairdocs/ilri/x5520b/x5520b1d.htm

Haugen, B.R., Brown, N.S., Wood, W.M., Gordon, D.F. and Ridgway, E.C. (1997). The thyrotrope-restricted isoform of the retinoid X receptor (gamma 1) mediates 9-cis

retinoic acid suppression of thyrotropin beta promoter activity. *Molecular Endocrinology*, 11: 481–489.

Heasman, L., Clarke, L. and Symonds, E.M. (2000). Influence of thyrotropin-releasing hormone administration at birth on thermoregulation in lambs delivered by cesarean. *American Journal of Obstetrics and Gynecology*, 183: 1257-1262.

Hefnawy, A., Youssef, S., Aguilera, P.V., Rodriguez, C.V. and Peres, J.L.T. (2014). The relationship between Selenium and T_3 in selenium supplemented and non-supplemented ewes and their lambs. *Veterinary Medicine International*, doi: 10.1155/2014/105236.

Hetzel, B.S. and Mano, M.T. (1989). A review of experimental studies of iodine deficiency during fetal development. *Journal of Nutrition*, 119: 145–151.

Hiroi, Y., Kim, H.H., Ying H., Furuya F., Huang, Z., Simoncini, T., Noma, K., Ueki, K., Nguyen, N.H., Scanlan, T.S., Moskowitz, M.A., Cheng, S.Y. and Liao, J.K. (2006). Rapid nongenomic actions of thyroid hormone," *Proceedings of the National Academy ofSciences of the United States of America*, 103(38): 14104–14109.

Hishinuma, A., Takamatsu, J., Ohyama, Y., Yokozawa, T., Kanno, Y., Kuma, K., Yoshida, S., Matsuura, N. and Ieiri, T. (1999). Two novel cysteine substitutions (C1263R and C1995S) of thyroglobulin cause a defect in intracellular transport of thyroglobulin in patients with congenital goiter and the variant type of adenomatous goiter. *Journal of Clinical Endocrinology and Metabolism*, 84: 1438–1444.

Hocquette, J.F., Vermorel, M., Bouix, J., Anglaret, Y., Donnat, J.P., Leoty, C., Meyer, M., and Souchet, R., (1992). Effects of cold, wind and rain on energy-expenditure and thermoregulation of ewes from 7 genetic types. *Genetics,Selection, Evolution*,24: 147–169.

Holsberger, D.R. and Cooke, P.S. (2005). Understanding the role of thyroid hormone in Sertoli cell development: a mechanistic hypothesis. *Cell and Tissue Research*, 322:133–40.

Huang, D.W., Wang, J.X., Liu, Q.Y., Chu, M.X., Di, R., He, J.N., Cao., G.L., Fang, L., Feng, T. and Li, N. (2013). Analysis on DNA sequence of TSHB gene and its association with reproductive seasonality in oats. *Molecular Biology Reports*, 40(2): 1893-1904.

Huang, S.A. and Bianco, A.C. (2008). Reawakened interest in type III iodothyronine deiodinase in critical illness and injury. *Nature Clinical Practice Endocrinology and Metabolism*, 4:148–155

Huszenicza, G., Fodor, M., Gacs, M., Kulcsar, M., Dohmen, M.J.V., Vamos, M., Porkolab, L., Kegl, T., Bartyik, J., Lohuis, J.A.C.M., Janosi, S. and Szita, G. (1999). Uterine bacteriology, resumption of cyclic ovarian activity and fertility in postpartum cows kept in large-scale dairy herds. *Reproduction in Domestic Animals*, 34, 237–245.

Huszenicza, G., Kulcsar, M. and Rudas, P. (2002). Clinical endocrinology of thyroid gland function in ruminants.*Veterinarni Medicina,* 47(7): 199–210.

Iacobellis, G., Ribaudo, M.C., Zappaterreno, A., Iannucci, C.V. and Leonetti, F. (2005). Relationship of thyroid function with body mass index, leptin, insulin sensitivity and adiponectin in euthyroid obese women.*Issues in Clinical Endocrinology*, 62(4): 487–491.

Igono, M.O. and Aliu, Y.O. (1982). Environmental profile and milk production of Friesian-Zubu crosses in Nigerian Guinea Savannah. *International Journal of Biometeorology*, 26: 115-120.

Ikegami, K. and Yoshimura, T. (2012). Circadian clocks and the measurement of daylength in seasonal reproduction. *Molecular and Cellular Endocrinology*, 349: 76–81.

Ikwuebu, O. A., Tarawali, G. and Njwe, R. M. (1994). The role of the West African Dwarf goats in the economy of the small-holder arable farmer in the sub-humid zone of Nigeria. *In: Proceedings of Second Biannual Conference of the African Small RuminantResearch Network* AICC, Arusha, Tanzania, 7-11 December, Pp. 19-22.

Issi, M., Gul, Y. and Basbug, O. (2011). The effect of classical theileriosis treatment on thyroid hormones levels in cattle naturally infected *Theileria annulata*. *Asian Journal of Animal and Veterinary Advances*, 6: 531-536.

Jack, L.J., Kahl, S., St Germain, D.L. and Capuco, A.V. (1994). Tissue distribution and regulation of 5‘-deiodinase processes in lactating rats. *Journal of Endocrinology*, 142: 205-215.

Jana, N.R. and Bhattacharya, S. (1994). Binding of thyroid hormone to the goat testicular Leydig cell induces the generation of a proteinaceous factor which stimulates androgen release. *Journal of Endocrinology*, 143: 549–556.

Jana, N.R., Halder, S. and Bhattacharya, S. (1996). Thyroid hormone induces a 52 kDa soluble protein in goat testis Leydig cell which stimulates androgen release. *Biochimica et Biophysica Acta*, 1292: 209–214.

Jannini, E.A., Ulisse, S. and D’Armiento, M. (1995). Thyroid hormone and male gonadal function. *Endocrine Review*, 16: 443–459.

Jánosi, S., Huszenicza, G, Kulcsár, M. and Kóródi, P. (1998). Endocrine and reproductive consequences of certain endotoxin-mediated diseases in farm mammals. A review. *Acta Veterinaria Hungarica*, 46: 71–84.

Johnsen, L., Kongsted A.H. and Nielsen M.O. (2013). Prenatal undernutrition and postnatal overnutrition alter thyroid hormone axis function in sheep. *Journal of Endocrinology*, 216: 389 402.

Johnson, A.L. (1986). Serum concentrations of prolactin, thyroxine and triiodothyronine relative to season and the estrous cycle in the mare. *Journal of Animal Science*, 62: 1012-1020.

Johnson, D.D., McGowan, C.H., Nurse, G. and Anous, M.R. (1995). Breed type and sex effects on carcass traits, composition and tenderness of young goats. *Small Ruminant Research*, 17: 57-63.

Juss, T.S., Meddle, S.L., Servant, R.S., King, V.M.(1993). Melatonin and photoperiodic time measurement in Japanese quail (*Coturnix coturnix japonica*). *Proceedings of Royal Society, London B, Biological Science*, 254, 21–28.

Kabuga, J.D. (1992). The influence of thermal conditions on rectal temperature, respiration rate and pulse rate of lactating Holstein-Friesian cows in the humid tropics. International. *Journal of Biometeorology*, 36(3): 146-50.

Kahl, S., Elsasser, T.H. and Blum, J.W. (2000). Effect of endotoxin challenge on hepatic 5'-deiodinase activity in cattle. *Domestic Animal Endocrinology*, 18: 133–143.

Kaiser, C.A., Goumaz, M.O. and Burger, A.G. (1986). In vivo inhibition of the 50-deiodinase type II in brain cortex and pituitary by reverse triiodothyronine. *Endocrinology*, 119: 762–770.

Kawu, M.U. (2011). Influence of seasonal changes on prostaglandin F2α-induced estrus synchronization, endocrine and nutritional etabolites during the oestrus cycle in Savana Brown goats. Ph.D. thesis. Ahmadu Bello University, Zaria.

Kawu, M.U., Lakpini, C.A.M., Ayo, J.O., Fatihu, M.Y., Yaqub L.S., Habibu, B., Shittu, M., Aluwong, T., and Ambali, S.F. (2013). Influence of season and oestrus cycle on serum progesterone and thyroxine profiles in Savanna Brown goats. In: *Book of Abstract 50th Annual Congress of Nigeria Veterinary Medical Association, ECOWAS Secretariat, Abuja, Nigeria*, pp. 57.

Kenessey, A. and Ojamaa, K. (2006). Thyroid hormone stimulates protein synthesis in the cardiomyocyte by activating the AktmTOR and p70S6K pathways. *The Journal of Biological Chemistry*, 281(30): 20666–20672.

Khan, A. and Akhter, S. (2001). Effect of age, sex and seasons on the concentration of thyroid and thyroid stimulating hormones. *The Sciences*, 1(4): 224-227.

Khan, J.R. and Ludri, R.S. (2001). Hormonal profiles during periparturient period in single and twin fetus bearing goats. *Asian-Australian Journal of Animal Science*, 15(3): 346–351.

Knudsen, N., Laurberg, P., Rasmussen, L.B., Bulow, I., Perrild, H., Ovesen, L. and Jørgensen T. (2005). Small differences in thyroid function may beimportant for body mass index and the occurrence ofobesity in the population. *Journal of Clinical Endocrinology and Metabolism*, 90(7): 4019–4024.

Kohrle, J., Jakob, F., Contempre, B. and Dumont, J.E. (2005). Selenium, the thyroid, and the endocrine system. *Endocrine Reviews*, 26: 944–984.

Kohrle, J. (2007). Thyroid hormone transporters in health and disease: advances in thyroid hormone deiodination. *Best Practice & Research Clinical Endocrinology & Metabolism*, 21(2): 173–191.

Kok, K., van Dijk, J.E., Sterk, A., Baas, F., Van Ommen, G.J.B. and De Vijlder, J.J.M. (1987). Autosomal recessive inheritance of congenital goiter in Dutch goats. *Journal of Heredity*, 78: 298–300.

Kong, W.M., Martin, N.M., Smith, K.L., Gardiner, J.V., Connoley, I.P., Stephens, D.A., Dhillo, W.S., Ghatei, M.A., Small, C.J. and Bloom, S.R. (2004). Triiodothyronine stimulates food intake via the hypothalamic ventromedial nucleus independent of changes in energy expenditure. *Endocrinology*,145: 5252–5258.

Koritschoner, N.P., Alvarez-Dolado, M., Kurz, S.M., Heikenwa¨lder, M.F., Hacker, C., Vogel, F., Munoz, A. and Zenke, M. (2001). Thyroid hormone regulates the obesity gene tub. *EMBO Reports*, 2: 499 504.

Kouakou, B., Marable, D.R. and Kannan, G. (2012).Assessment of cortisol and thyroid hormones (T3 and T4) in mature and youngdairy and meat goats. In: *Book of Abstracts, XI International Conference on Goats, Gran Canaria, Spain, 23-27 September 2012, pp. 116*.

Kozat, S., Mert, H., Yüksek, N., Mert, N. and Ekin, S. (2007). Serum levels of some trace elementsand thyroid hormones in yearling rams with retardation in growth. *Bulletin of Veterinary Institute Pulawy*, 51: 117-120.

Krezel, W., Kastner, P., and Chambon, P. (1999). Differential expression of retinoid receptors in the adult mouse central nervous system. *Neuroscience*.89: 1291–1300.

Kuiper, G.G., Kester, M.H., Peeters, R.P. and Visser, T.J. (2005). Biochemical mechanisms of thyroid hormone deiodination. *Thyroid*, 15: 787–798.

Kumar, A., Varshney, J.P. and Varshney, V.P. (2006). Endocrine dysfunction in chronic severe ehrlichiosis with or without babesiosis in dogs. *Veterinary Research Communication*, 30: 911-916.

Lanyasunya, T.P., Wang, H.R., Mukisira, E.A., Abdulrazak, S.A. and Ayako, W.O. (2006). Effect of seasonality on feed availability, quality and herd performance on smallholder farms in Ol-joro-orok location/nyandarua district, Kenya. *Tropical and Subtropical Agroecosystems*, 6: 87 – 93.

Lawal-Adebowale, O.A. (2012). Dynamics of ruminant livestock management in the context of the nigerian agricultural system. http://dx.doi.org/10.5772/52923. (Retrieved October 29th, 2013; 03:36 pm)

Lebbie, S.H.B. (2004). Goats under household conditions. *Small Ruminant Research*, 51(2): 131-136.

Leonard, J.L. and Visser, T.J. (1986). Biochemistry of deiodination. In: Hennemann, G. (ed.) Thyroid Hormone Metabolism. Marcel Dekker, New York, pp. 189–229.

Lin, M.T., Chu, P.C. and Leu, S.Y. (1983). Effects of TSH, TRH, LH and LHRH on thermoregulation and food and water intake in the rat. *Neuroendocrinology*, 37(3): 206–211.

Lin, H.Y., Sun, M., Tang, H.Y., Luidens, M.K., Mousa, M,A., Incerpi, S., Drusano, G.L., Davis, F.B. and Davis, P.J. (2009). L-Thyroxine vs. 3,5,30-triiodo-L-thyronine and cell proliferation: activation of mitogen-activated protein kinase and phosphatidylinositol 3-kinase. *American Journal of Physiology, Cell Physiology*, 296: C980–C991.

Lin, J.Z., Martagón, A.J., Hsueh, W.A., Baxter, J.D., Gustafsson, J., Webb, P. and Phillips, K.J. (2012). Thyroid hormone receptor agonists reduce serum cholesterol independent of the LDL receptor. *Endocrinology*, DOI: 10.1210/en.2011-2081.

Lisboa, P.C., Pires, L., de Oliveira, E., Lima, N.S., Bonomo, I.T., Reis, A.M., Passos, M.C.F. and Moura, E.G. (2010). Prolactin inhibition at mid-lactation influences adiposity and thyroid function in adult rats. *Hormone and Metabolic Research*, 42: 562–569.

Lohuis, J.A.C.M., Verheijden, J.H.M., Burvenich, C. and Miert van, A.S.J.P.A.M. (1988): Pathophysiological effects of endotoxin in ruminants. 2. Metabolic aspects. *Veterinary Quarterly*, 10: 117–125.

Lomo, P.O, Makawiti, D.W., and Konji, V.W. (1995). The effect of L-thyroxine on the anaemia response in *Trypanosoma congolense* infected rabbits. *Veterinary Parasitology*, 58(3): 227-34.

Loubière, L.S., Vasilopoulou, E., Glazier, J.D., Taylor, P.M., Franklyn, J.A., Kilby, M.D. and Chan, S.Y. (2012). Expression and function of thyroid hormone transporters in the microvillous plasma membrane of human term placental syncytiotrophoblast. *Endocrinology*, DOI: 10.1210/en.2012-1753

Lucas, J.J., Bruhsted, G.E. Fowler, S.H. (1958). The relationship of altered thyroid activity to various reproductive phenomena in gilts. *Journal of Endocrinology*, 17: 54-61.

Mack, S.D. (1983). Evaluation of the productivities of West African Dwarf sheep and goats in southwest Nigeria.Humid zone programme. In: Document 7. International Livestock Centre for Africa (ILCA), Ibadan, Nigeria. PP. 39.

Maina, J.A. (2002). Legal framework for the advancement and protection of the veterinary profession in Nigeria. In: Proceedings of the 39th N.V.M.A Conference Sokoto, Nigeria, pp. 10–13.

Martins, G.B., Rodger, J. and Blache, O. (2004). Nutitional and environmental effect on reproduction in small ruminant. *Reproduction, Fertility and Development*, 16: 499-501.

Marwaha, R.K., Tandon, N., Garg, M.K., Ganie, M.A., Narang, A., Mehan, N. and Bhadra, K. (2013). Impact of body mass index on thyroid functions in Indian children.*Clinical Endocrinology*, 79(3): 424–428.

Matthews, R.G. (1999). Cobalamin-dependant methionine synthase. In: *Chemistry and Biochemistry of B12. R. Banerjee, ed. John Wiley & Sons, Inc., New York, NY*. PP. 681–706.

Maurenbrecher, S. and Barrell, G.K. (2003). Suppression of thyroid gland function and its effects on the breeding season of Coopworth ewes. *New Zealand Journal of Agricultural Research*, 46:1, 1-7.

Mayahi, S., Mamouei, M., Tabatabaei, S. and Mirzadeh, K. (2014). Reproductive characteristics and thyroidal function in relation with season in Khuzestan buffalo (*Bubalus bubalis*) bulls. *Veterinary Research Forum*,5(3): 201 – 205.

McDonald, B.J., Stocks, D.C., Connell, J.A. and Hoey, W.A. (1988). Thyroxine concentration in maternal and foetal plasma during pregnancy in Australian feral goats. *Journal of Agricultural Science*, 110: 25–30.

McNitt, J.I. (1983). Livestock Husbandry Techniques, Low priced edition. Granada publishing company limited, Frogmore, St. Albans A122 NF and 36 Golden Square, London WIR 4AH.

Medina, D.L. and Santisteban, P. (2000). Thyrotropin-dependent proliferation of *in vitro* rat thyroid cell systems. *European Journal of Endocrinology*, 143: 161-178.

Menegatos, J., Goulas, C. and Kalogiannis, D. (2006). The productivity, ovarian and activity of ewes in an accelerated lambing system in Greece. S*mall Ruminant Research,* 65: 209–216.

Meschy, F. (2000). Recent progress in the assessment of mineral requirements of goats. *Livestock Production Science*, 64: 9–14.

Milionis, A. and Milionis, C. (2013). Correlation between body mass index and thyroid function in euthyroid individuals in Greece.*ISRN Biomarkers*, doi.org/10.1155/2013/651494.

Moenter, S.M., Woodfill, C.J.I. and Karsch, F.J. (1991). Role of thyroid gland in seasonal reproduction: Thyroidectomy blocks seasonal suppression of reproductive neuroendocrine activity in ewes. *Endocrinology*, 128: 1337-1344.

Mohammed, I.D. and Amin, J.D. (1996). Estimating body weight from morphometric measurement of Sahel (Borno White) goats. *Small Ruminant Research*, 24: 1-5.

Montsma, G., Luiting, P., Verstegen, M.W.A., van der Hel, W., Hofs, P. and Zijlker, J.W. (1985). Effects of high ambient temperatures on the metabolism of West African dwarf goats. *International Journal of Biometeorology*, 29(1): 23-35.

Morand-Fehr, P., Boutonnet, J.P., Devendra, C., Dubeuf, J.P., Haenlein, G.F.W., Holst, P.,Mowlem, L. and Capote, J. (2004). Strategy for goat farming in the 21st century. *Small Ruminant Research*, 51: 175–184.

Morley, J.E., Damassa, D.A., Gordon, J., Pekary, A.E. and Hershman, J.M. (1978). Thyroid function and vitamin A deficiency. *Life Science*,22:1901–1906.

Moruppa, S.M. and Ngere, L.O. (1984). Biometrics studies on Bufalo White and Red Sokoto (Maradi) goat breeds. Paper presented at the 2nd Convention Lecture of Ahmadu Bello University, Shika-Zaria. Nigeria.

Murphy, M.,Jethwa, P.H., Warner, A., Barrett, P., Nilaweera, K. N., Brameld, J. M. and Francis, J. P. (2012). Effects of manipulating hypothalamic triiodothyronine concentrations on seasonal body weight and torpor cycles in siberian hamsters. *Endocrinology*, 153: 101-112.

Mutayoba, B.M., Gombe, S., Kaaya, G.P. and Waindi, E.W. (1988). Effect of the experimental *T.congolense* infection on the ovaries, pituitary, thyroid and adrenal gland in female goats. *Research in Veterinary Science*, 44: 140-146.

Nakao, N., Ono, H., Yamamura, T., Anraku, T., Takagi, T., Higashi, K., Nakao, N., Ono, H., Yamamura, T., Anraku, T., Takagi, T., Higashi, K., Yasuo, S., Katou, Y., Kageyama, S., Uno, Y., Kasukawa, T., Iigo, M., Sharp, P.J., Iwasawa, A., Suzuki, Y., Sugano, S., Niimi, T., Mizutani. M., Namikawa, T., Ebihara, S., Ueda, H.R. and Yoshimura, T. (2008). Thyrotrophin in the *pars tuberalis* triggers photoperiodic response. *Nature*, 452: 317–322.

Nazifi, S., Saeb, M., Abangah, E. and Karimi, T. (2008). Studies on the relationship between thyroid hormones and some trace elements in the blood serum of Iranian fat-tailed sheep. *Veterinarski Arhiv*,*78*(2): 159-165.

Nelson R.W. (1998). Endocrine disorders. *Small Animal Internal Medicine.* Mosby Inc. St. Louis, Missouri, USA. pp. 671-807.

Ngere, L.P., Adu, I.F. and Okubanjo, O. (1984). The indigenous goats of Nigeria. *Animal Genetics Research and Information*, 3: 1-9

Nicholls, T.J., Follett, B.K., Goldsmith, A.R. and Pearson, H. (1988). Possible homologies between photorefractoriness in sheep and birds: the effect of thyroidectomy on the length of the ewe's breeding season. *Reproduction, Nutrition, Development*, 28: 375–385.

Nicholls, D.G. and Locke, R.M. (1984)Thermogenic mechanisms in brown fat. *Physiology Review*, 64: 1-64.

Nicholls, T.J., Follett, B.K. and Robinson, J.E. (1983). A photoperiodic response in gonadectomized Japanese quail exposed to a single long day. *Journal of Endocrinology*, 97: 121–126.

Novoselec, J., Antunović, Z., Šperanda, M., Steiner, Z. and Šperanda, T.(2009). Changes of thyroid hormones concentration in blood of sheep depending on age and reproductive status. *Italian Journal of Animal Science,* 8(3): 208-210.

Nudda, A., Battacone, G., Bomboi, G., Floris, B., Decandia, M. and Pulina, G. (2013). Effect of dietary iodine on thyroid hormones and energy blood metabolites in lactating goats. *Animal*, 7(1): 60–65.

Oetting, A. and Yen, P.M. (2007). New insights into thyroid hormone action. *Best Practice andResearch in Clinical Endocrinology and Metabolism*, 21: 193–208.

Okab, A.B., Elebanna, I.M., Mekkawy, M.Y., Hassan, G.A., Elnouty, F.D. and Salem, M.H. (1993). Seasonal-changes in plasma thyroid-hormones, total lipids, cholesterol and serum transaminases during pregnancy and at parturition in Barki and Rahmani ewes. *Indian Journal of Animal Sciences*, 63: 946–951.

Oluwole, O.A., Bartlewski, P.M. and Hahnel, A. (2013). Relationships of serum thyroid hormones and follicle-stimulating hormone concentrations to Sertoli cell differentiation during the first wave of spermatogenesis in euthyroid ram lambs. *Reproductive Biology*, 13: 150–160.

Omran, F.I., Shafie, M.M., Ashour, G.H., Youssef, M.M. and Hassan, L.R. (2013). Response of buffalo calves exposed to first and second acute thermal shocks. *Egyptian Journal of Agricultural Research,* 91(3):1113-1127.

Orth, J.M., Gunsalus, G.L. and Lamperti, A.A. (1988). Evidence from Sertoli cell-depleted rats indicates that spermatid number in adults depends on numbers of Sertoli cells produced during perinatal development. *Endocrinology*, 122: 787–794.

Osuhor, C.U., Alawa, J.P. and Lufadeju, E.A. (1998). Overnight manure production from Red Sokoto goats in Zaria, Nigeria. In: *Proceedings of the Silver Anniversary Conference of Nigerian Society for Animal Production, 21 – 26th March, 1998. Abeokuta, Nigeria*, pp. 434 – 435.

Otoikhian, C.S.O. and Orheruata, A.M. (2010). White bornu goats: untapped meat-breed in Nigerian small ruminant industry. *Bioscience Research Communications,* 22(6): 307-311.

Padron, A,S., Neto, R.A.L., Pantaleao, T.U., dos Santos, M.C.D., Araujo, R.L., de Andrade, B.D., Leandro, M.D., de Castro, J.P.S.W., Ferreira1 A.C.F. and de Carvalho, D.P. (2014). Administration of 3,5-diiodothyronine (3,5-T2) causes central hypothyroidism and stimulates thyroid-sensitive tissues. *Journal of Endocrinology*, 221: 415–427.

Pallavi C., Modi, B., Mangukiya, S., Jadav, P. and Shah, R. (2011).Variation in thyroid hormones level among People of different age, gender and seasons, Piparia, Gujarat. *National Journal of Medical Research*, 1(2): 57-59.

Paller, M.S. (1986). Hypothyroidism protects against free radical damage in ischemic acute renal failure. *Kidney International*,29: 1162–1166.

Pang, X.P., Hershman, J.M., Mirell, C.J., Pakery, A.E. (1989). Impairment of hypothalamic-pituitary-thyroid function in rats treated with human recombinant tumor necrosis factor-α (cachectin). *Endocrinology*, 125: 76–83.

Parkinson ,T.J. and Follett, B.K. (1994). Effect of thyroidectomy upon seasonality in rams. *Journal of Reproduction and Fertility*, 101: 51–58.

Parkinson, T.J. and Follett, B.K. (1995). Thyroidectomy abolishes seasonal testicular cycles of Soay rams. *Proceedings of Royal Society of London B*, 259: 1–6.

Pavlata, L., Prasek, J., Filipek J. and Pechova, A. (2004). Influence of parenteral administration of seleniumand vitamin E during pregnancy on selected metabolicparameters and colostrum quality in dairy cowsat parturition *Veterinarni Medicina*,49(5): 149–155.

Pearce, E.N. (2012). Effects of iodine deficiency in pregnancy. *Journal of Trace Elements in Medicine and Biology*, 26(2–3): 131–133.

Peeters, R., Buys, N., Pauwels, T., Kuhn, E.R., Decuypere E., Siau, O. and Van Isterdael, J. (1989). Relationship between the thyroidal and gonadal axes during the estrus cycle of ewes of different breeds and ages. *Reproduction Nutrition Development*, 29: 237-245.

Peeters, R., Buys, N., Vanmontfort, D., van Isterdael, J., Decuypere, E. and Kuhn, E.R. (1992). Preferential release of triiodothyronine following stimulation by thyrotropin or thyrotropin releasing hormone in sheep of different ages. *Journal of Endocrinology*, 132: 93–100.

Pennock, G.D., Raya, T.E., Bahl, J.J., Goldman, S. and Morkin, E. (1992). Cardiac effect of 3,5-diiodothyropropionic acid, a thyroid hormone analog with ionotropic selectivity. *Journal of Pharmacology and Experimental Therapeutics*,263: 163-169.

Pereira, A.M.F., Baccari, J. F. Titto, E.A.L. and Almeida, J.A.A. (2008). Effect of thermal stress on physiological parameters, feed intake and plasma thyroid hormones concentration in Alentejana, Mertolenga, Frisian and Limousine cattle breeds. *International Journal of Biometeorology*, 52(3): 199-208.

Pezzi, C., Accorsi, P.A., Vigo, D., Govoni, N. and Gaiani, R. (2005). 5'-deiodinase activity and circulating thyronines in lactating cows. *Journal of Dairy Science*, 86: 152–158.

Pierce, J.G. and Parson, T.F. (1981). Glycoprotein hormones: structure and function. *Annual Review of Biochemistry*, 50: 465–475

Qin, F., Zhu, X., Zhang, W., Zhou, J., Zhang, S. and Jia, Z. (2011). Effects of dietary iodine and selenium on nutrient digestibility, serum thyroid hormones, and antioxidant

status of Liaoning Cashmere goats. *Biological Trace Element Research*, 143, 1480–1488.

Qin F., Li, J., Zhu, X., Zhou, J., Yang, J. and Jia, Z. (2013). Dietary iodine and selenium affected the mRNA expression levels of skin monodeiodinase (II, III) in liaoning Cashmere goats. *Biological Trace Element Research*, 151(3): 360-364.

Rae, M.T., Rhind, S.M., Miller, D.W. and Brooks, A.N. (2002). Maternal undernutrition alters triiodothyronine concentrations and pituitary response to GnRH in fetal sheep. *Journal of Endocrinology*, 173: 449–455.

Ragno, P., Montuori, N., Covelli, B., Hoyer-Hansen, G. and Rossi, G. (1998). Differential expression of a truncated form of the urokinase-type plasminogen-activator receptor in normal and tumor thyroid cells. *Cancer Research*, 58: 1315–1319.

Randhawa, C.S. and Randhawa, S.S.(2001). Epidemiology and diagnosis of subclinical iodine deficiency in crossbred cattle of Punjab. *Australian Veterinary Journal*, 79, 349–351.

Ravaglia, G., Forti, P., Maioli, F., Nesi, B., Pratelli, L., Savarino, L., Cucinotta, D. and Cavalli, G. (2000). Blood micronutrient and thyroid hormone concentrations in the oldest-old. *Journal of Clinical Endocrinology and Metabolism,* 85: 2260-2265.

Ravagnolo, O., Misztal, I., and Hoogenboom, G. (2000). Genetic component of heat stress in dairy cattle, development of heat index function. *Journal of Dairy Science*, 83: 2120–2125.

Reddy, I.J., Varshney, V.P., Sanwal, P.C., Agarwal, N. and Pande, J.K. (1996). Peripheral plasma oestradiol-17β and progesterone levels in female goats induced to hypothyroidism. *Small Ruminant Research,* 22(2): 149–154.

Reincke, M., Arlt, W.,Heppner, C.,Petzke, F.,Chrousos, G.P. andAllolio, B. (1998).Neuroendocrinedysfunction in Africantrypanosomiasis. The role of cytokines. *Annals ofNew YolkAcademy ofScience,* 840:809–821

Reineke E.P., Bergman A.J. and Turner. C.W.(1941). Effect of thyroidectomy of young male goats upon certain hormones. *Endocrinology,* 29(3): 306-312.

Reiter, R.J. (1987). The melatonin message: duration versus coincidence hypotheses. *Life Science*, 40: 2119–2131.

Reiter, R.J. (1991). Pineal melatonin: cell biology of its synthesis and of its physiological interactions. *Endocrinology Review*, 12: 151– 180.

Revel, F.G., Saboureau, M., Pevet, P., Mikkelsen, J.D., Simonneaux, V.(2006). Melatonin regulates type 2 deiodinase gene expression in the Syrian hamster. *Endocrinology*, 147, 4680–4687.

Rhind, S.M., McMillen, S.R., Duff, E., Kyle, C.E. and Wright, S. (2000). Effect of long term feed restriction on seasonal endocrine changes in Soay sheep. *Physiology and Behavior*, 71: 343–451.

Rhind, S.M., Kyle, C.E., Riach, D.J. and Duff, E.I.(2006). Effects of nutrition on hormone profiles and patterns of deiodinase activity in the skin and associated patterns of hair follicle activity and moult in cashmere goats. *Animal Science*, 82: 723–730.

Ribeiro, N.L., Pimenta Filho, E.C., Arandas, J.K.G., Ribeirob, M.N., Saraiva, E.P., Bozzi, R. and Costa, R.G. (2015). Multivariate characterization of the adaptive profile in Brazilian and Italian goat Population. *Small Ruminant Research*, 123: 232–237.

Riis, P.M. and Madsen, A. (1985). Thyroxine concentration and secretion rates in relation to pregnancy, lactation and energy balance in goats. *Journal of Endocrinology*, 107: 421–427.

Ritar, A.J., Robertson, J.A. and Evans, G.(1994). Ovulatory activity, hormonal induction of ovulation and fertility of young Cashmere and Angora female goats in a temperate environment.*Reproduction, Fertility and Development*, 6: 737–747.

Rom Bugoslavskaia, E.S. and Shcherbakova, V.S. (1986). Seasonal characteristics of the effect of melatonin on thyroid function. *Bulletin of Experimental Biology and Medicine*, 101: 268–269.

Rooke, J.A., Robinson J.J. and Arthur J.R. (2004).Effects of vitamin E and selenium on the performance and immune status of ewes and lambs. *Journal of Agricultural Science*, 142: 253-262.

Salem, M.H., Elsherbiny, A.A., Khalil, M.H. and Yousef, M.K. (1991). Diurnal and seasonal rhythm in plasma-cortisol, triiodothyronine and thyronine as affected by the wool coat in barki sheep. *Indian Journal of Animal Sciences*, 61: 946–951.

Salvatore, D. (2011).Deiodinases: keeping the thyroid hormone supply in balance. *Journal of Endocrinology*, 209: 259-260.

Samson, F.E. and Nelson, S.R. (2000). The aging brain, metals and oxygen free radicals. *Cell Molecular Biology*, 46(4): 699-707.

Schäffler, A., Binart, N., Scholmerich, J. and Buchler, C. (2005). Hypothesis paper: brain talks with fat—evidence for a hypothalamic-pituitary- adipose axis? *Neuropeptides*, 39(4): 363–367.

Schillo, K.K. (1992). Effects of dietary energy on control of luteinizing hormone secretion in cattle and sheep. *Journal of Animal Science*, 70: 1271–1282.

Schlumberger, H.G. (1955). Spontaneous goiter and cancer of the thyroid in animals. *The Ohio Journal of Science*, 55: 23-43

Schwartz, H.L. and Oppenheimer, J.H. (1978). Physiologic and biochemical actions of thyroid hormone. *Pharmacology and Therapeutics*,3: 349–376.

Sejian, V. and Srivastava, R.S. (2009). Effects of melatonin on adrenal cortical functions of Indian goats under thermal stress. *Veterinary Medicine International*, doi.org/10.4061/2010/348919.

Sejian, V., Singh, A.K., Sahoo, A. and Naqvi, M.S. (2014). Effect of mineral mixture and antioxidant supplementation on growth,reproductive performance and adaptive capability of Malpura ewes subjected to heat stress. *Journal of Physiology and Animal Nutrition*, 98: 72-83.

Sensky, P.L., Roy, C.H., Barnes, R.J. and Heath, M.F. (1994). Changes in fetal thyroid hormone levels in adrenalectomized fetal sheep following continuous cortisol infusion 72 h before delivery. *Journal of Endocrinology*, 140: 79–83.

Seymen, H.O., Seven, A., Civelek, S., Yiğit, G., Hatemi, H. and Burçak, G. (1999). Evaluation of antioxidant status in liver tissues: effect of iron supplementation in experimental hyperthyroidism. *Journal of Basic and Clinical Physiology and Pharmacology*, 10(4): 315-325.

Shahat, K.H.E. and Abdel Monem, U.M. (2011).Effects of dietary supplementation with vitamin e and /or selenium on metabolic andreproductive performance of egyptian baladi ewes under subtropical conditions.*World Applied Sciences Journal*, 12(9): 1492-1499.

Sharma, S., Ramesh, K., Hyder, I., Uniyal, S., Yadav, V.P., Panda, R.P., Maurya, V.P., Singh, G., Kumar, P., Mitra, A. and Sarkar, M. (2013). Effect of melatonin administration on thyroid hormones, cortisol and expression profile of heat shock proteins in goats (*Capra hircus*) exposed to heat stress. *Small Ruminant Research*, 112: 216–223.

Sherman, S.I., Gopal, J., Haugen, B.R., Chiu, A.C., Whaley, K., Nowlakha, P. and Duvic, M. (1999). Central hypothyroidism associated with retinoid X receptor-selective ligands. *Northern England Journal of Medicine*,340: 1075–79.

Shetaewi, M.M. and Ross, T.T. (1991). Effects of concentrate supplementation and lasalocid on serum chemistry and hormone profiles in Rambouillet ewes. *Small Ruminant Research*, 4: 365–377.

Shirpour, A., Khameneh, S., Zarghami, N. and Eskandari, M. (2003). The influence of hypothermia on thyroid functionin rats. *International Journal of Endocrinology and Metabolism*, 1: 27-32.

Shupnik, M.A., Chin, W.W., Habener, J.F. and Ridgway, E.C. (1985). Transcriptional regulation of the thyrotropin subunit genes by thyroid hormone.*Journal of Biological Chemistry*, 260: 2900-2903.

Shupniks, M.A., Greenspang, S.L. and Ridgway, E.C. (1986). Transcriptional regulation of thyrotropin subunit genes by thyrotropin-releasing hormone and dopamine in pituitarycell culture. *Journal of Biological Chemistry*, 261(27): 12675-12679.

Silanikove, N. (2000). Physiological basis of adaptation in goats to harsh environment. *Small Ruminant Research*, 35: 181-193.

Singh R. and BeighS.A. (2013). Diseases of Thyroid in Animals and Their Management. In: Payan-Carreira, R. (Ed) *Insights from Veterinary Medicine*. Intech Open Science, pp. 234-240.

Slebodzinski, A. (1972). Acute depletion of the hormonal-iodine stores from the thyroid gland after birth in lambs. *Journal of Endocrinology*, 53: 195–200.

Solanki, A., Bansal, S., Jindal, S., Saxena, V. and Shukla, U.S. (2013). Relationship of serum thyroid stimulating hormone with body mass index in healthy adult. *Indian Journal of Endocrine Metabolism*, 17(1): 167-169.

Soliman, E.B., Abd El-Moty, A.K.I. and Kassab, A.Y. (2012).Combined effect of vitamin E and selenium on some productive and physiological characteristics of ewes and their lambs during suckling period. *Egyptian Journal of Sheep & Goat Sciences*, 7(2): 31-42.

Soriguer, F., Morcillo, S.V., Esteva, I., Almaraz, M.C., Tapia, M.A., Gutierrez-Repiso, M.D.C.,Rubio-Martin, E., Garrido-Sanchez, L., Perez, V., Garriga, M.J., Rojo-Martinez, G. and Garcia-Fuentes, E. (2011). Thyroid hormone levels predict the change in body weight: a prospective study. *European Journal of Clinical Investigation*, 41: 1202–1209.

Souza, M.I.L., Bicudo, S.D., Uribe-Velásquez, L.F. and Ramos, A.A. (2002). Circadian and circannual rhythms of T3 and T4 secretions in Polwarth–Ideal rams. *Small Ruminant Research*, 46: 1–5.

Spicer, L.J., Alonso, J. and Chamberlain, C.S. (2001). Effects of thyroid hormones on bovine granulosa and thecal cell function in vitro: dependence on insulin and gonadotropins. *Journal of Dairy Science*, 84: 1069–1076.

Stafford, K.J., Kenyon, P.R., Morris, S.T. and West, D.M. (2007). The physical state and metabolic status of lambs of different birth rank soon after birth. *Livestock Science*, 111(1–2): 10–15.

Stager, J.M. (1983). Effect of triiodothyronine on body temperature at rest and during exercise in dogs.*Journal of Applied Physiology*, 54(4): 1115-1119

Stangl, G.I., Schwartz, F.J. and Kirchgessner, M. (1999). Cobalt deficiency effects on trace elements, hormones and enzymes involved in energy metabolism in cattle. *International Journal for Vitamin and Nutrition Research*,69: 120-126.

Stempak, G. (1962). Maternal hypothyroidism and its effect on fetal development. *Endocrinology*, 70: 443-445.

Stephenson, T., Budge, H., Mostyn, A., Pearce, S., Webb, R. and Symonds M.E. (2001). Fetal and neonatal adipose maturation: A primary site of cytokine and cytokine-receptor action. *Biochemical Society Transactions*, 29: 80–85.

Stockman, C.A. (2006). The physiological and behavioral responses of sheep exposed to heat load within intensive sheep industries. Ph.D. Thesis, School of Veterinary and Biomedical Sciences, Murdoch University, Western Australia.

Swaroop, A. and Ramasarma, T. (1985). Heat exposure and hypothyroid conditions decrease hydrogen peroxide generation in liver mitochondria. *Biochemical Journal*,226:403–408.

Symonds, M.E., Andrews, D.C., Buss, D.S., Clarke, L., Darby, C.J., Johnson, P., Lamax, M.A. (1996). Effect of rearing temperature on perirenal adipose tissue development and thermoregulation following methimazole treat-ment of postnatal lambs. *Experimental Physiology*, 81: 995-1006.

Symonds, M.E., Andrews, D.C. and Johnson, P.J. (1989). The control of thermoregulation in the developing lamb during slow wave sleep. *Journal of Developmental Physiology*, 11: 289-298.

Symonds, M.E., Clarke, L. and Lomax, M.A. (1994). The regulation of neonatal metabolism and growth. In: Ward, R.H., Smith, S.K., Donnai, D., (Eds). Early fetal growth and development. London: Royal College of Obstetricians and Gynaecologists. PP. 403-419.

Taiwo, B.B.A., Buvenandron V. and Adu I.F. (2005). Effect of body condition on the reproduction performance of Red Sokoto goats. *Nigerian Soceity for Animal Prduction*, 32: 1-6.

Tanaka,T., Akaboshi, N., Inoue, Y., Kamomae, H. and Kaneda, Y. (2002). Fasting induce suppression of pulsatile L.H secretion is related to body energy status in ovariectomized goats. *Animal Reproduction Science*, 72: 185-196.

Tanaka, T., Yamaguchi, T., Kamomae, H. and Kaneda, H. (2003). Nutritionally induced weight body loss and ovarian quiescence in shiba goats. *Journal of Reproduction and Development*, 49(1): 113–119.

Thrun, L. A., G. E. Dahl, N. P. Evans, and F. J. Karsch. (1996). Time course of thyroid hormone involvement in the development of anestrus in the ewe. Biology of Reproduction, 55:833–837.

Thrun, L.A., Dahl, G.E., Evans, N.P. and Karsch, F.J. (1997a). A critical period for thyroid hormone action on seasonal changes in reproductive neuroendocrine function in the ewe. *Endocrinology*, 138: 3402–3409.

Thrun, L.A., Dahl, G.E., Evans, N.P. and Karsch, F.J. (1997b). Effect of thyroidectomy on maintenance of seasonal reproductive suppression in the ewe. *Biology of Reproduction*, 56: 1035–1040.

Timisjarvi, J., Ojutkangas, V., Eloranta, E., Nieminen, M., Leppaluoto, J., Liimatainen, S. and Vuolteenaho, O. (1994). Annual variations in serum thyroid-stimulating hormone and thyroid hormones and in their responses to thyrotropin-releasing hormone in the reindeer. *Journal of Endocrinology*, 141: 527–533.

Todini, L., Lucaroni, A., Malfatti, A., Debenedetti, A. and Costarelli, S. (1992). Male–female differences in the annual profiles of the thyroid hormones blood level by the goat. *Atti della Societa` Italiana della Scienze Veterinarie*, 46: 169–173.

Todini, L., Malfatti, A., Barbato, O., Trabalza-Marinucci, M., Acuti, G., Antonini, M. and Debenedetti, A. (2005). Plasma thyroid hormones, fibre characteristics and hair follicle activity in angora kids: effects of supplementation with horse bean (Vicia faba minor). *Atti della Societa` Italiana della Scienze Veterinarie*, 59: 39–40.

Todini, L., Delgadillo, J.A., Debenedetti, A. and Chemineau, P. (2006). Plasma total T3 and T4 concentrations in bucks as affected by photoperiod. *Small Ruminant Research*, 65: 8–13.

Todini, L. (2007) Thyroid hormones in small ruminants: effects of endogenous, environmental and nutritional factors. *Animal*, 1: 997–1008

Tucker, H.A. (1979). Endocrinology of lactation. *Seminars in Perinatology*, 3: 199-223.

Tucker, H.A. (1994). Lactation and its hormonal control. In:The physiology of reproduction, second edition (ed. Knobil, E. and Neil, J.D.), Raven Press, New York. pp. 1065–1098.

Tucker, H.A. (2000). Hormones, mammary growth, and lactation: a 41-year perspective. *Journal of Dairy Science*, 83: 874–884.

Underwood, E.J. and Suttle, N.F. (2001). The Mineral Nutrition of Livestock, 3rd Ed., Biddles Ltd, London, PP. 47-63.

Valtorta, S., Hahn, L. and Johnson, H.D. (1982). Effect of high ambient temperature (35 degrees), and feed intake on plasma T4 levels in sheep. In: *Proceedings of the Society for Experimental Biology and Medicine*, 169: 260–265.

Valyasevi, R.W., Harteneck, D.A., Dutton, C.M. and Bahn, R.S. (2002). Stimulation of adipogenesis, peroxisome proliferator activated receptor-γ (PPARγ), and thyrotropin receptor by PPARγ agonist in human orbital preadipocyte fibroblasts. *Journal of Clinical Endocrinology and Metabolism*, 87(5): 2352–2358.

Van de Graaf, S.A.R, Cammenga, M., Ponne, N.J., Veenboer, G.J.M., Gons, M.H., Orgiazzi, J. de Vijlder, J.J. andRis-Stalpers, C. (1999). The screening for mutations in the thyroglobulin cDNA from six patients with congenital hypothyroidism. *Biochemie*, 81: 425–432.

Van Haaster, L.H., De Jong, F.H., Docter, R. and de Rooij, D.G. (1992). The effect of hypothyroidism on Sertoli cell proliferation and differentiation and hormone levels during testicular development in the rat. *Endocrinology*, 131: 1574–1576.

Vaughan, M.K., Richardson, B.A., Petterborg, L.J., Holtorf, A.P., Vaughan, G.M., Champney, T.H. and Reiter, R.J. (1984). Effects of injections and/or chronic implants of melatonin and 5-methoxytryptamine on plasma thyroid hormones in male and female Syrian hamsters. *Neuroendocrinology*, 39: 361–366.

Venditti, P., Balestrieri, M., Meo, S. and Leo, T. (1997). Effect of thyroid state on lipid peroxidation, antioxidant defences, and susceptibility to oxidative stress in rat tissues*Journal of Endocrinology*, 155: 151-157.

Viguié, C., Battaglia, D.F., Krasa, H.B., Thrun, L.A. and Karsch, F.J. (1999). Thyroid hormones act primarily within the brain to promote the seasonal inhibition of luteinizing hormone secretion in the ewe. *Endocrinology*, 140: 1111-1117.

Vijay, P., Meenaxi, S. and Anil, M. (2014). Influence of age on thyroid hormone profile and its correlation with other serum biochemical indices in goat of aid tropical region. *Indian Journal of Small Ruminants*, 20(2): 124–128.

Vijayan, E. and McCann, S.M. (1977). Suppression of feeding and drinking activity in rats following intraventricular injection of thyrotropin releasing hormone (TRH). *Endocrinology*, 100(6): 1727–1729.

Visser, T.J. (1990). Importance of deiodination and conjugation in the hepatic metabolism of thyroid hormone. In: Greer MA. (Ed). *The Thyroid Gland*, Raven Press, New York, PP. 255–283.

Wade, G.N., Schneider, J.E. and Li, H.Y. (1996). Control of fertility by metabolic cues. *American Journal of Physiology*, 270: E1–E19.

Walkden-Brown, S.W., Davidson, R.H., Milton, J.T.B. and Martin, G.B. (1996). Thyroidectomy late in the breeding season advances the onset of seasonal anovulation in cashmere goats. In: *Proceedings of the 13th international congress on animal reproduction, Sydney, Australia*, pp. 1-19.

Wang, H., Chu, W.S., Lu, T., Hasstedt, S.J., Kern, P.A. and Elbein, S.C. (2004). Uncoupling protein-2 polymorphisms in type 2 diabetes, obesity, and insulin secretion. *American Journal of Physiology, Endocrinology and Metabolism*, 286: E1–E7.

Wartofsky, L. and Burman, K.D. (1982). Alterations in thyroid function in patients with systemic illness: the ‘‘euthyroid sick syndrome’’. *Endocrine Reviews*, 3: 164–217.

Webster, J.R., Moenter, S.M., Woodfill, C.J.I. and Karsh, F.J. (1991). Role of the thyroid gland in seasonal reproduction. II. Thyroxine allows a season-specific-suppression of gonadotropin secretion in sheep. *Endocrinology*, 129: 176–183.

Weiss, W.P., Todhunter, D.A., Hogan, J.S. and Smith, K.L. (1990). Effect of duration of supplementation of selenium and vitamin E on periparturient dairy cows. *Journal of Dairy Science*, 73: 3187–3194.

West, J.W. (2003). Effects of heat stress on production in dairy cattle. *Journal of Dairy Science*, 86: 2131- 2144.

West, K.L., Ramer, J., Brown, J.L., Sweeney, J., Hanahoe, E.M., Reidarson, T., Proudfoot, J. and Bergfelt, D.R. (2014). Thyroid hormone concentrations in relation to age, sex, pregnancy, and perinatal loss in bottlenose dolphins (Tursiops truncatus). *General and Comparative Endocrinology*, 197: 73–81.

Williams, C.C., Calmes, K.J., Fernandez, J.M., Stanley, C.C., Lovejoy, J.C., Bateman, H.G., Gentry, L.R., Gantt, D.T. and Harding, G.D. (2004). Glucose metabolism and insulin sensitivity in Gulf Coast native and Suffolk ewes during late gestation and early lactation. *Small Ruminant Research*, 54: 167–171.

Williams, G.R and Bassett, D. (2011). Local control of thyroid hormone action-role of type 2 deiodinase. *Journal of Endocrinology*, 209: 261–272.

Wipff, P. and Hinz, B. (2008). Integrins and the activation of latent transforming growth factor beta1: an intimate relationship. *European Journal of Cell Biology*, 87: 601–615.

Wisdom, G.B. (1976). Enzyme-Immunoassay. *Clinical Chemistry*, 22: 1243-55.

Wolf, M., Weigert, A. and Kreymann, G. (1996). Body composition and energy expenditure in thyroidectomized patients during short-term hypothyroidism and thyrotropin-suppressive thyroxine therapy. *European Journal of Endocrinology*, 134(2): 168–173.

Wood, W.M., Kao, M.Y., Gordon, D.F. and Ridgway, E.C. (1989). Thyroid hormone regulates the mouse thyrotropin beta subunit gene promoter in transfected primary thyrotropes. *Journal of Biological Chemistry*,264: 14840–14847.

Yakubu, D.P., Mostyn, A., Wilson, V., Pearce, S., Alves-Guerra, M.C., Pecqueur, C., Miroux, B., Budge H., Stephenson, T. and Symonds, M.E. (2007). Different effects of maternal parity, cold exposure and nutrient restriction in late pregnancy on the abundance of mitochondrial proteins in the kidney, liver and lung of postnatal sheep. *Reproduction*, 133: 1241–1252.

Yamamura, T., Hirunagi, K., Ebihara, S. and Yoshimura, T. (2004). Seasonal morphological changes in the neuro-glial interaction between gonadotropin- releasing hormone nerve terminals and glial endfeet in Japanese quail. *Endocrinology*,145: 4264–4267.

Yamamura, T., Yasuo, S., Hirunagi, K., Ebihara, S. and Yoshimura, T. (2006). T3 implantation mimics photoperiodically reduced encasement of nerve terminals by glial processes in the median eminence of Japanese quail. *Cell and Tissue Research*, 324: 175–179.

Yasuo, S., Watanabe, M., Nakao, N., Takagi, T., Follett, B.K., Ebihara, S., Yoshimura, T. (2005). The reciprocal switching of two thyroid hormone-activating and -inactivating enzyme genes is involved in the photoperiodic gonadal response of Japanese quail. *Endocrinology*, 146: 2551 2554.

Yasuo, S., Nakao, N., Ohkura, S., Iigo, M., Hagiwara, S., Goto, A., Ando, H., Yamamura T., Watanabe, M.,Watanabe, T., Oda, S., Maeda, K., Lincoln, G.A., Okamura, H., Ebihara, S. and Yoshimura, T. (2006). Long-day suppressed expression of type 2 deiodinase gene in the mediobasal hypothalamus of the Saanen goat, a short-day breeder: implication for seasonal window of thyroid hormone action on reproductive neuroendocrine axis. *Endocrinology*, 147: 432–440.

Yasuo, S., Yoshimura, T., Ebihara, S. and Korf, H.W. (2007). Temporal dynamics of type 2 deiodinase expression after melatonin injections in Syrian hamsters. *Endocrinology*, 148: 4385–4392.

Yen, P.M. (2001). Physiological and molecular basis of thyroid hormone action. *Physiological Reviews*, 81: 1097–1142.

Yokus, B., Cakir, D.U., Kanay, Z., Gulten, T. and Uysal, E. (2006). Effects of seasonal and physiological variations on the serum chemistry, vitamins and thyroid hormone concentrations in Sheep.*Journal of Veterinary Medicine. A, Physiology, Pathology and Clinical Medicine*, 53: 271–276.

Yoshimura, T., Yasuo, S., Watanabe, M., Iigo, M., Yamamura, T., Hirunagi, K. and Ebihara, S. (2003). Light-induced hormone conversion of T4 to T3 regulates photoperiodic response of gonads in birds. *Nature*, 426: 178–181.

Yoshihara, A., Hara, T., Kawashima, A., Akama, T., Tanigawa, K., Wu, H., Sue, M., Ishido, Y., Hiroi, N., Ishii, N., Yoshino, G. and Suzuki, K. (2012). Regulation of dual oxidase expression and H_2O_2production by thyroglobulin. *Thyroid*, 22(10): 1054-1062.

Zahediasl, S. (2010). Importance of thyroid hormones in intrauterine programming. *International Journal of Endocrinology and Metabolism*, 8(4): 186-187.

Zarei, M.A., Farshad, A. and Akhondzadeh, S. (2009). Variations in thyroidalactivity during estrous cycle and natural in Markhoz goats breed. *Pakistan Journal of Biological Sciences*, 12: 1420-1424.

Zhang, S., Blache, D., Blackberry, M.A. and Martin, G.B. (2004). Dynamics of the responses in secretion of luteinizing hormone, leptin and insulin following an acute increase in nutrition in mature male sheep. *Reproduction, Fertility and Development*, 16(8): 823-829.

Appendices

Appendix I:Effect of sex and age on serum concentration of T_3, T_4, TSH and T_3:T_4 in Red Sokoto and Sahel goats during the cold-dry season

RSG – Red Sokoto goats and SHG – Sahel goats. Values of the same parameters with different superscript are statistically significant ($P < 0.05$). a,b:between sexes, x,y: between season, c,d: between breeds

	RSG		SHG	
	Male	Female	Male	Female
T_3 (ng/ml)				
Young	2.46 ± 0.14^{x}	2.47 ± 0.19	1.83 ± 0.19^{a}	2.35 ± 0.002^{b}
Adult	2.02 ± 0.10^{y}	2.27 ± 0.10	1.92 ± 0.16	2.34 ± 0.29
T_4 (ng/ml)				
Young	$47.03 \pm 1.04^{a, x}$	49.64 ± 3.70^{b}	46.93 ± 2.75^{x}	46.57 ± 4.22
Adult	$34.26 \pm 0.87^{a, y}$	50.55 ± 4.97^{b}	$39.07 \pm 1.88^{y, a}$	46.92 ± 1.77b
TSH (µIU/ml)				
Young	0.76 ± 0.018	0.71 ± 0.022	0.91 ± 0.10	0.93 ± 0.15
Adult	0.76 ± 0.031	0.79 ± 0.035	0.86 ± 0.083	0.76 ± 0.031
T_3:T_4				
Young	0.048 ± 0.004	0.055 ± 0.0039	0.040 ± 0.0051^{a}	0.053 ± 0.0053^{b}
Adult	0.058 ± 0.0040^{a}	0.048 ± 0.0038^{b}	0.049 ± 0.0032	0.050 ± 0.0054

Appendix II:Effect of sex and age on serum concentration of T_3, T_4, TSH and T_3:T_4 in Red Sokoto and Sahel goats during the hot-dry season

	RSG		SHG	
	Male	Female	Male	Female
T_3 (ng/ml)				
Young	2.12 ± 0.19^{x}	1.76 ± 0.22^{x}	$2.42 \pm 0.21^{x, a}$	1.45 ± 0.24^{b}
Adult	1.21 ± 0.03^{y}	1.38 ± 0.14^{y}	$0.92 \pm 0.009^{y, a}$	1.62 ± 0.30^{b}
T_4 (ng/ml)				
Young	51.34 ± 3.82	49.39 ± 2.20	57.04 ± 5.20^{x}	46.88 ± 5.96
Adult	43.35 ± 2.75^{a}	50.00 ± 0.99^{b}	$28.75 \pm 6.78^{y, a}$	43.93 ± 4.45^{b}
TSH (µIU/ml)				
Young	0.76 ± 0.03	0.72 ± 0.02	$0.89 \pm 0.07^{x, a}$	0.65 ± 0.01^{b}
Adult	0.76 ± 0.057	0.69 ± 0.021	$0.655 \pm 0.01^{y, a}$	0.82 ± 0.08^{b}
T3:T4				
Young	0.039 ± 0.0019^{x}	0.039 ± 0.0090	0.044 ± 0.0036^{a}	0.030 ± 0.0038^{b}
Adult	0.029 ± 0.0023^{y}	0.026 ± 0.0029	0.042 ± 0.0094	0.034 ± 0.0078

RSG – Red Sokoto goats and SHG – Sahel goats. Values of the same parameters with different superscript are statistically significant ($P < 0.05$). a,b:between sexes, x,y: between season, c,d: between breeds

Appendix III:Effect of sex and age on serum concentration of T_3, T_4, TSH and T_3:T_4 in Red Sokoto and Sahel goats during the rainy season

	RSG		SHG	
	Male	Female	Male	Female
T_3 (ng/ml)				
Young	2.48 ± 0.14[a]	2.90 ± 0.09[x, b]	1.87 ± 0.11	2.08 ± 0.15
Adult	2.15 ± 0.18	2.46 ± 0.11[y]	2.12 ± 0.10	2.18 ± 0.19
T_4 (ng/ml)				
Young	51.88 ± 6.47[x]	54.48 ± 4.29	41.59 ± 2.61	39.62 ± 3.69[x]
Adult	37.27 ± 2.37[y]	43.61 ± 3.10	41.40 ± 3.41	50.07 ± 4.73[y]
TSH(µIU/ml)				
Young	0.67 ± 0.059	0.72 ± 0.072	0.67 ± 0.10	0.93 ± 0.12
Adult	0.93 ± 0.10	0.93 ± 0.19	0.91 ± 0.13	0.93 ± 0.13
T_3:T_4				
Young	0.050 ± 0.0026	0.063 ± 0.0095	0.048 ± 0.0014[a]	0.064 ± 0.009[b]
Adult	0.057 ± 0.0057	0.064 ± 0.007	0.047 ± 0.0023[a]	0.040 ± 0.003[b]

RSG – Red Sokoto goats and SHG – Sahel goats. Values of the same parameters with different superscript are statistically significant ($P < 0.05$). a,b:between sexes, x,y: between season, c,d: between breeds