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THYROID ANTIBODIES IN DIFFERENT TRIMESTERS OF PREGNANCY AMONG WOMEN ATTENDING ANTE-NATAL CLINICS IN YENAGOA, BAYELSA STATE, NIGERIA

Medical Science

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ABSTRACT

Background: The changes in thyroid functions and the consequences of thyroid antibodies during pregnancy have grown recently. It has been established that the presence of thyroid auto antibodies is relatively high in women of child bearing age with the risk of spontaneous and recurrent pregnancy loss and preterm delivery. **The objective** of the study was to determine the prevalence and establish the level of serum thyroid antibodies in the different trimesters of pregnancy among Euthyroid pregnant women attending ante-natal clinics in Yenagoa, Bayelsa State. **Design/Method:** A total number of 648 pregnant women and 224 non pregnant women were used for the study. The serum thyroid Peroxidase (TPO-ab), and thyroglobulin (TG-ab) antibodies were measured using Enzymes Linked Immuno Sorbent Assay (ELISA) method. **Result:** The result of the study showed that 94.14% of the screened pregnant women were euthyroid, 2.62% were hyperthyroid and 1.08% hypothyroid. The result revealed significant elevations ($P<0.05$) in the mean values for TPO – antibody in the first trimester (21.4 ± 4.75 iu/ml) when compared to the control groups (16.09 ±2.30) and a steady decrease in the second trimester (18.19±2.71 iu/ml) and third trimester (17.65 ±1.81 iu/ml) of pregnancy. The decrease in the Tg-antibody for the three trimesters were not statistically significance ($P>0.05$). The levels of the TPO-ab and Tg-ab parallel the result obtained for the Free T4 in euthyroid pregnant women in Yenagoa, Bayelsa State with a significant decrease in the mean value for third trimester (13.55 ± 6.23 pmol/l) as compared to the control value (20.15 ±5.31 pmol/l). The result also showed a steady increase in thyroid stimulating hormone with progression of pregnancy. Further analysis showed a negative correlation between the different gestational period of pregnancy and the thyroid antibodies. A total of 2.16 percent of the screened euthyroid pregnant women in Yenagoa had TPO-Ab elevated, signifying the TPO-Ab positivity and it is the major cause of thyroid autoimmunity among pregnant women. **Conclusion:** The study has revealed the presence of TPO antibody among pregnant women in Yenagoa, Bayelsa State, Nigeria especially in the first trimester of pregnancy with a statistically significant mean value when compared with the control group. This elevated level of the serum TPO-Ab and Tg-Ab decreases with the progression of the pregnancy.

KEYWORDS

Thyroid antibodies, Thyroid peroxidase, Thyroglobulin, Trimesters, Pregnancy.

INTRODUCTION

Thyroid peroxidise (TPO-Ab) antibody is a beta (β)-cell type, Y-shaped protein that is produced by the immune system essential for the identification and neutralization of bacteria and viruses[1]. However when the immune system mistakenly targets components of the thyroid gland or proteins, this antibody becomes an auto antibody and leads to chronic inflammation of the thyroid gland (thyroiditis), tissue damage and disruption of thyroid functions[2,3]. Apart from thyroid peroxidise antibody, there are two other types and these are: Thyroglobulin antibody (TG-Ab) and thyrotropin receptor antibody (TR-Ab), which includes thyroid stimulating antibody (TS-Ab) and thyrotropin blocking antibody (TB-Ab) and neutral-thyrotropin receptor antibody based on their effect on thyroid stimulating hormone receptor[4,5]

Pregnancy, otherwise known as gestation is the timing during which one or more offspring develops inside a woman and can occur by sexual intercourse or assisted reproductive technology [6, 7]. It is also referred to as the state of carrying a developing embryo or foetus within the female body and usually lasts for about nine months, measured from the date of the woman's last menstrual period (LMP) and conventionally divided into three trimesters, each about three months long [8, 9]. In order to nurture and accommodate the developing foetus, a pregnant mother undergoes significant anatomical and physical changes. These changes begin immediately after conception and affect every organ system in the body. For most women experiencing an uncomplicated pregnancy, these changes resolve after with minimal residual effects[10]. As the pregnancy progresses, a pregnant mother experiences physical and emotional changes ranging from increased moodiness to darkening of the skin in various areas such as the areolar [8, 11]. Certain symptoms and early signs of pregnancy that begins includes the absence of menstrual periods, changes in the breast including swelling or tenderness, nausea and vomiting, tiredness, frequent urination and weight gain[8, 12]. Nevertheless. It has been recognised that Euthyroid pregnant women screened during the first trimester of pregnancy have an increased prevalence up to 20% of thyroid peroxidase antibody and are at increased risk of various complications of pregnancy including miscarriage, preterm birth, pregnancy-induced hypertension (PIH), intrauterine death (IUD) and growth retardation [13,14,15].

Hence there is need for screening of thyroid peroxidase antibody precisely during the first trimester of pregnancy as studies have shown that it is essential for maternal health and also to reduce adverse obstetrical outcome and subsequent development of the child [16,17]. Anti – TPO and anti – TG antibodies are related to levels of thyroid stimulating hormone (TSH) and both alone or in combination have been used to predict development of hypo/hyperthyroidism[18]. It has been determined in different studies that altered levels of anti-thyroid antibodies and TSH in euthyroid subjects have been associated with development of hypothyroidism in future [5, 18]. Anti-thyroid antibodies (specifically anti TPO antibody) are more often present when TSH is deranged. The individuals with deranged thyroid profile (specifically TSH) should also be screened for anti-thyroid antibodies to rule out underlying autoimmune phenomenon[19].

Thyroid peroxidase is an antibody produced by the immune system that is usually expressed in the thyroid gland and also involved in the synthesis of thyroid hormone such as thyroxine (T4) and Triiodothyronine (T3). During pregnancy, thyroid peroxidase antibody is usually present in much higher titers than other thyroid antibodies and if not monitored could lead to various complications of pregnancy [20,21]. This study was carried out to investigate the prevalence rate of these antibodies among euthyroid pregnant women in Yenagoa, Bayelsa State to provide verifiable data that will enable healthcare practitioners care for and manage pregnant women having this antibodies above the accepted limit in order to reduce the risk of adverse obstetrical outcomes.

MATERIALS/METHOD

Study Area

The study was carried out in Yenagoa, Bayelsa State. Bayelsa is a state in southern Nigeria in the core region of Niger Delta. Its capital is Yenagoa and the main language spoken is Ijaw. The hospitals involved in this study are Diete-koki memorial hospital Opolo, Federal Medical Centre, and family support program clinic (FSPC) all in Yenagoa.

Study Population

This was a cross sectional study carried out from February 2017 to

April 2018. A total number of eight hundred and seventy-two (872) euthyroid pregnant and non-pregnant women were used for this study. This comprised of 234 pregnant women in their first trimester (4-12wks), 210 in the second trimester (13-26wks) and 204 in the third trimester (27-40wks) attending the antenatal clinics in the hospitals with 224 non pregnant women within the same age range that serves as control group. All apparently healthy pregnant women attending antenatal clinics were included in the study after filling a questionnaire form that included the information of age, last date of menstrual period and whether on any medication for a specific illness. Excluded from the study were pregnant and non-pregnant women that were not willing to participate in the study and pregnant women under the age of 18 years. The sample size were calculated using the Fisher's formula[22] and the calculated sample size was 201 for each study group based on the projected population of pregnant women in Yenagoa, Bayelsa State, Nigeria.

Ethical Clearance

Ethical approval was obtained from the committee for human research, Federal Medical Centre, Yenagoa with the clearance certificate number FMC/REC/ECC/2016S/JAN/155. Consents were gotten from the subjects while filling the questionnaire form used to collect the demographic data.

SAMPLE COLLECTION AND PREPARATION

Aseptically, about 5.0ml of venous blood samples were collected from the subjects following the standard venepuncture procedure. The collected blood was transferred into a plain container and allowed to clot at room temperature for about 20 - 30minutes. The samples were then centrifuged at 3500 rpm for about 5 minutes and the serum separated into a properly labelled plain containers. The samples were stored frozen at -20^{0c} and measurement done within 7days of sample collection.

METHOD OF THE STUDY

Analysis of the thyroid hormones (thyroid peroxidase-TPO, Thyroglobulin-Tg) antibodies and thyroid profiles thyroxine (FT4), thyroid stimulating hormone (TSH) were measured using Enzyme Linked Immunosorbent Assay (ELISA) method[5, 23, 24]. The ELISA kits were purchased from Elabscience Biotechnology Co. LTD (USA). This uses the competitive (sandwish) and non-competitive ELISA principles and the Biotechnology Awareness plate reader (UK) was used to read the sample absorbance at 450nm with a differential wave length of 490nm.

STATISTICALANALYSIS

Data analysis was performed using Microsoft Excel Version 10 and IBM statistical package for social Science (SPSS) version 20. Descriptive statistic was used to determine the mean, standard deviation. The correlation analysis was performed using the Pearson's correlation analysis and 95% confidence interval, P<0.05) were considered to be statistically significant.

RESULTS

A total of 872 subjects comprising 224 euthyroid non pregnant controls and 648 euthyroid pregnant subjects were studied. The age range for the non-pregnant women were between 22 – 43 years with an average of 29.3 years and 21 – 41 years for the pregnant subjects with an average age of 29.8 years. The analysis of the data obtained and as presented in the tables below showed that 94.14% of the pregnant women were euthyroid, 2.62% hyperthyroid and 1.08% hypothyroid.

Table 4.1: Prevalence of thyroid diseases and anti-thyroid (anti-TPO and anti-TG) antibody status among the euthyroid pregnant and non-pregnant women in Yenagoa, Bayelsa State, Nigeria.

Subjects:	ThyroidFunctionStatus						
	Euthyroids(%)	Hypothyroid(%)	Hyperthyroid(%)	TPOElevated(%)	TGElevated(%)	Total(%)	P-Value(%)
Controls(n=224)	96.88(217)	0.89(2)	2.23(5)	0(0)	0(0)	100(224)	
Pregnant(n=648)	94.14(610)	1.08(7)*	2.62(17)*	2.16(14)*	0(0)	100(648)	P>0.05
1st trimester(n=234)	88.03(206)	1.71(4)*	5.56(13)*	4.70(11)*	0(0)	100(234)	P>0.05
2nd trimester(n=210)	97.14(204)	0.95(2)*	0.95(2)*	0.95(2)*	0(0)	100(210)	P>0.05
3rd trimester(n=204)	98.04(200)	0.49(1)*	0.98(2)*	0.49(1)*	0(0)	100(204)	P>0.05

*Were not statistically significant

The characteristics of the findings from this study as shown in the table 4.1 indicated that 2.16 % of the studied subjects had TPO-Ab elevated above accepted upper limit (TPO-Ab positivity) with zero percent for TG-Ab. The result from the table also showed that 2.62 % had hyperthyroidism and 1.08 % with hypothyroidism. A total of 11 pregnant women, representing 4.70% of the screened 234 women in the 1st trimester had TPO-Ab elevated. The values were not statistically significant at P>0.05 against the control group.

Table 4.2: Trimester wise values for mean ±S.D and median (range) for Thyroid Peroxidase antibody (TPO-Ab) from studied Euthyroid pregnant women.

Groups	Age(yrs) Mean ± S.D	Value(ui/ml) Mean± S.D	Range	Ft_4 Mean±S.D	TSH Mean ± S.D	P-Value
Control (n-224)	29.3 ± 5.71	16.09 ± 2.30	13.79-18.39	20.15 ± 5.31	1.76 ± 0.83	
1st Trimester (n=234)	30.4 ± 4.93	21.41 ± 4.75	16.66-26.16	18.72 ± 4.88	2.09 ± 0.92	P=0.0398*
2nd Trimester (n=210)	28.6 ± 6.40	18.19 ± 2.71	15.48-20.90	16.91 ± 5.11	2.95 ± 0.75	P=0.0716NS
3rd Trimester(n=204)	30.2 ± 5.79	17.65 ± 1.81	18.84-19.46	13.55± 6.23*	3.73 ± 0.98*	P=0.0823NS

*Statistically significant; NSNot statistically significant

The TPO-Ab mean value for the first trimester was statistically significant with respect to the control group and is in contrast to the second and third trimesters that were not significant. The mean values for the three gestational pregnant periods were not statistically significant against each other. The mean value for the Thyroxine (FT4) and Thyroid stimulating hormone (TSH) were statistically significantly increased (P<0.05) with respect to the control group.

Table 4.3: Trimester-wise values for mean ± S.D and median (range) for Throglobulin antibody (Tg-Ab) from studied Euthyroid pregnant women.

Groups	Age (yrs) mean ± S.D	Value (iu/ml) mean ± S.D	Range	FT_4	TSH	P-Value
Control (n=224)	29.3 ± 5.71	9.94 ± 1.06	8.88 – 11.00	20.15 ± 5.31	1.76 ± 0.83	
1st trimester (n=234)	30.4 ± 4.93	11.14 ± 1.95	9.19 – 13.09	18.72 ± 4.88	2.09 ± 0.92	P=0.0591NS
2nd trimester (n=210)	28.6 ± 6.40	10.73 ± 1.49	9.24 – 12.22	16.91 ± 5.11	2.95 ± 0.75	P=0.0733NS
3rd trimester (n=204)	30.2 ± 5.79	10.48 ± 1.60	8.88 – 12.08	13.56 ± 6.23	3.73 ± 0.98	P=0.0803NS

NSNot statistically significant

The result from the table has shown that the values for Tg-Ab, decreases with the age of pregnancy but with no significant different (P>0.05) among the groups studied for the antibody.

Fig 4.1 A graph plot of the mean values of TPO-Ab measured in the three trimesters of euthyroid pregnant women in Bayelsa State.

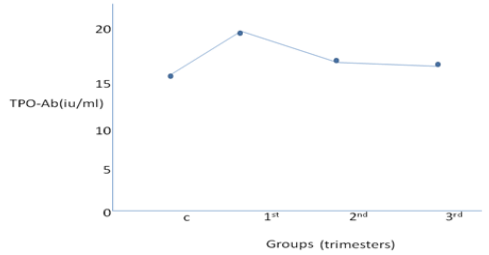

Fig 4.2: A graph plot of the mean values of Tg-Ab measured in the three trimesters of euthyroid pregnant women in Bayelsa State.

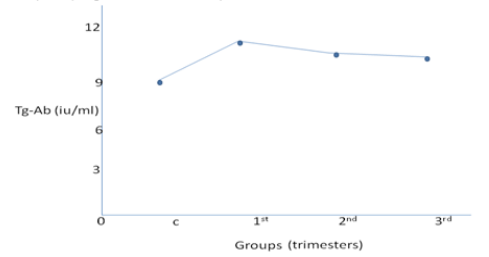

Fig 4.1 and 4.2 are graphs shown the mean values of TPO-Ab and TG-Ab measured in the four groups of control, 1st, 2nd, and 3rd trimesters.

Table 4.4: Pearson's correlation analysis of the relationships between the thyroid antibody levels and the age of gestational period of pregnancy in Euthyroid pregnant women.

Thyroid antibody	TP - Ab	T_G-Ab
1st trimester	-0.232	-0.189
2nd trimester	-0.217	-0.194
3rd trimester	-0.193	-0.203

The correlation analysis has shown a weak negative correlation between the antibodies secreted and the different trimesters of pregnancy.

DISCUSSION

The study was conducted to investigate the prevalence of Thyroid Peroxidase (TPO-Ab) and Thyroglobulin (TG-Ab) antibodies, as well as the titter levels of the antibodies in different gestational period among euthyroid pregnant women attending antenatal clinics in Yanegoa, Bayelsa State, Nigeria. The results obtained from this study revealed that the mean values of TPO-Ab in the first trimester were statistically significantly increased (P= 0.0398) with respect to the control group and subsequently diminishes during the second and third trimesters (table 4.2, fig 4.1). However, the obtained mean values for TPO-Ab among the studied subjects were within the recommended TPO-Ab reference range for pregnancy which is ≤35 iu/ml [25, 26]. The study did not indicate any significant difference statistically between the control group and the three trimester for TG-Ab in the studied subjects (Table 4.3, fig. 4.2). During the first trimester, the antibodies increased with respect to the control group, but were still within the established normal range [27,28].

A total of 2.16 percent of the screened euthyroid pregnant women had TPO-Ab elevated above the accepted upper limit, signifying the TPO-Ab positivity (Table 4.1). This is the major cause of thyroid autoimmunity among pregnant women as reported by Galofre and Davies[29]. This is in contrast to the Tg-Ab that has zero percent elevation (above normal range) among the screened euthyroid pregnant women in Yanegoa, Bayelsa State.

The 2.16% TPO-Ab positivity in this study contributed to the 32.70 percent derangement in the mean value of FT_4 and 52.82 percent for TSH [19, 30] as compared to when the antibody is negative. The findings from the study indicated that TSH is increased with the age of pregnancy, and was statistically significant when compared to the control group (table 4.2, 4.3). This obviously explained that with the derangement of thyroid profile might likely lead to TPO positivity and subsequent thyroid disorder. This probably is due to the comprisement in the ability of thyroid functions to increase its production during gestation, especially in the situation of limited thyroid hormone reserve like thyroid autoimmunity and iodine deficiency which causes imbalance between supply and increasing demand [17, 26, 31]. There is a negative correlation between the studied TPO-Ab, Tg-Ab and the different gestational periods (Table 4.4).

In the study, thyroid peroxidase were observed to be more prevalence than thyroglobulin antibodies in the euthyroid pregnant subjects. This may reflect the fact that TPO-Ab is more specific test than Tg-Ab for detecting autoimmune thyroid diseases[32]. The anti-thyroid antibodies have long been known to affect thyroid function and influence thyroid profile testing [33]. These antibodies are most probably elevated in the subjects with deranged thyroid profile as seen in this study and other studies [34,35]. This means that individuals with deranged thyroid profile should be screened for anti-thyroid antibodies to rule out underlying autoimmune phenomenon. The presence of thyroid autoantibodies is relatively low this study compared to other studies [17, 26, 36] and positive thyroid peroxidase antibody even in euthyroid women may increase the risk of spontaneous and recurrent pregnancy loss and preterm delivery.

CONCLUSION:

The study has revealed the presence of Thyroid Peroxidase antibody (TPO-Ab) among euthyroid pregnant women, especially in the first trimester of pregnancy with non-statistically significant (P>0.05) percentage of hypo/hyperthyroidism in yenagoa, Bayelsa State of Nigeria. Screening for antibodies in the early months of pregnancy is justifiable to reduce adverse pregnancy outcomes.

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Conflict of Interest

Nil

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