

Effect of Reproductive Status and Body Mass Index on Serum Concentrations of Thyroid Hormones and Thyroid-stimulating Hormone in Women in Zaria, Northern Nigeria

Ogbe SE¹, Kawu MU², Olorunshola KV³, Danborno AM¹

¹Department of Human Physiology, Faculty of Basic Medical Science, Bingham University, Karu, Nasarawa State. ²Department of Veterinary Physiology, Faculty of Veterinary Medicine, Ahmadu Bello University, Zaria, Kaduna State. ³ Department of Human Physiology, Faculty of Basic Medical Science, University of Abuja, FCT, Abuja.

Article Metrics

Date submitted: 2021-08-23

Date Accepted: 2021-10-13

Date Published: 2021-12-09



ABSTRACT

Background: Optimum thyroid hormones level is important for the well-being of the fetus and mother. Thyroid hormones disorders have negative impact on female reproduction resulting in reduced fertility and pregnancy morbidities. There is paucity of data on normal levels of circulating thyroid hormones in women of reproductive age in Zaria, Nigeria. The aim of the study was to determine reference values of serum thyroid hormones and thyroid stimulating hormones and the influence of reproductive status and body mass index (BMI) on the reference values of thyroid hormones and thyroid-stimulating hormone in women of reproductive age in Zaria. **Methodology:** This is a cross-sectional study conducted on 176 women, comprising 65 pregnant, 51 lactating and 60 non-lactating women living within Zaria metropolis. A single blood sample was collected from each of the subjects for the purpose of this study (total blood samples = 176). Blood serum was used to assay for thyroxine (T4), free triiodothyronine (fT3) and thyroid stimulating hormones (TSH) using an ELISA kit. **Results:** Lactating women had significantly lower ($P < 0.01$) serum fT3, T4 and TSH than non-lactating and pregnant women. Serum fT3 and T4 were higher in second trimester than in first and third trimesters ($P < 0.05$). Pregnant women had significantly lower ($P < 0.01$) BMI compared to lactating and non-lactating women. There was a negative correlation between BMI and fT3 which was only significant ($P < 0.01$) in pregnant women. A significant ($P < 0.01$) positive correlation between BMI and TSH was obtained in pregnant women, and a negative correlation ($P < 0.05$) in non-pregnant women was observed. **Conclusion:** The present study, provided preliminary reference values of thyroid hormones (fT3, T4) and TSH; and demonstrated that reproductive status and BMI significantly affect these values in women in Zaria, Nigeria

Keyword: Thyroxine, Thyroid, Hormones, Body mass index, Pregnant, Lactating

*Correspondence: Ogbe Susan Enechojo, Bingham University, Karu.

Email: susanogbe07@gmail.com

[Access to the article](#)



website: <http://www.jmbsr.com.ng>

doi: doi.org/10.5281/zenodo.5809627

[Find our articles on Google Scholar, fully indexed](#)

How to cite this article

Ogbe SE, Kawu MU, Olorunshola KV, Danborno AM. Effect of Reproductive Status and Body Mass Index on Serum Concentrations of Thyroid Hormones and Thyroid-stimulating Hormone in Women in Zaria, Northern Nigeria. J Med Bas Sci Res 2021;2(2):57-69. DOI: 10.5281/zenodo.5809627

INTRODUCTION

Thyroid disorders are more common in women and may manifest before or during pregnancy, post-delivery, or later in life.^[1,2] It is recommended that the thyroid hormone activity of pregnant women should be assessed regularly due to the extra demand for thyroid hormones during this crucial period in the life of the fetus and the pregnant mother.^[2,3] Female reproduction depends on adequate levels of thyroid hormones and thyroid disorders, exert negative effects on the female reproduction.^[4,5] Overt hypothyroidism and subclinical hyperthyroidism caused by autoimmune thyroid diseases have been linked to reduced fertility and increased pregnancy-related morbidity such as premature delivery and/or low birth weight, spontaneous abortion, fetal distress in labor, placental abruption and gestation-induced hypertension.^[6-9] Optimum function of the thyroid gland is essential for normal fertility. Menstrual disorders and infertility due to altered peripheral estrogen metabolism, hyperprolactinemia and abnormal pulsatile release of luteinizing hormone are common in women with hypothyroidism.^[7] Obstetric complications in mothers^[8, 10, 11] and impaired neurodevelopment in early fetal brain^[12, 13] are associated with inadequate thyroid function. The first 12 to 14 weeks of gestation is a critical period for the developing fetus as their thyroxine supply depends on placental transfer of maternal hormones.^[14] It has been reported that maternal hypothyroidism affects the intelligence quotient (IQ) of the unborn child.^[12,15] In a general population, mild thyroid failure is estimated to occur frequently in pregnant women with compensated hypothyroidism antedating pregnancy.^[16,17]

Researchers have studied the interaction of thyroid disorders with body mass index (BMI). Manji *et al*^[18] found no association between serum concentrations

of TSH and free thyroxine concentrations within the normal range and BMI. In contrast, Knudsen *et al*.^[19] reported that thyroid function could be one of several factors that act in harmony to determine body weight. However, Figueroa *et al*.^[20] found serum TSH to be significantly associated with BMI, and that higher and more variable TSH levels were associated with obesity. Despite the importance of thyroid hormones in female reproduction and fetal developments, little or no information is available on the pattern of serum profile of thyroid hormones in Nigerian females during gestation and lactation periods. The present study is aimed at determining the serum concentrations of fT_3 , T_4 and TSH, in a population of pregnant, lactating and non-lactating women in Zaria, Northern Nigeria, and environs and their correlations with BMI.

METHODOLOGY

Population Sampling

The study was a cross-sectional study conducted on 176 women, who were within the reproductive age and gave their informed consent to participate in the study. The study was approved by Ahmadu Bello University Teaching Hospital Ethics Committee (Approval No: MSc/Med/00228/11-12). The study was conducted in Zaria and environs in Northern, Nigeria. Zaria lies within latitude $11^{\circ} 12'N$, longitude $7^{\circ} 33'E$, and altitude of 610m above sea level; average rainfall of 00 816 mm/month; ambient temperature of $15.3\ 36.25^{\circ}C$ and relative humidity of 20.26 15.65. It is predominantly populated by the Hausa-Fulani speaking people of Nigeria.

A convenience sampling method was adopted for this study with a sample population of 176 women of reproductive age that comprised of 65 pregnant

women attending antenatal care, 51 lactating women attending postnatal care in various hospitals in Zaria; and 60 non-pregnant (non-lactating) women that served as the control group. Women with history of thyroid disease, diabetes mellitus and hypertension were excluded from this study. The women were served questionnaires from which their biodata was obtained. Body mass index (BMI) was determined using the weight/mass and height of the subjects and calculated as described by Eknoyan and Garabed (2007): $BMI = Mass (Kg)/Height (m)^2$. The BMI was measured at different gestational ages because the subjects booked for antenatal clinic at different trimesters. The BMI of each subject was measured alongside the recording biodata and blood sampling.

Hormonal Assay

About 2 ml of blood from the median cubital vein were collected into plain sample bottles using a 2 ml syringe between 8-10am. The serum was obtained from the blood samples by centrifuging the blood at 3000 g for 15 minutes. The sera were stored in freezer at a temperature of -20°C until assay. The fT₃, T₄ and TSH were determined using an ELISA kit (Diagnostic Automation® /Cortez Diagnostics, USA).

Determination of T4

This is a competitive immunoassay technique where a fixed amount of labeled T4 competes with the unlabeled T4 in the sample, standard, or quality control serum for a fixed number of binding sites on the specific T4 antibody. Two T4 Elisa kits of 96 wells each were used for this assay with batch number, 3149- 16, specificity of 96.30% and sensitivity of 0.5µg/dL and a total run time of 80 minutes.

Reagent Preparation

The T4-HRPO conjugate reagent was prepared by

adding 0.1ml of T4-HRPO conjugate concentrate to 2.0 ml of T4 conjugate diluent (1:20 dilution), and mixed thoroughly at a temperature of 19-20°C. 15 ml volume of wash buffer (50x) was diluted with distilled water to prepare 750 ml of washing buffer.

Assay Procedure

About 50 µl of standard, samples and controls were dispensed into appropriate wells. A 100 µl of enzyme conjugate reagent was dispensed also into each well. The contents of the well were thoroughly mixed for 10s and then incubated at room temperature of 18-22°C for 60 mins. During the incubation period, the conjugated T4 competes with T4 from the sample for available binding sites on the antibody.

After the incubation period, the micro titer wells were rinsed and flicked five times with a washing buffer solution. The wells were sharply struck onto an absorbent paper towels to remove all residual water droplets. Both conjugated and unconjugated T4 bound to the antibody during the incubation will remain on the solid phase. 100 µl of TMB solution was dispensed into each well, which turned the pale-yellow color of contents of the well into blue; the mixture was then incubated at room temperature for 20mins.

A stop solution of about 100µl was added to each well and gently mixed for 5s to stop the reaction. The wells were read with a microplate reader at an optical density of 450 nm. Standards of known T4 concentrations which were run concurrently with the samples were used to plot a standard curve. The unknown T4 concentrations in each sample were then calculated from the curve^[21-23].

Determination of FT3

The MICRO-EIA free T3 test was used for the determination of fT3. The principle of the assay is based on the principle of a solid phase competitive

enzyme immunoassay (EIA). Two free T3 Elisa kits of 96 wells each with batch number, 3148-16, specificity of 97%, sensitivity of 0.05pg/mL and total run time of ~75 minutes was used for this assay.

Reagent Preparation

Wash buffer was made by diluting wash concentrate with distilled water up to 1000ml. The working substrate was prepared by adding the substrate A into substrate B solution and mixed thoroughly.

Assay Procedure

About 50 µl of standard, samples and controls were dispensed into appropriate wells. Then 100 µl of FT3-enzyme reagent solution was added into each well and the microplate was swirled gently for 20-30s to mix and covered. The mixture was incubated at room temperature for 60s.

The contents of the microplate were discarded by decanting and the microplate was blotted dry with absorbent paper. 300 µl of wash buffer was added to each well and decanted; this procedure was repeated two more times making a total of three washes. A working substrate solution of 100 µl was added into each well and incubated at room temperature for 15mins. After incubation, 50 µl of stop solution was added to each well and gently mixed for 15-20.

The absorbance in each well was read using a micro titer plate reader at a wavelength of 450nm and a reference wavelength of 620nm was used to minimize well imperfections. Standards of known FT3 concentrations which were run concurrently with the samples were used to plot a standard curve. The unknown FT3 concentrations in each sample were calculated from the curve^[24,25].

Determination of TSH

The TSH EIA test is based on the principle of a solid phase enzyme-linked immunosorbent assay^[26,27]. Two

TSH Elisa kits of 96 wells each with batch number 3122-16, sensitivity of 0.20 µIU/mL and sensitivity of 100% and a total run time of ~80mins was used for this assay.

Reagent preparation

15 ml of wash buffer (50x) was diluted into distilled water and 750 ml of wash solution was made.

Assay Procedure

About 50 µl of standard, samples and controls were dispensed into appropriate wells. Enzyme conjugate reagent of 100 µl was dispensed into each well, thoroughly mixed for 30s and incubated at room temperature for about 60mins.

The incubation mixture was removed by flicking the contents of the plate into a waste container and rinsed about five times with washing buffer. The wells were struck over absorbent paper towels to remove every residual droplets of water. 100 µl of TMB solution was dispensed into each well, gently mixed for 5s and incubated at room temperature for 20mins. After incubation, the stop solution of 100 µl was dispensed into each well to stop the reaction. The wells were read with a microplate reader at an optical density of 450nm. Standards of known T4 concentrations which were run concurrently with the samples were used to plot a standard curve. The unknown T4 concentrations in each sample were then calculated from the curve

Data Analysis

Data collected from this study were expressed in percentage and mean (\pm SEM). Results were analyzed using one-way analysis of variance and Tukey's post-hoc test. Pearson's correlation analysis was done to test for relationship between serum T_4 , ft_3 and TSH with pregnancy, lactation and parity. Values of $P < 0.05$ were considered statistically

significant. The statistical package used was Graphpad prism for windows (Chicago, 2003). Non-parametric data were subjected to Kruskal-Wallis test.

RESULTS

Table 1 shows the mean (\pm SEM) serum fT_3 , T_4 and TSH concentrations in non-lactating, pregnant and lactating women.

Serum fT_3 was significantly ($P < 0.001$) lower in lactating than in non-lactating and pregnant women. Serum T_4 was significantly ($P < 0.001$) lower in lactating than in non-lactating and pregnant women. Serum TSH was significantly ($P < 0.002$) lower in lactating women than in non-lactating and pregnant women. There was no significant difference in serum fT_3 , T_4 and TSH concentrations between pregnant and non-lactating women.

Table 1: Mean (\pm SEM) serum concentrations of thyroxine, triiodothyronine and thyroid stimulating hormone in a female sample population in Zaria, Nigeria.

Status	n	fT_3 (ng/ml)	T_4 (ng/ml)	TSH (μ IU/ml)
Non-Lactating	60	3.37 ± 0.12^a (1.55 – 3.60)	101.09 ± 0.68^a (87.47–114.72)	5.25 ± 0.32^a (1.35 – 5.89)
Pregnant	65	3.34 ± 0.11^a (1.28 – 3.56)	116.7 5 ± 0.67^a (103.40 - 130.09)	4.67 ± 0.33^a (0.56 – 5.32)
Lactating	51	2.40 ± 0.11^b (0.40 -2.61)	61.41 ± 0.64^b (48.54 – 74.28)	3.54 ± 0.29^b (0.27 – 4.12)
Total	176	3.08 ± 0.72	95.37 ± 0.42	4.50 ± 0.19

a, b = values with different subscript letters within the same column are significantly ($p < 0.001$) different.

fT_3 - Free triiodothyronine; T_4 - Thyroxine; TSH –Thyroid Stimulating hormone; () – Range

Table 2: Effect of trimester of pregnancy on serum thyroxine, triiodothyronine and thyroid stimulating hormone in a female sample population in Zaria, Nigeria.

Trimester	n	fT_3 (ng/ml)	T_4 (ng/ml)	TSH (μ IU/ml)
First	12	2.81 ± 0.20^a (1.27 – 3.25)	82.10 ± 1.303^a (53.39 - 110.62)	4.77 ± 0.67 (0.20 – 5.35)
Second	41	3.22 ± 0.30^a (1.28 – 3.88)	129.20 ± 0.83^b (112.39 – 146.01)	6.00 ± 0.66 (0.56 – 5.64)
Third	12	3.52 ± 0.13^b (1.54 – 3.79)	108.90 ± 1.47^a (76.52 – 141.18)	6.02 ± 0.93 (0.95 – 5.82)
Total	65	3.34 ± 0.11	116.75 ± 0.67	5.72 ± 0.47

a, b = values with different superscript letters within the same column are significantly different ($p < 0.05$).; fT_3 - Free triiodothyronine

T_4 - Thyroxine; TSH - Thyroid Stimulating Hormone; () – Range

Table 2 shows the effect of trimester of pregnancy on serum concentrations of fT_3 , T_4 and TSH. Mean serum fT_3 concentration was significantly higher in the second trimester than in the first and third trimester pregnancies ($P < 0.05$). Mean serum T_4 level was significantly ($P < 0.05$) higher in second trimester than in first and third trimester pregnancies (. Mean serum TSH concentrations in the first, second and third trimester pregnancies were not significantly different.

Table 3: Pattern of body mass index in non-lactating, pregnant and lactating female sample population in Zaria, Nigeria

Status	n	BMI (kg/m ²)
Non-Lactating	60	26.57 ± 0.93 ^a
Pregnant	65	23.91 ± 0.59 ^b
Lactating	51	25.85 ± 1.11 ^a
Total	176	25.01 ± 0.51

DISCUSSION

In the present study, lactating women had significantly lower fT_3 , T_4 and TSH levels compared to pregnant and non-lactating women. The low thyroid hormone concentrations observed in lactating women in this study is within normal range. Similarly, Fukuda *et al.* [28] observed a persistent decrease in thyroid hormones concentration in rats from pregnancy through lactation, which later returned to normal after weaning their pups. The later report agrees with the observation of the present study. The possible reason for the decreased thyroid hormones concentrations in lactating women could be due to loss of thyroid hormones into the breast milk [28] also, thyroid hormones influence milk synthesis as well as the intensity and duration of milk secretion. [29] This leads to increased thyroid hormones

utilization and thus, decreases in serum thyroid hormones level. The low fT_3 concentration observed in the lactating women in this study is also in agreement with the report of Zhang *et al.* [30], who studied thyroid hormone concentration in 56 lactating women in China and reported that the milk concentrations of T_4 and fT_3 were 29.6 mcg/L and 2.3 ng/L, respectively. Lactating women in the current study had TSH level of 3.68 μ IU/ml, which is within the normal recommended reference range of 0.4 4.0 mIU/l in a non-pregnant population. [31]

Table 3 shows the pattern of body mass index in non-lactating, pregnant and lactating women. The BMI (kg/m²) in non-pregnant women was significantly higher than in pregnant and lactating women, ($P < 0.01$).

Table 4 shows the correlation coefficients between BMI and fT_3 , T_4 and TSH, in non-lactating, pregnant and lactating women. There was a significant ($P < 0.01$) negative correlation between BMI and fT_3 and significant ($P < 0.005$) positive correlation between BMI and TSH in pregnant women.

Table 4: Pearson's correlation coefficient of body mass index, thyroid hormones and thyroid stimulating hormone

Status	BMI vs fT_3	BMI vs T_4	BMI vs TSH
Non-Lactating	-0.064	-0.079	-0.068
Pregnant	-0.32**	-0.072	0.345**
Lactating	-0.057	-0.004	0.181

** - $p < 0.001$

Serum concentrations of fT_3 , T_4 and TSH were mostly lower in pregnant women compared to the non-lactating women. There was however, no significant difference between them. The American Thyroid Association has established that the

reference range of TSH during pregnancy decreases throughout the period of gestation. Thus, both the lower and upper normal limit of serum TSH are decreased by about 0.10.2 mIU/L and 1.0 mIU/L, respectively, compared with the usual TSH reference interval of 0.44.0 mIU/L of non-pregnant women.^[31] The reason for the decrease in the concentrations of thyroid hormones in the pregnant women could be due to the fact that the thyroid gland produces 50% more thyroid hormone during pregnancy to provide enough thyroid hormone for the developing fetus and the expectant mother.^[32, 33] During pregnancy, estrogen levels stimulate the expression of thyroxine binding globulin (TBG), a protein that is produced in the liver. This rise in estrogen during pregnancy induces a double-fold increase in serum TBG. Thyroxine binds to the excess TBG, resulting in a negative feedback increase in TSH secretion by the pituitary gland and thus, improving the synthesis and secretion of thyroid hormones. The high levels of human chorionic gonadotropin (HCG) (which is similar to TSH) during first trimester of pregnancy can also lead to increased binding to TSH receptors, thereby transducing signals on the thyroid epithelial cells.^[34, 3] The reference value observed in the non-lactating population of this study (1.35–5.89 mIU/L) is slightly higher as compared to values reported from Australia (0.40–4.00 mU/L).^[35] Similar trend was also observed in the pregnant population of this study (0.56–5.32 mU/L) and that of Gilbert *et al.*^[35] in first trimester of pregnant women in Australia (0.02–2.15 mU/L). Also a recent study in Iranian pregnant women reported hypothyroidism in the first trimester.^[2] The level of iodine supplementation in diet, racial difference, socio-economic and nutritional status, and many other factors could be responsible for the difference in the reference values of this study, as compared to other studies. In this study, the serum fT₃ concentration showed a

progressive increase through the three trimesters. This observation corresponds with the studies carried out in iodine sufficient areas^[37] and countries, where iodine supplementation is practiced.^[38-40] This observation also agrees with the report of Striker *et al.*^[41] and Marwaha *et al.*,^[42] who reported a progressive increase in the fT₃ levels through the three trimesters of pregnancy. It is believed that the increase is due to physiological adaptation, which enables energy conservation due to high metabolic demand of pregnancy.^[43] The increase in fT₃ level is due to down-regulation of the thyroid hormone action to conserve energy during pregnancy.^[43,44] It has been reported that total T₃ and fT₃ remain the same or increase, when maternal iodine level is low thus avoiding an increase in circulating TSH.^[45,46] Diversion of a part of maternal iodine to fetal thyroid gland during the second half of pregnancy also shifts the maternal thyroid gland to prefer rational synthesis of fT₃, instead of fT₄ to maintain euthyroidism during the period of relative iodine deficiency.^[47] In this study, the T₄ level increased significantly in the second trimester and later decreased in the third trimester. This observation is similar to earlier reports^[41, 48, 49] where a progressive increase in T₄ level was reported in the three trimesters.

The lowest concentration of serum TSH obtained in the present study was observed during the first trimester after which a non-significant increase in TSH level in the second trimester was obtained. This could relate to hCG levels, which are highest in early gestation. Serum TSH and its reference range rises gradually in the second and third trimesters.^[39, 50] This agrees with earlier findings,^[41, 47, 51-54] of an increase in TSH in second and third trimesters, although some other workers^[39, 44, 48, 55] had reported an increase in TSH only during the third trimester. Striker *et al.*^[41] observed an increase in TSH in the second trimester and a decrease in the third trimester, while Marwaha

et al. [42] reported an increase in TSH in the third trimester. This discrepancy suggests that other factors, including endogenous or exogenous, may play a role in the dynamics of thyroid hormones and TSH disposition in pregnant women.

Although the reference value of fT_3 , T_4 and TSH obtained in this study are in line with other studies reported, the reference values obtained in the present study were apparently higher than some of the values reported. The discrepancies could be due to ethnic/racial background, maternal iodine status, laboratory techniques, definition of population, exclusion criteria, method of statistical analysis and also the sensitivity of kits used.

Pregnant women had significantly lower BMI compared to lactating and non-lactating women, this is in contrast to the report of Danborno *et al.* [56] who reported high BMI of pregnant women attending antenatal clinic in LAUTECH, Osogbo, as pregnancy advances towards term. A possible reason for the significantly lower BMI in pregnant and lactating as compared to non-lactating women observed in this study may be due to the fact that the pregnant women were predominantly sampled from the rural area of Zaria were booking for antenatal is often done in an arbitrary manner without cognizance to the trimester of pregnancy. While the lactating and non-lactating women were predominantly sampled from women that attend the University health care facility and other government and private hospitals within Zaria urban settlement. The latter are largely elitist and more prone to being overweight. This could be a confounding factor. Thus, this finding should be interpreted with caution. However, it should also be noted that low BMI has been reported in women living in rural areas of Northern Nigeria [58].

Body mass index also showed a significant negative correlation with fT_3 in pregnant women. This is in

contrast with the finding of Iacobellis *et al.*, [59] who reported a positive correlation of BMI and fT_3 in uncomplicated obese women. Milionis and Milionis [60] also reported a positive correlation between BMI and fT_3 in Greek women. The possible reason for the negative correlation between BMI and fT_3 observed in this study could be the pregnancy status of the women. During pregnancy, there is increased metabolism and utilization of fT_3 in order to generate the energy needed to sustain the pregnant mother and the growing fetus. In contrast to the findings of this study, results of other studies [42,61] showed a positive correlation between BMI and fT_3 . Similarly, Ren *et al.* [62] observed an increase in fT_3 levels in overweight and obese individuals than in normal weight subjects. However, Knudsen *et al.* [19] did not find any association between BMI and fT_3 . This means that other confounding factors may influence the relationship between BMI and thyroid hormones activity in women, and may require further investigation.

A positive correlation was observed between BMI and TSH in pregnant women. This observation is in agreement with the findings of earlier researchers, who reported positive associations between BMI and serum TSH. [20, 60, 61, 63, 64] The BMI in pregnant women could be the stimulating factor for increased TSH secretion in a negative feed-back fashion. In other words, as BMI increases in pregnant women, fT_3 levels decrease due to increased utilization to meet the metabolic needs of pregnancy. Consequently, this elicits a negative feed-back response on the anterior pituitary to release more TSH.

CONCLUSION

This study has provided preliminary reference values of thyroid hormones (fT_3 and T_4) and TSH in women of reproductive age in Zaria, Nigeria. The study has

also demonstrated that serum thyroid hormones (fT₃ and T₄) and TSH values were affected by reproductive status and BMI in women in Zaria, Nigeria.

Acknowledgements

I wish to acknowledge the contributions of Dr Elijah Ekah Ella of the Department of Microbiology, Ahmadu Bello University, Zaria. I want to acknowledge the contributions of Dr Habibu Buhari of the Department of Veterinary Physiology, Ahmadu Bello University, Zaria. I acknowledge also, the University Health Service of Ahmadu Bello University, Salama Infirmary, Zaria, St Luke's Hospital, Wusasa, Zaria and Gambo Sawaba General Hospital, Zaria and the Staff of Department of Human Physiology, Faculty of Medicine, Ahmadu Bello University, Zaria.

Conflict of Interest

I wish to state that there is no conflict of interest in this manuscript

All authors have gone through this manuscript and have made reasonable input to this work

REFERENCES

- Janssen OE, Mehlmauer N, Hahn S. High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. *European Journal of Endocrinology*. 2004;3:363-369.
- Sepasi, F., Rashidian, T., Shokri, M. et al. Thyroid dysfunction in Iranian pregnant women: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2020;20, 405.
- Mansourian AR. Female reproduction physiology adversely manipulated by thyroid disorders: A Review of Literature. *Pakistan Journal of Biological Sciences*. 2013;16:112-120.
- Poppe K, Velkenier B, Glinoeer D. The role of thyroid autoimmunity in fertility and pregnancy. *Nature Clinical Practice of Endocrinology and Metabolism*. 2008;4(7):394-405.
- Anderson SL and Anderson S. Turning to Thyroid Disease in Pregnant Women. *European Thyroid J*. 2020;9:225-233.
- Poppe K, Glinoeer, D. Thyroid autoimmunity and hypothyroidism before and during pregnancy. *Human Reproduction Update*. 2003;9:140-161.
- Krassas GE, Poppe K, Glinoeer D. Thyroid function and the human reproductive health. *Endocrine Review* 2005; 31: 702-755.
- Mirghani Dirar A, Kalhan A. Hypothyroidism during pregnancy: Controversy over screening and intervention. *World J Obstet Gynecol*. 2018;7(1):1-16
- FIGO Working Group on Good Clinical Practice in Maternal- Fetal Medicine. Good clinical practice advice: Thyroid and Pregnancy. *International Journal of Gynecology and Obstetrics*. 2019; 144(3): 347-351
- Casey BM, Dashe JS, Spong CY, McIntire DD, Leveno KJ. Perinatal significance of isolated maternal hypothyroxinemia identified in the first half of pregnancy. *Obstetrics and Gynecology*. 2007; 109: 1129-1135.
- Lazarus JH. Thyroid function in pregnancy. *British Medical Bulletin*. 2011; 97(1): 137148.
- Haddow JE, Palomaki GE, Allan WC. Maternal Thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *New England Journal of Medicine*. 1999; 341: 549-555.
- Idris I, Srinivason R, Simm A, Page RC. Maternal hypothyroidism in early and late

- gestation: effect on neonatal and obstetric outcome. *Endocrinology*. 2005; 63(5): 560-565.
14. Morreale d Escobar G, Obregon MJ, Escobar del Rey F. Maternal thyroid hormone early in pregnancy and fetal brain development. *Best Practice Research and Clinical Endocrinology and Metabolism*. 2004; 18: 225-248.
 15. Van den Boogaard E, Vissenberg R, Land JA, van Wely M, van der Post JA, Goddijn M, Bisschop PH. Significance of (sub) clinical thyroid dysfunction and thyroid autoimmunity before conception and in early pregnancy: a systematic review. *Human Reproduction Update*. 2011; 17(5): 605-619.
 16. Glinoe D, Fernandez SM, Bordoux P, Lejeune B, Delange F, Lemone M, et al. Pregnancy in patients with mild thyroid abnormalities: maternal and neonatal repercussions. *Journal of Clinical Endocrinology and Metabolism*. 1991; 73: 421-427.
 17. Glinoe D, Riahi M, Grun JP, Kinthaert J. Risk of subclinical hypothyroidism in pregnant women with asymptomatic autoimmune thyroid disorders. *Journal of Clinical Endocrinology and Metabolism*. 1994; 79: 1972-1974.
 18. Manji N, Boelaert K, Sheppard MC, Holdert RL, Gough SC, Franklyn JA. Lack of association between serum TSH or free T4 and body mass index in euthyroid subjects. *Clinical Endocrinology*. 2006; 64(2): 125-128.
 19. Knudsen N, Laurberg P, Rasmussen LB, Bulow I, Perrild H, Ovesen L, et al. Small differences in thyroid function may be important for body mass index and the occurrence of obesity in the population. *Journal of Clinical Endocrinology and Metabolism*. 2005; 90(7): 4019-4024.
 20. Figueroa B, Ve´lez H, Irizarry-Rami´rez M. Association of thyroid-stimulating hormone levels and body mass index in overweight Hispanics in Puerto Rico. *Journal of Ethnicity and Disease*. 2008; 18: 151-154.
 21. Skelley D, Brown L, Besch, P. Radioimmunoassay. *Clinical Chemistry*. 1973; 19: 146.
 22. Wistom GB. Enzyme immunoassay. *Clinical Chemistry*. 1976; 22: 1243
 23. Schuurs AHMW, van Weeman BK. Review, enzyme immunoassay. *Clinical Chemistry Acta*. 1977; 81: 1.
 24. Bhagat CI, Garcia-Webb P, Watson F, Beilby JP. Interference in radioimmunoassay of total serum thyroxine and free thyroxine due to thyroxine binding auto-antibodies. *Clinical Chemistry*. 1983; 29: 1324-1325.
 25. Wild, D. (1994). *Immunoassay Handbook*, Stockton Press. Pp. 339-8
 26. Engall, E. *Methods in Enzymology*. Van Vunakis, H and Langone, J.J (eds), Academic Press, New York. 1980; pp 419-492
 27. Uotila, M. Ruoslahti, E. and Engvall, E. *Journal of Immunological Methods*. (1981) 42, 11-15
 28. Fukuda H, Oshima K, Mori M, Kobayashi S, Greer MA. Sequential changes in the pituitary-thyroid axis during pregnancy and lactation in rat. *Endocrinology*. 1980; 107(6): 1711-1716.
 29. Peter F. and Muzsnai A. Congenital disorders of the thyroid: Hypo/hyper. *Pediatric Clinics of North America*. 2011; 58(5): 1099-1115.
 30. Zhang Q, Lian X, Chai X, Bai Y, Dai W. Relationship between Maternal Milk and Serum Thyroid Hormones in Patients with Thyroid Related Diseases. *CAMS*. 2013; 35(4): 427-431.
 31. American Thyroid Association. Hypothyroidism: A booklet for patients and their families. http://www.thyroid.org/wpcontent/uploads/patients/brochure/hypothyroidism_web_booklet published 2013, accessed January 23, 2014.
 32. Vissenberg R, Van Den Boogaard E, Van Wely

- M, Van Der Post J A, Fliers E, Bisschop PH, Goddijn M. Treatment of thyroid disorders before conception and in early pregnancy: A systematic review. *Human Reproduction Update*. 2012; 4: 360-373.
33. Negro R, Stagnaro-Green A. Diagnosis and management of subclinical hypothyroidism in pregnancy. *Biomedical Journal*. 2014; 349(10): g4929
34. Braverman L, Barbour L. Pregnancy and thyroid disease page-(2012). National Endocrine and Metabolic disease Information Services Homepage. Retrieved September 21, 2013. <http://www.endocrine.niddk.nih.gov/pubs/pregnancy>
35. Gilbert RM, Hadlow NC, Walsh JP, Fletcher SJ, Brown SJ, Stuckey BG, et al. Assessment of thyroid function during pregnancy: first-trimester (weeks 9-13) reference intervals derived from Western Australian women. *Med J Aust*. 2008; 189(5):2503.
36. Tsegaye B, Ergete W. Histopathologic pattern of thyroid disease. *East African Journal*. 2003; 80(10): 525-528.
37. Berghout A, Endert E, Ross A, Hogerzeil HV, Smits NJ, Wlarsluga WM. Thyroid function and thyroid size in normal pregnant women in an iodine replete area. *Clinical Endocrinology*. 1994; 41(3): 375-379.
38. Kung AWC, Lao TT, Chau MT, Tam SCF, Low LCK. Goitrogenesis during pregnancy and neonatal hypothyroidism in a borderline iodine sufficient area. *Clinical Endocrinology*. 2000; 53(6): 725-731.
39. Panesar NS, Li CY, Rogers MS. Reference intervals for thyroid hormones in pregnant Chinese women. *Annals of Clinical Biochemistry*. 2001; 38: 329-332.
40. Zarghami N, Rohbani-Noubar M, Khosrowbeygi A. Thyroid hormones status during pregnancy in normal Iranian women. *Indian Journal of Clinical Biochemistry*. 2005; 20(2): 182-185.
41. Stricker R, Echenard M, Eberhart R, Chevailler MC, Perez V, Quinn FA. Evaluation of maternal thyroid function during pregnancy: the importance of using gestational age-specific reference intervals. *European Journal of Endocrinology*. 2007; 157: 509514.
42. Marwaha RK, Tandon N, Garg MK, Ganie MA, Narang A, Mehan N, et al. Impact of body mass index on thyroid function in Indian children. *Clinical Endocrinology*. 2013; 79(3): 424-428.
43. Lof M, Olausson H, Bostrom K, Janerot-Sjoberg B, Sohlstrom A, Forsum E. Changes in basal metabolic rate during pregnancy in relation to changes in body weight and composition, cardiac output, insulin-like growth factor I, and thyroid hormones and in relation to fetal growth. *American Journal of Clinical Nutrition*. 2005; 81(3): 678-685.
44. Ardawi MM, Nasrat HA, Mustafa BE. Urinary iodine excretion and maternal thyroid function during pregnancy and postpartum. *Saudi Medical Journal*. 2002; 23(4): 413-422.
45. Glinoe D, De Nayer P, Bourdoux P. et al. Regulation of maternal thyroid during pregnancy. *Journal of Clinical Endocrinology and Metabolism*. 1990; 71(2): 276-287.
46. Sanchez-Vega J, del Rey FE, Farinas-Seijas H, de Escobar GM. Inadequate iodine nutrition of pregnant women from Extremadura (Spain). *European Journal of Endocrinology*. 2008; 159 (4): 439-445.
47. Elahi S, Hussain Z. A longitudinal study of changes in thyroid hormones among pregnant women residing in an iodine deficient urban area. *ISRN Endocrinology*. 2013; 2013.

48. Kahric-Janjicic N, Soldin SJ, Soldin OP, West T, Gu J, Jonklass J. Tandem mass spectrometry improves the accuracy of free T4 measurements during pregnancy. *Thyroid*. 2007; 17: 303-11
49. Soldin OP, Soldin D, Sastoque M. Gestation-specific thyroxine and thyroid stimulating hormone levels in the United States and worldwide. *Therapeutic Drug Monitoring*. 2007; 29(5):553-559.
50. Haddow JE, Knight GJ, Palomaki GE, McClain MR, Pulkkinen AJ. The reference range and within-person variability of the thyroid stimulating hormone during the first and second trimesters of pregnancy. *Journal of Medical Screening*. 2004; 11: 170-174.
51. Gong Y, Hoffman BR. Free thyroxine reference interval in each trimester of pregnancy determined with the Roche Modular E-170 electrochemiluminescent immunoassay. *Clinical Biochemistry*. 2008; 41: 902-906.
52. Lambert-Messerlian G, McClain M, Haddow JE, Palomaki GE, Canick JA, Cleary-Goldman J, et al. First- and second-trimester thyroid hormone reference data in pregnant women: a FaSTER (First- and Second- Trimester Evaluation of Risk for aneuploidy) Research Consortium study. *American Journal of Obstetrics and Gynecology*. 2008; 199: 62.e61-62.e66.
53. Moleti M, Lo Presti VP, Campolo MC, Mattina F, Galletti M, Mandolino M, et al. Iodine prophylaxis using iodized salt and risk of maternal thyroid failure in conditions of mild iodine deficiency. *Journal of Clinical Endocrinology and Metabolism*. 2008; 93: 2616-2621.
54. Raverot V, Bournaud C, Sassolas G, Orgiazzi J, Claustrat F et al. Pregnant French women living in the Lyon area are iodine deficient and have elevated serum Thyroglobulin concentrations. *Thyroid*. 2012; 22: 522-528.
55. Bocos-Terraz JP, Izquierdo-alvarez-Lahuerta R, Aznar-Sauca A, Real-Lopez E, Ibanez-Marco R, Bocanegra-Garcia V, et al. Thyroid hormones according to gestational age in pregnant Spanish women. *Biomedical Central Resource Notes*. 2009; 2: 237
56. Danborno AM, Fabusuyi OM and Ogbe SE. Effect of BMI, Pulse Rate and Age on Hypertension in Pregnant Women Attending Ante Natal Clinic in LAUTECH Teaching Hospital, Osogbo, Nigeria. *LASU Journal of Medical Sciences*. 2019; 4(2): 44-48
57. Danborno AM, Adelaiye AB, Olorunshola KV and Danborno B. Serum Thiamine Level in Pregnant and Non-Pregnant Women in Zaria, Nigeria. *The Internet Journal of Nutrition and Wellness*. 2008; 6:1.
58. Glew RH, Chuang LT, Berry T, Okolie H, Crossey MJ, Vanderjagt. Lipid profiles and trans fatty acids in serum phospholipids of semi nomadic Fulani in Northern Nigeria. 2010; 28(2): 159-166.
59. Jacobellis G, Ribaudo MC, Zappaterreno A, Iannucci CV, Leonetti F. Relationship of thyroid function with body mass index, leptin, insulin sensitivity and adiponectin in euthyroid obese women. *Clinical Endocrinology*. 2005; 62(4): 487-491.
60. Milionis A, Milionis C. Correlation between body mass index and thyroid function in euthyroid individuals in Greece. *International Scholarly Research Notices Biomarkers*. 2013 (2013):
61. Dvorkova M, Hill M, Cerovska J, Pobisova Z, Bilek R, Hoskovcova P, et al. Relationship between pituitary-thyroid axis hormones and some anthropometric parameters in Czech adult

- population. *Physiology Research*. 2008; 57(1): S127-S1234.
62. Ren R, Jiang X, Zhang X, Guan Q, Yu C, Li Y, et al. Association between thyroid hormones and body fat in euthyroid subjects. *Clinical Endocrinology*. 2014; 80(4): 585-59
63. Sajid MI, Mehboob R, Ahmed S, Jamshaid M, Majeed I, Siddiqui FA, et al. Association of serum thyroid hormones and serum leptin with body mass index. *International Journal of Current Biotechnology*. 2013; 1(8); 4-8.
64. Solanki A, Bansal S, Jindal S, Saxena V, Shukla, US. Relationship of serum thyroid stimulating hormone with body mass index in healthy adults. *Indian Journal of Endocrinology and Metabolism*. 2013; 17(1): S167S169.