Original Article

Thyroid autoimmunity in pregnant Nigerians

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ABSTRACT

Context: Thyroid autoimmunity is a recognized disorder in pregnancy and is associated with a number of adverse pregnancy outcomes. **Aim:** This study set out to determine the relationship between pregnancy and thyroid autoimmunity in Nigerian women. **Settings and Design:** This was an analytical cross-sectional study carried out in a tertiary hospital in South Western Nigeria with a total study population of 108 pregnant and 52 nonpregnant women. **Subjects and Methods:** Serum thyroid stimulating hormone, free thyroxine and thyroid peroxidase antibodies (TPO-Ab) were quantitatively determined using enzyme linked immuno-assays. Pregnant women were grouped into three categories (<14 weeks, 14–28 weeks and > 28 weeks). The relationship between pregnancy and thyroid autoimmunity was determined using Spearman correlation. Analysis of variance was used in comparison of means, Chi-square test used in analyzing proportions while $P \leq 0.05$ was considered as significant. **Results:** The mean age of the pregnant women was 30.4 ± 6.0 years while the mean gestational age of all pregnant women was 20.6 ± 9.6 weeks. The mean TPO-Ab of 11.58 IU/ml in the pregnant was significantly higher than that of the controls of 7.23 IU/ml ($P < 0.001$). Out of 108 pregnant women, 27 (25%) had elevated TPO-Ab as against about 2% of the nonpregnant women levels $P < 0.001$. The number of pregnant women with elevated TPO-Ab levels decreased from 33.3% in the first group to 25.6% and 15.2% in the second and third groups. **Conclusion:** Thyroid autoimmunity expressed by the presence of TPO-Ab is high among pregnant Nigerian women and the frequency of autoimmunity appears to decline with advancing gestational age.

Key words: Autoimmunity, pregnancy, thyroid

Introduction

Thyroid disorders are the second most common endocrine disorders found in pregnancy.[1] Imbalances in thyroid homeostasis are expressed as hypothyroidism or hyperthyroidism.[2-4] Autoimmune thyroid disease is a common cause of both hyperthyroidism and hypothyroidism in pregnant women.[5] The presence of antibodies to thyroid peroxidase (TPO-Ab) or thyroglobulin during pregnancy is associated with a significant increment in miscarriages, premature deliveries, gestational diabetes mellitus, postpartum thyroiditis and permanent hypothyroidism.[5-8] Children of pregnant women with normal thyroid function, but increased TPO-Ab are also at risk for impaired psychomotor development.[9]

The prevalence rates of thyroid disorders in 147 Tunisian pregnant women were 6.5%, 3.2%, and 1.3% for positive TPO-Ab, hypothyroidism and hyperthyroidism respectively.[10] The precise prevalence of thyroid autoimmunity in pregnant Nigerian women is not known. In view of the adverse pregnancy outcomes associated with thyroid autoimmunity this study set out to determine

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the prevalence of autoimmune thyroid disorders (AITD) in pregnant Nigerian women and also the relationship between gestational age and thyroid autoimmunity in Nigerian women.

Subjects and Methods

This analytical cross-sectional study was carried out at the Lagos University Teaching Hospital (LUTH), a Tertiary Hospital located in the South Western Region of Nigeria. This hospital is one of the main referral medical institutions in Lagos State. The hospital comprises 13 clinical departments, including: Medicine, Surgery, Paediatrics, Obstetrics and Gynaecology, Radiodiagnosis among others.[11] The Obstetrics and Gynaecology Department of LUTH run clinics in the mornings for pregnant and postpartum women four times in a week. The number of pregnant women attending the prenatal clinics is about 280 every week. Ethical approval was obtained from the Ethics Committee of LUTH.

The study participants were selected from pregnant women who attended the hospital for their antenatal care during the period of study from April to September 2012. The women were selected from a list obtained at each visit from the medical records officer. To be eligible singleton pregnancy must have been confirmed with an obstetric ultrasound scan. The controls were nonpregnant women selected from among the female members of the staff of LUTH with a similar age to the pregnant women in a 1:2 ratio. Pregnancy was excluded if the urine β human chorionic gonadotropin pregnancy test was negative. Women with a personal or family history of thyroid dysfunction or diabetes mellitus were excluded. All participants gave written informed consent.

Using a 95% confidence interval, a margin of error of 5% and a prevalence of autoimmune thyroid disease of 6.5%, a minimum sample size of 94 was obtained.[10]

All participants had their demographic information obtained using the questionnaires administered by trained research assistants. Information obtained from each participant included age at last birthday, marital status, and the highest level of education. Physical examination was carried out. Serum thyroid stimulating hormone (TSH), free thyroxine (fT4), and TPO-Ab were quantitatively determined using enzyme-linked immuno-assays in 108 pregnant and 52 nonpregnant women. Being euthyroid was defined as TSH of 0.17–4.81 μIU/ml and fT4 within 9.5–20.6 pmol/L. Levels of TPO-Ab above 14.4 IU/ml (the 97.5th percentile of the values obtained from the controls) were deemed elevated and indicative of autoimmune thyroid disease.[12] Data analysis was performed using Statistical Package for the Social Science version 17th edition. Analysis of variance was used in comparison of means, Chi-square test used in analyzing proportions, Spearman correlation was used to determine the relationship between TPO-Ab levels with gestational age while $P \leq 0.05$ was considered to be significant.[13]

Results

One hundred and eight pregnant and 52 nonpregnant women were studied [Table 1]. The mean age of the pregnant women of 30.4 ± 6.0 years was similar to that of the nonpregnant women of 30.5 ± 6.2 years ($P = 0.7$). The proportions of study participants in each age category are also shown in Table 1. The mean gestational age of all pregnant women was 20.6 ± 9.6 weeks ranging from 7 to 39 weeks with a median age of 19 weeks. Forty-one (38%) were primigravida, while 67 (62%) were multigravida.

Table 1 shows the proportions of study participants in each age category and in each pregnancy group.

The mean levels of TSH, fT4, and TPO-Ab in both the pregnant and control subjects are shown in Table 2. Thyroid disorders were observed in 32 (29.6%) pregnant women. Elevated TPO-Ab was observed in 27 (25%) women, hypothyroidism in 3 (2.8%) women while subclinical hyperthyroidism was observed in 2 (1.8%) women. Out of the 27 women with elevated TPO-Ab, 25 (92.6%) were euthyroid. One out of the 3 women (33.3%) with

Table 1: Distribution of study participants by chronological and gestational ages

Variables	Participants, *N* (%)	
	Pregnant women	Controls
Age category (years)		
21-25	27 (25)	14 (27)
26-30	26 (24.1)	12 (23)
31-35	25 (23.1)	12 (23)
36-40	30 (27.8)	14 (27)
Total	108 (100)	52 (100)
Gestational age		
1-13 weeks (first group)	36 (33.3)	
14-28 weeks (second group)	39 (36.1)	
>28 weeks (third group)	33 (30.6)	

Table 2: Thyroid function tests in pregnancy and controls

Variable	Mean (SD)		*T*-test statistic	*P*
	Pregnant women	Controls		
TSH (μIU/ml)	1.4 (1.26)	1.1 (1.0)	6.87	0.01
fT4 (pmol/L)	12.9 (3.4)	14.90 (3.0)	2.55	0.01
TPO-Ab (IU/ml)	11.58 (5.08)	7.23 (2.45)	5.85	<0.001

TSH: Thyroid-stimulating hormone, fT4: Free thyroxine, TPO-Ab: Thyroid peroxidase antibody, SD: Standard deviation

hypothyroidism had elevated TPO-Ab while one out of the 2 women (50%) with hyperthyroidism had elevated TPO-Ab.

The mean TPO-Ab levels in the three groups were 12.11 ± 5.49 IU/ml, 12.21 ± 5.37 IU/ml and 10.25 ± 4.06 IU/ml in the first, second, and third groups respectively.

The prevalence of autoimmune thyroid dysfunction in pregnancy was 25% while it was 1.9% in the nonpregnant women $P < 0.001$. Out of the 36 pregnant women who had TPO-Ab testing conducted in the first group, 12 (33.3%) had elevated TPO-Ab levels. Out of these 12 women, 10 of them were euthyroid. Ten (25.6%) of the 39 pregnant women in the second group had elevated TPO-Ab levels while 5 (15.2%) out of the 33 pregnant women in the third group had elevated TPO-Ab levels $P = 0.21$ [Figure 1]. Correlation analysis performed showed there was an insignificant negative correlation between TPO-Ab levels and gestational age (Spearman's correlation coefficient $r = -0.16$; $P = 0.09$). With increasing gestational age, TPO-Ab levels decline.

Discussion

In this study, the most common form of thyroid disorder was elevated levels of TPO-Ab. This finding was similar to what was reported in the Tunisian study where elevated levels of TPO-Ab was also the commonest thyroid disorder. Hypothyroidism was present in 2.8% of the women and is similar to that reported in American and European pregnant women.[14] During pregnancy, there is increased thyroid hormone production and increased foetal iodine requirements. Consequently, dietary iodine requirements are higher in pregnancy than they are for nonpregnant adults. Women with adequate iodine intake before and during pregnancy have adequate intra-thyroidal iodine stores and remain euthyroid. For those with inadequate iodine intake before and during pregnancy maternal hypothyroidism occurs as increased demand of pregnancy will outstrip supply.[2]

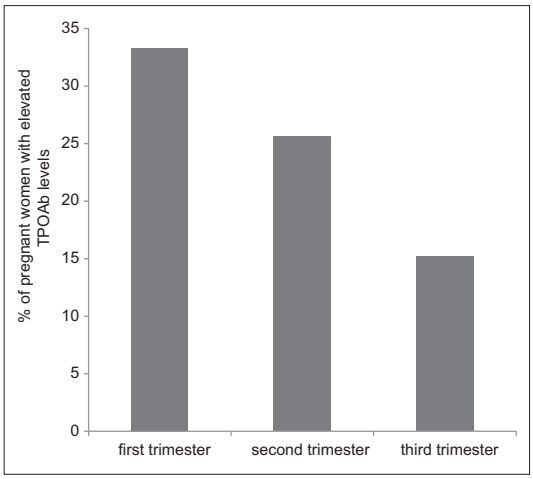

Figure 1: Relationship between Autoimmune Thyroid Disorder and Gestational Age. The chart shows that the number of pregnant women with elevated TPO-Ab levels decreased with pregnancy from 33.3% in the first trimester to 25.6% and 15.2% in the second and third trimesters.x^2= p = 0.21

Hypothyroidism was associated with elevated levels of TPO-Ab in 33.3% of women. This shows that auto immunity is a common cause of hypothyroidism in pregnant women.[10] The presence of hypothyroidism amongst the other women without autoimmunity could be as a result of iodine deficiency. Though Lagos is considered iodine sufficient area, studies carried out in some iodine sufficient areas have reported iodine deficits in women.[10] Subclinical hyperthyroidism was present in 1.9% of the pregnant women. Both women were in the first group. The cause of subclinical hyperthyroidism was related to autoimmunity in 50% while another cause could be transient gestational thyrotoxicosis since there was absence of elevated levels of TPO-Ab and this usually occurs in the first 13 weeks of pregnancy.

Autoimmune thyroid dysfunction was prevalent in 25% of pregnant women while it was 1.9% in the nonpregnant women. The value found in this study was higher than what was reported in pregnant women from Tunisia, Belgium, Japan, Turkey, Spain and the United States where 6.5%, 6.3%, 10%, 12%, 14.8%, and 20% respectively were positive for TPO-Ab.[10,15-18]

The reason for this high prevalence of autoimmune thyroid dysfunction 25% in these pregnant women is difficult to explain. It could be due to variations in the assays used to measure TPO-Ab in the different studies. At present, there is no international standardization of the assays. It was also observed that in all the studies, different cut-off values were used to define autoimmune thyroid dysfunction. In this study, cut off values of 14.4 IU/ml was used.

The prevalence of elevated TPO-Ab decreased with gestational age from 33.3% in the first group to 25.6% and 15.2% in the women in second and third groups respectively. The same trend was observed in the study in Tunisian women where there was a decrease of positive TPO-Ab (from 7.7% to 4.7%) through gestation.[10] Previous studies have demonstrated that thyroid antibodies TPO-Ab, TgAb, and TRAb all decline during pregnancy and increase in the postpartum period.[19-22] During pregnancy, thyroid antibody titers decline due to the immuno-suppressive effect of pregnancy and subsequently

titers increase in the postpartum period.[10,23-27] Important adaptations of the maternal immune system occur during pregnancy. Placental trophoblast cells secrete a variety of cytokines, several immunomodulatory molecules and hormones. These secretions induce a physiological immunosuppression response, which allows the maternal immune system tolerate the foetus. During pregnancy B-cell production and activity are down regulated, leading to a reduction in antibody production.[28] There is also an increase in plasma levels of estrogen, progesterone, and corticosteroids. Corticosteroids induce immune cell apoptosis and immunosuppression while estrogen produces negative regulation of B cell activity.[28] The immunomodulatory molecules like Fas-Ligand induces apoptosis on fetal antigen-reactive maternal lymphocytes while human leukocyte antigen-G inhibits both natural killer NK cell function and maturation of dendritic cells. All these changes result in a general improvement in autoimmune intolerance during gestation.[28]

This study found that 25 out of 27 (92.6%) women with elevated TPO-Ab were euthyroid. Pregnant women with asymptomatic AITD carry a significant risk of developing hypo-thyroidism.[29] It has been shown that 33–50% of women who are positive for TPO or Tg antibody in the first 13 weeks of pregnancy will develop postpartum thyroiditis.[30] Screening for antibodies in the early months of pregnancy is justified to reduce adverse pregnancy outcomes like the increased risk of spontaneous miscarriage; progressive hypothyroidism during gestation; postpartum thyroiditis after pregnancy; and the long-term risk of developing definitive hypothyroidism later on in life. It is important that all pregnant women with AITD should be monitored closely and jointly by obstetricians and endocrinologists.[31]

Conclusion

Thyroid autoimmunity expressed by the presence of TPO-Ab is high among pregnant Nigerian women, and the degree of autoimmunity decreases with advancing gestation. Screening for thyroid autoimmunity is best performed in the first 13 weeks of pregnancy. It is important that all pregnant women with AITD be monitored closely and jointly by obstetricians and endocrinologists to reduce adverse maternal and fetal outcomes.

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