Thyroid Autoimmunity in Pregnancy in a North-Central City in Nigeria

Terry Terfa Gbaa
The Department of Chemical Pathology, College of Health Science, Benue State University, Makurdi, Nigeria

Simeon Adelani Adebisi
The Department of Chemical Pathology, College of Health Science, Benue State University, Makurdi, Nigeria

Abstract:
Background: Pregnancy often increases the likelihood of adverse maternal and fetal outcomes in cases of thyroid dysfunction. The inherent variation and instability of the thyroid gland can predispose the pregnant woman and fetus to significant negative consequences. Although thyroid autoimmunity may become less common as pregnancy progresses, it remains a prevalent dysfunction during this period. Method: We conducted a hospital-based cross-sectional study involving 250 healthy pregnant women who volunteered to participate. Blood samples were collected from the participants and analysed using the Enzyme-Linked Immunosorbent Assay (ELISA) technique to measure serum levels of Thyroid Stimulating Hormone (TSH) and anti-TPO antibodies. Statistical analysis was performed using SPSS. Result: Among the participants, 31 (12.4%) were found to have thyroid dysfunction, with 12 (4.8%) exhibiting signs of thyroid autoimmunity. Specifically, 8 (3.2%) were diagnosed with hypothyroidism, while 4 (1.6%) showed hyperthyroidism. Conclusion: This study identified a prevalence of 4.8% for thyroid autoimmunity during pregnancy using the anti-TPO antibody assay. Furthermore, we determined that measuring thyroid stimulating hormone levels was a reliable indicator for detecting thyroid dysfunction during pregnancy.

Keywords: TSH, anti-TPO, Autoimmunity, Pregnancy.

Introduction
Thyroid dysfunction is common in pregnant women and is associated with an increased risk of adverse outcomes for both the mother and the fetus. Pregnancy significantly influences the thyroid gland and its functioning (Alexander et al., 2017). However, when pregnancy coincides with endocrine disorders, the potential for adverse maternal and fetal outcomes becomes substantial.

During pregnancy, there is a temporary decrease in Thyroid thyroid-stimulating hormone (TSH) levels during the first trimester. This is due to the structural similarity between TSH and Human Chorionic Gonadotropin (hCG) molecules and their respective receptors. The resemblance allows hCG to stimulate the thyroid gland, increasing thyroid hormone production.

Pregnancy is characterised by a suppressed immune system, which improves autoimmune diseases as pregnancy progresses. However, the presence of Thyroid Peroxidase (TPO) antibodies in pregnant women can lead to recurrent miscarriages (Xie et al., 2020). The prevalence of thyroid autoimmunity during

This work is licensed under a Creative Commons Attribution 4.0 International License. The license permits unrestricted use, distribution, and reproduction in any medium, on the condition that users give exact credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if they made any changes.
pregnancy in Nigeria has not been extensively studied. However, a group study showed a prevalence of hypothyroidism among pregnant women in Nigeria to be at 3.0%, with subclinical hypothyroidism which occurred in 2.7% and overt hypothyroidism in 0.3%, while 2.3% were hyperthyroid, anti-TPO antibodies were observed in 9.0% of the pregnant population (Kayode et al., 215).

Thyroid autoimmunity is thought to be less prevalent in the African population, and the presence of thyroid antibodies may be overlooked because most women in Nigeria present to the antenatal clinic after the first trimester. As a result, when these pregnant women present, the window for detecting autoantibodies may close as the pregnancy progresses because immunity gradually declines due to class switching from Th1 (T-helper 1) to Th2 (T-helper 2). Furthermore, pregnancy improves autoimmune disease due to the suppression of B-cell function (Iddah, & Macharia, 2013).

Method and Materials

Study Design and Setting

This descriptive cross-sectional study was conducted in multiple hospitals, involving pregnant women as the study population. Data were collected and analysed over approximately nine months, from June 2019 to February 2020. The recruitment of participants, collection of serum samples for thyroid function tests and urine iodine analysis, laboratory assessments, and evaluation of thyroid dysfunction in pregnancy were all carried out within this 9-month timeframe.

The study was conducted in Makurdi, a city in the North Central region of Nigeria. Participants were recruited from various healthcare facilities, including Benue State University Teaching Hospital (B.S.U.T.H), Federal Medical Center (F.M.C) Makurdi, Family Support Programme Clinic Makurdi, First Fertility Hospital Makurdi, and Foundation Hospital Makurdi. Data analysis and sample testing took place in the laboratory of the Chemical Pathology Department at B.S.U.T.H, Makurdi.

Study Population

The target population for this study consisted of pregnant women in Makurdi who were attending their routine antenatal clinic visits. The participants were selected using a simple random sampling technique based on a table of random numbers. They were provided with detailed information about the study objectives, and their written consent was obtained before administering the questionnaires.

The participants were categorised into three trimesters of pregnancy. Those included in the study had no history of thyroid dysfunction. In contrast, individuals with known thyroid dysfunction, acute or chronic illnesses, and those on specific medications such as lithium, amiodarone, antiseizure drugs, interferon-gamma, hormone replacement therapy (HRT) containing estrogen, and rifampicin were excluded. Finally, biofluid samples were collected from each participant for further analysis.

Ethical Consideration

Written consents for inclusion in the study were obtained after the study was explained to the participants, the procedures involved were presented, and written permissions were obtained from the heads of the Department of Obstetrics/Gynaecology, Chemical Pathology of B.S.U.T.H, and the Chief Medical Directors of B.S.U.T.H Makurdi, Federal Medical Centre, and First Fertility Hospital Makurdi. The Health Research Ethics Committee at each participating institute provided ethical approval for the study.

Sample Collection and Analysis

Nonfasting samples were collected, including venous blood and spot urine. Aseptic techniques were employed to collect 5 ml of blood using a syringe and needle, which was transferred into a plain vacutainer tube. A spot urine sample was collected in a wide-mouthed sterile urine bottle. The samples were separated using a tabletop centrifuge (StatSpin Express) at 3000 rpm for 10 minutes. The resulting serum samples were
carefully pipetted and stored in cryovials at -20°C.

The batched serum samples were analysed using the ultrasensitive enzyme-linked immunosorbent assay (ELISA) technique. The ELISA kits (AccuBind® ELISA kits, California, USA) from Monobind Inc. were utilised for the thyroid function test panel analysis. An automated machine equipped with a microstrip reader (STAT-FAX 303, USA) was employed for this analysis.

Statistical Analysis
Data analysis was conducted using Statistical Package for the Social Sciences (SPSS) version 21 (IBM, Chicago, IL, USA). Normally distributed data were presented as mean ± standard deviation (SD), while non-normally distributed data were expressed as the median.

Statistical comparisons were performed using the Mann-Whitney U-test and Kruskal-Wallis tests for non-Gaussian distributed data. In the case of Gaussian distributed data, comparisons were made using the unpaired Student’s t-test and one-way analysis of variance (ANOVA). Correlations were determined using Pearson’s correlations. A significance level of P < 0.05 was considered statistically significant.

A test for normality was conducted to determine the distribution pattern of the dataset, whether Gaussian or non-Gaussian. Based on the distribution, the appropriate statistical tool was applied. Gestational age exhibited Gaussian distribution. Thus, one-way ANOVA and unpaired Student’s t-test were used. On the other hand, TSH displayed a non-Gaussian distribution, leading to the utilisation of the Mann-Whitney U-test.

Results
Study Participants
The study included two hundred fifty pregnant women selected using a simple random sampling technique. Subsequently, the participants underwent blood and urine sample collection for analysis.

Population Distribution Pattern
The analysis included two hundred fifty participants and was categorised into three groups based on their trimesters. Group I comprised 51 participants, Group II formed 114 participants, and Group III included 85 participants, corresponding to the first, second, and third trimesters. Using the TSH assay, 31 participants were identified as having thyroid dysfunction, with a higher percentage of participants being hypothyroid (10% or 25 participants) compared to hyperthyroid (12.4% or 6 participants). Among the pregnant women, 12 (4.8%) were found to have thyroid autoimmunity, with 8 (3.2%) being hypothyroid and 4 (1.6%) euthyroid.

Table 1. TSH Values in each trimester

<table>
<thead>
<tr>
<th>Trimester</th>
<th>n</th>
<th>TSH (mIU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First trimester</td>
<td>51</td>
<td>2.76( ^{a} )</td>
</tr>
<tr>
<td>Second trimester</td>
<td>114</td>
<td>1.53( ^{b} )</td>
</tr>
<tr>
<td>Third trimester</td>
<td>85</td>
<td>3.50</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td>0.0001( ^{*} ) ( ^{a} )</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0001( ^{*} ) ( ^{b} )</td>
</tr>
</tbody>
</table>

Note: n = number of participants, TSH- thyroid stimulating hormone, \( ^{a} \) = statistically significant difference between first and second trimesters, \( ^{b} \) = statistically significant difference between second and third trimesters, \( ^{c} \) = statistically significant difference between first and third trimesters, \( ^{*} \) significant at the p<0.05 level ; ** very significant at the p<0.01 level

There was a significant decrease in the TSH values, as illustrated in Table 1, from the first trimester to the second trimester (P≤0.001). Still, there was an increase to 3.50 mIU/l in the third trimester.
trimester, falling within the average TSH diagnostic values.

Table 2. Chronological age of pregnant participants

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-25</td>
<td>96(38.4)</td>
</tr>
<tr>
<td>26-35</td>
<td>96(38.4)</td>
</tr>
<tr>
<td>31-35</td>
<td>43(17.2)</td>
</tr>
<tr>
<td>36-40</td>
<td>13(5.2)</td>
</tr>
<tr>
<td>41-45</td>
<td>2(0.8)</td>
</tr>
<tr>
<td>Total</td>
<td>250(100)</td>
</tr>
</tbody>
</table>

Table 2. illustrates the chronological age of the participants; the age group 17-25 and 26-30 showed the highest number of included study participants, with 96(38.4%), while the age group 41-45 included only 2(0.8) participants.

The age group with the highest positive thyroid antibodies is 31-35 years, and the none seen at the ages between 36-45 years, as shown in Table 3.

Table 3. Thyroid Autoimmunity in pregnancy and age group

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-25</td>
<td>2(33.3)</td>
</tr>
<tr>
<td>26-30</td>
<td>1(16.7)</td>
</tr>
<tr>
<td>31-35</td>
<td>3(50)</td>
</tr>
<tr>
<td>36-40</td>
<td>0(0)</td>
</tr>
<tr>
<td>41-45</td>
<td>0(0)</td>
</tr>
<tr>
<td>Total</td>
<td>6(100)</td>
</tr>
</tbody>
</table>

The comparative analysis of thyroid autoimmunity was analyzed with the highest number of positive hypothyroid participants, while there was no positive autoimmunity in the hyperthyroid group. However, some euthyroid participants presented with thyroid autoimmunity, as seen in Table 4.

Table 4. Comparative Analysis of Thyroid Autoimmunity in Pregnant Women

| TPO Positive | Hypothyroid | Euthyroid | Hyperthyroid | Total (%)
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TPO Positive</td>
<td>8(66.7)</td>
<td>4(33.3)</td>
<td>0(0)</td>
<td>12(100)</td>
</tr>
<tr>
<td>TPO Negative</td>
<td>17(7.1)</td>
<td>215(90.3)</td>
<td>6(2.5)</td>
<td>238(100)</td>
</tr>
</tbody>
</table>

Discussion

Thyroid dysfunction in pregnancy often goes without being screened at antenatal clinics despite being the second most common endocrinopathy following diabetes mellitus. In this study, we aimed to assess the occurrence of thyroid dysfunction and its association with thyroid autoimmunity in pregnant women.

This study found that the anti-TPO assay correctly identified the proportion of pregnant women with autoimmune thyroid disease (AITD). This is important because autoimmunity is one of the leading causes of thyroid dysfunction even after delivery due to the rebound effect of suppressed immunity during pregnancy (Muller, Drexhage, & Berghout, 2001). Compared to other studies, the presence of TPO-ab was not as high, with a prevalence of thyroid autoimmunity of 2.4% (n=6). This contrasts with a case-control study conducted in Jos, Nigeria, where TPO-ab was found in 11.4% of cases and 4.5% of controls (Samson et al., 2018). El-Bashir et al. (2015) found anti-TPO in 9% of the population (El-Bashir et al., 2015), and another cross-sectional study found thyroid autoimmunity in 4.0% (n=61) of 1519 pregnant Tunisian women (Feki et al., 2008). The African population has been shown to have lower thyroid autoimmunity than other racial groups (Soldin, Soldin, & Sastoque, 2007; La’ulu, & Roberts, 2007), indicating a lower prevalence in each preceding group. This is in comparison to a study done in Qatar on 7978 women, with a total of 33.33% having thyroid antibodies, a 15-fold increase (Athar et al., 2022). The risk of thyroid autoimmunity in this study was seen in more hypothyroid participants, who could present with postpartum thyroiditis weeks after a normalised TSH.
Thyroid autoimmunity in pregnancy is relatively uncommon, as the pregnant woman's immune system becomes suppressed as pregnancy progresses, primarily due to the diminishing effects of T-cell and B-cell activity. However, autoimmunity, such as autoimmune thyroiditis, may increase with age, a common cause of subclinical hypothyroidism. Our study utilised the anti-TPO assay to identify the proportion of pregnant women with autoimmune diseases, as autoimmunity significantly contributes to thyroid dysfunction. The prevalence of thyroid autoimmunity was 2.3% (n=12) among the participants.

Usually, about 20% of pregnant women have thyroid autoimmunity in the first trimester (Balucan, Morshed, & Davies, 2013), but no such cases were found in this study. Autoimmunity was found in both the hypothyroid and euthyroid populations but not in the hyperthyroid population. This was puzzling because antibodies are found in Graves' disease, the most common autoimmune disease that manifests as hyperthyroidism.

Autoimmunity was observed in hypothyroid and euthyroid participants, but none was detected in the hyperthyroid group. This finding aligns with a cross-sectional study conducted on 1,519 pregnant Tunisian women, which reported a prevalence of thyroid autoimmunity of 4.0% (n=61). Among the 12 participants identified with thyroid autoimmunity in our study, there were more cases of hypothyroidism (66.7%) than euthyroidism (33.3%).

The prevalence of thyroid autoimmunity in this study is almost like that of the African Americans in a survey by La’ulu and Roberts (2007), where they reported TPO antibody prevalence rates of 4.1, 12.4, 11.8,12.3 and 10.4% among second trimester pregnant Blacks, Asians, Hispanics, Whites and all the groups combined respectively. Okosie, Taylor, Ohwovoriele, Parkes, and Lazarus (2006) reported a TPO prevalence rate of 7.0% among the general population in Nigeria while the prevalence among pregnant women in Tunisia was 4.0%, as reported by Moncef et al in 2008, from my study, no hyperthyroid participant was observed to have TPOab.

Interestingly, the prevalence of thyroid autoimmunity was lower in the black population than in other racial groups, consistent with previous studies. None of the hyperthyroid pregnant participants in our study exhibited any form of thyroid autoimmunity. However, one study found that anti-TPO antibodies increased the risk of intrauterine foetal death in pregnant women (Kiran, Sheikh, & Islam, 2021). Furthermore, recurrent abortions were more common in women with thyroid autoimmunity than in pregnant controls (Lata et al., 2013). Whenever a pregnant woman tests positive for TPO antibodies, treatment is critical. Levothyroxine is beneficial, especially in hypothyroid patients with AITD. Evidence suggests that levothyroxine is essential in maintaining euthyroid status and lowering antibody titer (Negro et al., 2006).

In conclusion, our comparative analysis highlights the prevalence of thyroid autoimmunity in pregnant women. Despite being less common, thyroid autoimmunity can still occur in hypothyroid and euthyroid individuals. The lower prevalence in the black population and the absence of thyroid autoimmunity in hyperthyroid participants warrant further investigation. The low prevalence of thyroid autoimmunity in this study would result in better outcomes for the mother and foetus because the presence of thyroid antibodies increases the risk of miscarriage and foetal loss.

**Conclusion**

The prevalence of thyroid autoimmunity in pregnancy was 2.4%, and anti-TPO antibodies and thyroid-stimulating hormone assays were reliable indicators of thyroid dysfunction in pregnancy. The majority of AITD participants in this study were hypothyroid. Furthermore, early detection of thyroid antibodies lowers the risk of adverse maternal and foetal outcomes, and Levothyroxine is an effective treatment for established AITD.
Author Contributions
TT GBAA and SA ADEBISI contributed equally to this study. They participated in the study design, data collection, analysis, and manuscript preparation. TT GBAA was responsible for the study design, participant recruitment, sample collection, and laboratory analysis. SA ADEBISI conducted the statistical analysis interpretation of results and drafted the manuscript. Both authors reviewed and approved the final version of the manuscript.

Acknowledgements
The authors thank all the pregnant women who participated in this study. We also acknowledge the staff of the Benue State University Teaching Hospital and other healthcare facilities for their support in participant recruitment and sample collection.

Funding
This study received no specific funding from any agency or institution.

Conflict of Interest
The authors declare no conflicts of interest that could have influenced the results or interpretation of this study.

References


