Pattern and Prevalence of Thyroid Dysfunction in Nigerian Pregnant Females

Alfred Azenabor¹*, Joseph Paulinus Omumene² and Ayodele Oloruntoba Ekun¹

¹Department of Medical Laboratory Science, University of Lagos, Nigeria.  
²SMLS, Lagos University Teaching Hospital, Lagos, Nigeria.

Authors’ contributions

This work was carried out in collaboration between all authors. Author AA designed the study, wrote the protocol and wrote the first and final draft of the manuscript. Author JPO managed the literature searches and analyses of the biochemical analysis. Author AOE contributed to the final draft of the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2016/23754

Introduction: Thyroid associated endocrinopathies are the second most common endocrine disorders, after diabetes mellitus in women and are more prevalent in women during their reproductive ages. Diagnosing thyroid disease in pregnancy can be difficult as the clinical signs and symptoms mimic those of pregnancy. This study was done to document the pattern and prevalence of thyroid dysfunction in Nigerian pregnant women.

Materials and Methods: This was a cross sectional analytical study carried out on 264 Nigerian pregnant females and 75 aged matched healthy controls. Thyroid hormones, blood glucose, urinalysis and blood pressure were determined. Pregnant females were categorized into normal pregnancy, gestational hypertensive and gestational trimesters.

Results: The mean age (SD) of participants with normal pregnancy was 29.82 (4.39 years). This was comparable with those with gestational hypertensive 31.78 (4.46 years) (p = 0.062). The mean ± SD of plasma levels of free T4 (0.37±0.16 ng/dl) in participants with normal pregnancy was

ABSTRACT

Introduction: Thyroid associated endocrinopathies are the second most common endocrine disorders, after diabetes mellitus in women and are more prevalent in women during their reproductive ages. Diagnosing thyroid disease in pregnancy can be difficult as the clinical signs and symptoms mimic those of pregnancy. This study was done to document the pattern and prevalence of thyroid dysfunction in Nigerian pregnant women.

Materials and Methods: This was a cross sectional analytical study carried out on 264 Nigerian pregnant females and 75 aged matched healthy controls. Thyroid hormones, blood glucose, urinalysis and blood pressure were determined. Pregnant females were categorized into normal pregnancy, gestational hypertensive and gestational trimesters.

Results: The mean age (SD) of participants with normal pregnancy was 29.82 (4.39 years). This was comparable with those with gestational hypertensive 31.78 (4.46 years) (p = 0.062). The mean ± SD of plasma levels of free T4 (0.37±0.16 ng/dl) in participants with normal pregnancy was

*Corresponding author: E-mail: alfredaze@yahoo.com;
significantly higher than those with gestational hypertensive (0.28±0.33 ng/dl), (p = 0.034). Intra trimester comparison of the participants with thyroid dysfunction showed subclinical hypothyroidism was present in 11.11%, 3.85% and 20.35% in first, second and third trimester respectively. **Conclusion:** Subclinical hypothyroidism is the most commonly documented of the thyroid dysfunctional status in Nigerian pregnant females.

**Keywords:** Thyroid dysfunction; hypothyroidism; hyperthyroidism; normal pregnancy; gestational hypertension and gestational trimesters.

**1. INTRODUCTION**

Thyroid disease is prevalent in women of child bearing age, and thyroid physiology changes significantly during pregnancy [1]. Thyroid associated endocrinopathies are the second most common endocrine disorders, after diabetes mellitus in women [2]. These disorders are 4 – 5 times more prevalent in women during their reproductive ages and may likely be more frequent in those with other co – morbid conditions such as gestational hypertension. During pregnancy, there is a transient fall in Thyroid Stimulating Hormone (TSH) in the first trimester due to the structural homology between the TSH and Human Chorionic Gonadotrophin (HCG) molecules and their receptors, allowing HCG stimulation of the thyroid with an increase in thyroid hormone production [3]. Thyroid hormone concentrations are increased in pregnancy, partly due to the high levels of hyper-estrogenic state of pregnancy and due to the weak thyroid stimulating effects of HCG that acts like TSH. During pregnancy, the thyroid gland may enlarge by about 10% in countries where iodine sources are sufficient, and to a greater extent in iodine poor countries [4]. Several studies in different populations and countries with varying racial, socioeconomic and cultural differences have also shown differences in associations between thyroid function abnormalities and gestational hypertension [5]. In a previous study by Glinoer, production of thyroid hormones and iodine requirement each was reported to increase by approximately 50% during pregnancy. Consequently, pregnant women require additional iodine intake, and may be more prone to thyroid dysfunction.

Thyroid disease was earlier reported by Mannisto to affect 5% of all pregnancies [6]. Diagnosing thyroid disease in pregnancy can be difficult as the clinical signs and symptoms mimic those of pregnancy. Hypothyroidism is associated with weight gain, fatigue and constipation while hyperthyroidism causes nausea, and increased appetite [7,8]. Studies abound on the effect of free T 4 on the parasympathetic and sympathetic nerves through the vagal stimulus and as a result, constipation and diarrhea occurs at the hypo – hyper thyroidism status. [9,10].

This study was done to document the pattern and prevalence of thyroid dysfunction in Nigerian pregnant women. We also set out to evaluate possible associations of thyroid hormones with some biochemical and clinical variables.

**2. MATERIALS AND METHODS**

This was a cross sectional study conducted from April – September, 2015. The study participants included a convenient sampling of two hundred and sixty four (264) pregnant women attending the ante natal clinic of the Obstetrics and Gynaecology Department of Lagos University Teaching Hospital. The control group included seventy five (75) age – matched apparently healthy non pregnant females. Ethical approval was obtained from the Ethics and Research Committee of the Hospital and informed consent was obtained from the participants before the commencement of the study. A well structured questionnaire was used to obtain information concerning the clinical history of the participants. Exclusion criteria for the study included acutely ill participants requiring hospitalization and those who did not consent to participate. Blood pressure (mm/Hg) of all the participants was measured on the left arm using Accuson mercury Sphygmomanometer. An appropriate sized cuff was placed 2.5 cm above the antecubital fossa with participants sitting after resting for at least ten minutes. Subjects with gestational hypertension were also included in the study. Hypothyroidism has an adverse effect on atherosclerotic risk factors such as diastolic hypertension, leading to cardiovascular morbidity. 5.0 ml of venous blood samples were collected from the antecubital fossa of all the subjects into lithium heparin and fluoride oxalate specimen bottles after an overnight fast in a sitting position. Plasma samples were collected
after centrifugation and analyzed. Urine samples were collected and dip stick urinalysis was carried out on all participants.

2.1 Biochemical Analyses

Blood glucose was estimated spectrophotometrically by the glucose oxidase method [11]. The thyroid hormones – free thyroxine (f T4), tri iodothyronine (f T3) and Thyroid Stimulating Hormone (TSH) were analyzed by enzyme linked immunosorbent assay technique (Elisa), using a commercial test kit, Accu bind (USA); the absorbances of which were read by an elisa microplate reader (Stat fax, USA). The intra – assay coefficients of variation for f T3, f T4 and TSH were 4.9%, 10.98% and 8.15% while the inter assay coefficients of variation were 13.1%, 10.81% and 9.3% respectively.

2.2 Diagnostic Criteria

1. Subclinical hypothyroidism was diagnosed when serum TSH concentration was above 2.5µiu/ml and f T4 within reference range [12]
2. Subclinical hypothyroidism: first trimester - TSH above 2.5 µiu/ml and normal f T 4, second and third trimester: TSH above 3.0 µiu/ml and normal fT4
3. Overt hypothyroidism was diagnosed as elevated TSH and reduced fT4 or reduced fT3.
4. Subclinical hyperthyrodism was diagnosed as reduced TSH
5. Overt hyperthyroidism was diagnosed as reduced TSH and elevated fT4 or fT3.
6. Euthyroid was diagnosed as having normal serum TSH and fT3, f T4 [13,14].

2.3 Statistical Analysis

Data were analysed using SPSS version 17. Categorical variables were analysed using chi square tests. Independent t – test was used to compare continuous variables among the groups. The comparison within and between groups were done using one way analysis of variance (ANOVA). Correlations were explored with Pearson correlation coefficient. Logistic regression analysis determination was used to predict outcomes.

3. RESULTS

The mean age (standard deviation) of participants with normal pregnancy was 29.82 (4.39) years. This was comparable with those with gestational hypertensive 31.78 (4.46) years (p = 0.062). The plasma levels (mean ± SEM) of free T4 (0.37±0.16 ng/ml) in participants with normal pregnancy was significantly higher than those with gestational hypertension (0.28±0.33 ng/ml), (p = 0.034). These and other results are shown in Table 1. The number (percentage) of participants with proteinuria in gestational hypertensive, 1 (0.52%) and participants with normal pregnancy, 4 (1.89%), and this difference was statistically significant p = 0.025. The levels (mean ± SEM) of free T 4 was significantly higher in the first trimester of gestation when compared with second and third trimester (f = 4.876, p = 0.009). Intra trimester comparison of the participants with thyroid dysfunction showed subclinical hypothyroidism was present in 11.11%, 3.85% and 20.35% in first, second and third trimester respectively Fig. 1.

![Fig. 1. Intra trimester comparison of the prevalence of thyroid dysfunction in the study subjects](image-url)
Table 1. Concentrations of clinical and biochemical variables in subjects with normal
pregnancy and gestational hypertensives

| Variables                        | Normal pregnancy | Gestational hypertensives | p values |
|----------------------------------|------------------|---------------------------|----------|
| Free T3 (pg/ml)                  | 2.27±0.05        | 2.52±0.14                 | 0.035*   |
| Free T4 (ng/dl)                  | 0.37±0.02        | 0.28±0.17                 | 0.020*   |
| TSH (µIU/ml)                     | 2.11±1.11        | 1.84±0.66                 | 0.249    |
| Blood Glucose (mmol/l)           | 3.91±0.09        | 4.02±0.31                 | 0.664    |
| Systolic Blood pressure (mm/Hg)  | 113.06±1.06      | 150.50±9.59               | 0.000*   |
| Diastolic Blood pressure (mm/Hg) | 87.60±0.78       | 92.83±4.54                | 0.002*   |

*p values calculated using independent student ‘t’ test.
*significant

Table 2. Within group and between group comparison (analysis of variance) of thyroid
hormones in different trimesters of gestation

| Thyroid hormones | First trimester | Second trimester | Third trimester | p values |
|------------------|-----------------|------------------|-----------------|----------|
|                  | n = 54          | n = 102          | n = 108         |          |
| f T3 (pg/ml)     | 2.47±0.10       | 2.25±0.06        | 2.30±0.09       | 0.232    |
| f T4 (ng/dl)     | 0.40±0.04       | 0.37±0.02        | 0.30±0.02       | 0.009*   |
| TSH (µIU/ml)     | 1.81±0.09       | 1.93±0.09        | 2.31±0.20       | 0.066    |

*p values calculated using one way analysis of variance
*significant

Table 3. Post Hoc analysis of free T4 in the three trimesters of gestation
(Multiple comparison)

| Intra - Trimester comparison | Standard error | Significant |
|------------------------------|----------------|-------------|
| First trimester Vs Second trimester | 0.037          | 407         |
| Third trimester              | 0.037          | 0.006*      |
| Second trimester Vs First trimester | 0.037          | 407         |
| Third trimester              | 0.030          | 0.018*      |
| Third trimester Vs First trimester | 0.037          | 0.006*      |
| Second trimester              | 0.030          | 0.018*      |

*p values calculated using independent student ‘t’ test

Table 4. Prevalence of thyroid dysfunction in subjects with normal pregnancy and gestational
hypertensive

| Thyroid function status      | Normal pregnancy | Gestational hypertensive | P values |
|------------------------------|------------------|--------------------------|----------|
|                             | n = 212          | n = 52                   |          |
| Overt hypothyroidism        | 22(10.38)        | 2(3.85)                  | 0.905    |
| Sub clinical Hypothyroidism | 14(6.60)         | 8(15.38)                 | 0.7165   |
| Sub clinical hyperthyroidism| 0(0.0)           | 2(4.19)                  |          |
| Overt hyperthyroidism       | 0(0.0)           | 0(0.0)                   |          |
| Euthyroid                   | 178(83.96)       | 36(69.23)                | 0.1723   |

*p values calculated using Chi square

4. DISCUSSION

We report a high prevalence of thyroid dysfunction occurring mostly in the form of
hypothyroidism, where subclinical and overt hypothyroidism occurring mostly in the first
trimester had a prevalence of 11.1%. This is fairly high coming from Africa, when compared
with that reported elsewhere; though our result on the prevalence rate of subclinical
hypothyroidism is similar to that reported in North India. Hypothyroidism is reported to be common
in pregnancy with an estimated prevalence of 2-3% and 0.3 – 0.5% for subclinical and overt hypothyroidism in the Western world [15], 4.8% - 11% in India [16,17]. However the sharp difference in prevalence rate noted in different studies may be explained by the variability in the rates of subclinical hypothyroidism in different parts of the world, being lower in iodine-deficient areas and higher in areas of abundant iodine intake as well as the cut – off values used for TSH. This has often been reported to complicate 3% of pregnancies, of which 0.3 – 0.5% is overt and 2.0 – 2.5% is subclinical [18,13].

Our study may also be directly comparable to that of Dhanwal et al. [19] as a result of the similarity of subclinical hypothyroidism noticed in the first trimester. This corroborates the recommendation by the American Association of Clinical Endocrinologist in a report by Gharib et al. [20] on the importance of screening of all women in the first trimester of gestation. Probable causes of SCH are many and chronic autoimmune thyroiditis is said to be the most common cause. A report by Negro et al. [21] has shown that therapy in pregnant women with autoimmune thyroid disease, improves outcome and reduces the rate of miscarriage and pre term labour. This finding provides evidence for the importance of identification and treatment of thyroid dysfunction in pregnancy. It is instructive to note that autoimmune thyroiditis; a common cause of SCH increases with age [22]. This may aptly explain the inverse association of free T3 and T4 observed with age in our study.

Our data also showed a significant increase in free T4 in the first trimester compared with other trimesters, while TSH concentration showed a graded increase from the first trimester. Measuring free T4 concentration is seemingly more useful in pregnant women when trying to distinguish between overt and subclinical thyroid disease. It is pertinent to note that a cut off value of 0.80 ng/dl (2.5th percentile) of free T4 was observed in subjects without SCH in the first trimester in this study. This is similar to that reported elsewhere [23]. A fall in TSH during the first trimester is in tandem with an earlier report by Glinoer et al. [24] in which subnormal serum TSH values were observed in approximately 20% of normal pregnancies. In their study, the reduction in TSH during the first trimester of pregnancy was associated with a modest increase in free T4, which may lead to a spectrum of thyrotoxicosis symptoms (pregnancy hyperthyroidism).

We observed no significant differences in the occurrence of thyroid dysfunction when participants with normal pregnancy were compared with gestational hypertensive, although a significant increase in plasma levels of free T3 in gestational hypertensives was noted. This contradicts an earlier report from Vargas et al. in which the levels of free T4 was lower in pre- eclampsia. The interventions on our cohorts of participants as at the time of study may partly be responsible for the consequential effect of free T3. This is evident from the marked reduction in the prevalence of proteinuria observed. However, it is instructive to note that lower levels of free T4 reported elsewhere was associated with decreased plasma albumin concentration in preeclamptic women [25], due to the loss of protein and protein-bound hormones in the urine [26].

Logistic regression analysis was carried out to evaluate the possibility of using thyroid hormones in the prediction of thyroid dysfunction in gestational hypertensives. The independent variables entered into the model included free T3, free T4 and TSH, while various thyroid dysfunctions served as the dependent variables. It was observed that the thyroid hormones were possible predictors of SCH only, when compared with other thyroid dysfunction occurring in gestational hypertensives. Thyroid hormones are regulators of the mitochondria activity, it can be hypothesized that all the complications in SCH may be due to mitochondria dysfunction.

We have also shown in this report that an inverse association of both free T3 and free T4 with the participant’s history of gravidity and parity. This confirms the well expounded view of thyroid dysfunction as one of the possible causes of pre – term delivery (PTD). It is interesting to note that prior interventions aimed at decreasing the incidence of PTD have met with limited success. Over the last two decades, there have been major advances in understanding the deleterious impact that thyroid disease has on pregnancy outcome.
Table 5. Logistic regression analysis of thyroid hormones in the prediction of gestational hypertensive

| Variables | Overt hypothyroidism | Subclinical hypothyroidism | Subclinical hyperthyroidism | Euthyroid |
|-----------|----------------------|---------------------------|-----------------------------|-----------|
|           | O.R. | C.I. | P | O.R. | C.I. | P | O.R. | C.I. | P | O.R. | C.I. | P |
| fT3       | Ref  | 0.493 | 0.889 | 0.181 | -4.357 | 0.885 | 2.794, | 0.740 | -0.552 | 0.013* | 7.898E, | 0.00 | -0.00, | 0.999 |
| fT4       | Ref  | 0.485 | 0.899 | 0.183 | -4.406 | 0.896 | 2.825, | 0.748 | -10.670 | 0.013* | 7.988E9 | 0.00-0.00 | 0.999 |
| TSH       | Ref  | 0.463 | 0.930 | 0.189 | -4.580 | 0.929 | 2.924, | 0.770 | -11.100 | 0.012* | 8.267E9 | 0.00-0.00 | 0.999 |

*p values calculated using regression analysis
*significant;
O.R – Odds ratio; C.I. 95% Confidence Interval; P – Probability; Ref - reference

Table 6. Pearson correlation coefficient of thyroid hormones with clinical and biochemical parameters in the study subjects

| Thyroid hormones | Gravidity r (p) | Parity r (p) | Age r (p) | SBP r (p) | DBP r (p) | Blood glucose r (p) |
|-----------------|-----------------|--------------|-----------|-----------|-----------|---------------------|
| fT3             | -0.436(0.000)*  | -0.3100(0.000)* | -0.259(0.001)* | 0.105(0.233) | 0.064(0.466) | -0.064(0.448)     |
| fT4             | -0.343(0.000)*  | -0.295(0.001)* | -0.233(0.003)* | 0.022(0.798) | -0.078(0.372) | 0.275(0.001)*     |
| TSH             | 0.143(0.105)    | 0.090(0.308)  | 0.051(0.533) | -0.036(0.688) | 0.013(0.881) | -0.191(0.018)*   |

*p values calculated using Pearson correlation coefficient analysis
*significant
SBP – Systolic blood pressure DBP – Diastolic blood pressure
5. CONCLUSION

Although thyroid dysfunction may not be common in pregnant Nigerian females, its prevalence is comparable with gestational hypertensive. Sub clinical hypothyroidism is the most commonly documented of the thyroid dysfunctional status in Nigerian pregnant females. Thyroid function tests should ensure that free T4 does not exceed 0.8 ng/dl in the first trimester in addition to increased TSH.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. Endocr Rev. 2010;31:702–705.
2. Glinoer D. The regulation of thyroid function in pregnancy: Pathways of endocrine adaptation from physiology to pathology. Endocr Rev. 1997;18:404–433.
3. Mohanty R, Patnaik S, Ramani B. Subclinical hypothyroidism during pregnancy: A clinical review. 2007;25(5):449–454.
4. Van Raaji JM, Vermaat – Miedema SH, Schonk CM, Peek ME, Haustvast JG. Energy requirements of pregnancy in the Netherlands. Lancet. 1987;2(8565):953–5.
5. Abdulsalam K, Yahaya IA. Prevalence of thyroid dysfunction in gestational hypertensive Nigerians. Sub – Saharan Afr J Med. 2015;2:19–27.
6. Mannisto T, Vaaramaki M, Pouta A, Hartikainen AL, Roukonen A, Surcel HM. Perinatal outcome of children born to mothers with thyroid dysfunction or antibodies: A prospective population – Based cohort study. J Clin Endocrinol Metab. 2009;94(3):772–9.
7. Bahn RS, Burch HB, Cooper DS. Hyperthyroidism and other causes of thyroxicosis management guidelines of the American thyroid association and American association of clinical endocrinologists. Endocr Pract. 2011; 17(3):456–520.
8. Garber JR, Cobin RH, Gharib H. Clinical practice guidelines for hypothyroidism in adults co sponsored by the American association of clinical endocrinologists and the American thyroid association. Thyroid. 2012;22(12):1200–1235.
9. Arda Isik, Deniz Firat, Kemal Peker, Ilyar Sayar, Oguz Idiz, Nehmet Sayturk. A case report of esophageal perforation: Complication of nasogastric tube placement. Am J Case Rep. 2014;15:168–71.
10. Isik A, Alimoglu, okan I, Bas G, Turguf H. Dieulafoy lesions in the stomach. Case Rep Gastroenterol. 2008;2(3):469–73.
11. Barham D, Trinder P. An improved colour change for the determination of blood glucose by the oxidase system. Analyst. 1972;142:130.
12. Kratzsch J, Fiedler GM, Leichtle A. New reference intervals for thyrotrophin and thyroid hormones based on National Academy of clinical biochemistry criteria and regular ultrasonography of the thyroid. Clin Chem. 2005;51:1480–1486.
13. De Grooth JJ, Abalovich M, Alexander EK. Management of thyroid dysfunction during pregnancy and postpartum: An endocrine society clinical practise. J Clin. Endocrinol. 2009;97(8):2543–2565.
14. Casey BM, Levono KJ. Thyroid disease in pregnancy. Obstet Gynaecol. 2006;108:1283–92.
15. Klein RZ, Haddow JE, Faix JD, Brown RS, Hermons RJ, Pulkkinen A. Prevalence of thyroid deficiency in pregnant women. Clin Endocrinol. 1991;35(1):46–6.
16. Nambiar V, Jagtap VS, Sarathi V, Lila AR, Kamalanathan S, Bandgar TR. Prevalence and impact of thyroid disorders maternal outcome in Asian – Indian pregnant women. J Thyroid Res. 2011;429097.
17. Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. Arch Gynaecol Obstet. 2010; 281(2):215–20.
18. Stagnaro – Green A, Abalovich M, Alexander E. Guidelines of the American thyroid association for the diagnosis and management of the thyroid disease during pregnancy and postpartum. Thyroid. 2011;21(10):1081–1125.
19. Dhanwal DK, Prasad S, Agarwal AK, Dixit V, Banerjee AK. High prevalence of subclinical hypothyroidism during first
trimester of pregnancy in North India. Indian J Endocrinol Metab. 2013;17(2):281–4.

20. Gharib H, Cobin RH, Dickey RA. Subclinical hypothyroidism during pregnancy: Position statement from the American Association of Clinical Endocrinologists. Endocr Pract. 1999;5(6):367–8.

21. Negro R, Formoso G, Mangieri T, Pezzarossa A, Sazzi D, Hassan H. Levothyroxine treatment in euthyroid pregnant women with autoimmune thyroid disease: Effects on obstetrical complications. J Clin Endocrinol Metab. 2006;91:2587–91.

22. Fatourechi V. Subclinical hypothyroidism: An update for primary care physicians. Mayo Clin Proc. 2009;84(1):65–71.

23. Soldin OP, Soldin D, Sastoque M. Gestational specific thyroxine and thyroid stimulating hormone levels in the United States and worldwide. The Drug Monit. 2007;29:553–559.

24. Ginoir D, De NP, Bourdoux P. Regulation of maternal thyroid during pregnancy. J Clin Endocrinol Metab. 1999;71(2):276–287.

25. Goldenberg RL, Culhane JF, Iams JD, Romero R. Preterm birth 1: Epidemiology and causes of preterm birth. Lancet. 2008;371:75–84.

26. Meis PJ, Klebanoff M, Thom E, Dombrowski MP, Sibai B, Moawad AH, Spong CY, Hauth JC, Miodovnik M, Varner MW, Leveno KJ, Caritis SN, Iams JD, Wapner RJ, Conway D, O'Sullivan MJ, Carpenter M, Mercer B, Ramin SM, Thorp JM, Peaceman AM. Prevention of recurrent preterm delivery by 17α-hydroxyprogesterone caproate. N Engl J Med. 2003;348:2379–2385.

© 2016 Azenaor et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/13206