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Original Research Article

Title: Status of Thyroid Autoimmunity in the First Trimester of Pregnancy in a Tertiary Medical College of Kolkata, WB

Mamata Majumdar[1], Swati Bhattacharyya[1*], Mayukh Bhattacharyya[2]

1. *Final year post graduate trainee (MD Biochemistry) Dept. of Biochemistry, Calcutta National Medical College, Kolkata.*
1. *Professor, Dept. of Biochemistry, Calcutta National Medical College, Kolkata.*
2. *Final year, BSc (Microbiology), St. Xavier,s College, Kolkata.*

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A B S T R A C T

Background- Thyroid disorder is the second most common endocrinological disorder in pregnancy. If kept undetected it may lead to various complication like fetal loss and interference with fetal neurological development. Autoimmunity is a major factor that leads to subclinical and clinical hypothyroidism. Hence the current investigators explored autoimmunity status along with thyroid profile in first trimester of pregnancy in the present observational cross sectional study.

Methodology -36 cases were included following inclusion & exclusion criteria within 4-12wks of pregnancy. Fasting serum was collected for estimation of FT4, TSH, anti TPO Ab and anti TG antibody by CLIA & ELISA.

Results- Mean TSH value was 1.69±mIU/L, fT4- 1.14±0.18 ng /dl anti TPO ab-47.03±0.18IU/ml, anti T G ab index- 0.05±0.056.

Conclusion- Inspite of having normal thyroid profile the mean of anti TPO antibody was found to be higher than normal reference interval. If explored longitudinally a large number of these patients may be seen developing subclinical and clinical hypothyroidism. We propose further vertical studies for analysing the implication and effect of raised anti TPO antibodies in first trimester in follow up.

Introduction:

Thyroid dysfunctions are the second most common endocrine disorders seen during pregnancy. For overall growth, development and maturation of fetal nervous system maternal euthyroid status in early gestation period and optimal transfer of thyroxine to fetus is very crucial. Autoantibodies to thyroglobulin(TG) and thyroid peroxidase(TPO) and TSH Receptor antibody are common in the euthyroid population and are considered secondary responses and indicative of thyroid inflammation. A landmark study done by Stagnaro et al on the adverse outcome of antithyroid antibodies in euthyroid women drew the attention of researchers [1]. Though the exact reason of these adverse effects is unknown, it has been hypothesized that a generalized autoimmune imbalance caused by antithyroid antibodies may be responsible for increased complications inspite of euthyroid status. Thyroid diseases are common in pregnancy and uncontrolled thyroid dysfunction (both overt hypothyroidism and overt hyperthyroidism) is associated with infertility, pregnancy loss, and maternal and fetal /neonatal complications [2]. Most thyroid diseases affecting childbearing women are autoimmune and up to 20% of pregnant women screened during the first trimester of gestation had positive thyroid autoantibodies [3]. There is a measurable amount of change in thyroid hormone in first trimester especially due to influence of estrogen induced increase in TBG & hCG induced increase in thyroid hormone & release [11].

*Correspondence:
Dr. Swati Bhattacharyya,
Professor,
Dept. of Biochemistry, Calcutta National Medical College, Kolkata.
Phone: 8240211537,
Email id: drmukulbhattacharyya@gmail.com

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The American Thyroid Association recently identified that thyroid hormone pattern in first trimester is of research priority as it may vary throughout pregnancy. The fetus-in-utero does not produce its own thyroid hormone & is dependent on maternal T4 crossing the placenta. Numerous factors that may include smoking & content of iodine in food & supplements influence availability of thyroid hormone to fetus & fetal brain development. Moreover, autoimmunity against thyroid hormones results in loss of fetus & further complication of pregnancy.

Therefore, the current investigators performed the study which include TSH & FT4 level, anti-TPO antibody, TG antibody in first trimester of pregnancy.

Research Hypothesis: antiTPO antibody level along with thyroid status may undergo changes in as early as first trimester of pregnancy.

MATERIALS AND METHODS:

The present study was a hospital based case control non-interference study conducted during the period of January 2020 to July 2020.

Study population-A total of 50 antenatal women attending Gynecology and Obstetrics department in Calcutta National Medical college and hospital were selected in their first trimester using the method of convenience within the study period of six months from January 2020 to July 2020. Patients having uncontrolled diabetes, thyroid disorder, any other endocrinal abnormality, severe anaemia, on hormonal supplements, and suffering from chronic or acute inflammatory disorder were excluded from the study. Following the inclusion and exclusion criteria ultimately 36 patients were selected for the study. Informed consent was taken from all patients & patients willing to participate were included in the study. The whole study protocol followed the Helsinki declaration for human studies and the guidelines for human studies adopted by the ICMR, India. The study was conducted after obtaining the written permission from the institutional ethical committee Laboratory investigations performed were:

a) Hb%

b) Fasting plasma glucose- by GOD_POD method

c) Thyroid profile (FT4, TSH)-by CLIA Method with a reference range for the first trimester for TSH and FT4 being 0.1-2.5 mIU/L and 0.8-1.53ng/dl respectively.

d) Anti TPO antibody- by ELISA with a reference range for females of l-30 IU/ml

e) Anti TG(thyroglobulin) antibody- By ELISA with the detection range as:

f) <0.9 No detectable TG antibody.

g) 0.9-1.1 Borderline positive

h) >1.1 detectable.

i) Results were verified time to time with CLIA. For all laboratory investigations coefficient of variation (CV) remained less than 10%.

j) Data were collected by:

k) a) Interviewing patient and relatives b) going through clinical records c) laboratory measurements.

l) Data obtained from laboratory investigations after being validated using the quality control methods.

STATISTICAL METHOD

Data obtained were analysed for difference between mean values of study parameters by independent t tests or Mann Whitney test according to their pattern of distribution. Distribution of data, whether parametric or nonparametric, were determined by Kolmogorov-Smirnov test (K-S test).TG ab showed non-parametric distribution($p>0.5$), all other parameters are parametric. Association studies were performed using the correlation analysis. For all studies P value was considered to be significant if < 0.05 for a 95% confidence interval. Data was analyzed in SPSS 26 software.

RESULTS AND ANALYSIS-

The study was conducted with 36 pregnant patients in their first trimester after excluding few miscarriages & outliers. Mean age of the cases were found to be 24.89 ± 5.28 yrs.

Table 1: Comparative analysis between the study parameters of the case group and their normal reference range.

	Study group	Control group	P value *
Age in years	24.89 ± 5.28	26.25 ± 6.84	P = 0.61
Serum TSH in mIU/ml	1.69 ± 0.28	1.98 ± 0.32	P = 0.54
Serum fT4 in ng/dl	1.14 ± 0.18	1.43 ± 0.28	P = 0.65
Anti TPO ab in IU/ml	47.03 ± 14.1	19.65 ± 5.1	P < 0.001

*P value considered significant at P < 0.001 for 95% confidence interval.

Mean value of the calculated Anti-TG Ab (index) at first trimester was found to be 0.05±0.056. Though it is within normal range, mean anti TPO antibody is significantly higher than normal. But TSH & FT4 did not show any difference compared to trimester specific reference range.

Table 2: Correlation analysis between the Anti-TPO antibody & Anti-TG antibody in the case group.

	Correlation coefficient	P value*	
Pearson's correlation	0.13	0.35	
Spearman correlation	0.18	0.39	

*P value considered significant at P < 0.001 for 95% confidence interval

In the Table 2 Pearson's correlation analysis (correlation coefficient: 0.13, P = 0.35) as well as Spearman's rho (coefficient: 0.18, P = 0.39) with 2-tailed analysis also failed to show any correlation between Anti-TPO antibody & Anti-TG antibody. Both Pearson's correlation and Spearman's Rho tests were applied here to strengthen this statistical analysis because the sample size is small.

DISCUSSION-Thyroid disorders are one of the most common disorders in women of child bearing age most of which is due to thyroid autoimmunity [4]. Previous studies show a prevalence of 5-20% Thyroid autoimmunity in pregnancy [5]. Recent researches show that recurrent & unexplained miscarriage is associated with raised anti-TPO antibody in euthyroid patients. With such alteration level of TSH and loss of fetus is more [6]. The present study was conducted based on the above information & also from other corroborative studies globally [1,7,8]. The aim was to find out whether there was any trimester specific change in Thyroid function as well as in thyroid autoimmunity in the urban pregnant ladies in Kolkata. The study group was selected from uncomplicated primi or multipara who is thyroid supplement naïve. Inclusion and Exclusion criteria were stringently selected. Any endocrinological abnormality, past or present, any acute or chronic inflammatory disease, degenerative diseases, gross metabolic disorders, organ derangements were excluded from the study as they can interfere with thyroid status.

The mean age was around 25 years though few teenage pregnancies were seen. But no conclusion has been drawn on that basis.

The present study was conducted with the idea of observing change of thyroid status and its autoimmunity in first trimesters of uncomplicated pregnancy. Changes in plasma protein concentration, TSH suppression by hCG and suppression of autoimmunity in later stages of pregnancy influence thyroid status [9]. Thyroid auto antibodies can be utilized as a marker for at risk pregnancies that end in preterm delivery & fetal loss.

In the present study we have used a cut off of 2.5miu/l for TSH which is reasonable as it was suggested in 2011 by a publication of American Thyroid Association [9].

In a study conducted by American thyroid association taskforce on thyroid disease during pregnancy it was noted that thyroid autoantibody titre decreased during pregnancy.in antibody positive euthyroid pregnancy TSH level increases progressively (from mean 1.7mIU/L to 3.5 mIU/L at term). Our study is in accordance with the above fact as we checked TSH & anti-TPO ab in early trimester of pregnancy to assess thyroid autoimmunity. The importance of the present study lies in the fact that if identified early it can be taken care of & subsequently fetal loss and associated complications can be reduced greatly.

In the context of FT4 and TSH values (Table 1), they were found within reference intervals. Beta hCG level is at peak at 10-12 weeks which leads to a high FT4 concentration and thus TSH decreases. FT4 might also show falsely lower value at later stage of pregnancy due to interference from low albumin & high thyroglobulin [10]. Our study utilized ELISA & CLIA method & observed a stable FT4 & TSH in 1st trimester. But the mean anti TPO ab is raised by 56.66% than the higher level in euthyroid mothers.

If followed up many of these pregnancies may lead to complications. Such skewed result may be due to small sample size for the prevailing COVID situation.

In general population Anti-TG Ab is seen to be elevated in 10% cases. It is not as sensitive a biomarker as Anti TPO Ab but can be used as a surrogate marker [12]. In a study conducted by Sun Y. Lee [13]. The authors proposed that abnormal Anti TG Ab along with Anti TPO Ab may interfere with thyroidal response in pregnancy. In an Indian study using anti TPO antibody assay by CLIA it is seen that women with elevated antibody(>29kIU/L) had associated overt and subclinical hypothyroidism [14] It is also recommended by American Thyroid Association that pregnant women with raised anti TPO antibody should be checked monthly to decide on treatment modality. The present study highlights an increased Anti-TPO Ab which is not associated with change in TSH. Ethnic factors, socio-cultural practices may be responsible for such outcome. [14]

Conclusion: The present study showed that pregnancy in first trimester population has significantly raised anti TPO ab (mean) with a normal TSH distribution. The study can further be extended as a longitudinal study across the trimester where we can appreciate the change of autoimmunity as well as thyroid status in normal pregnancy.

Limitation of the study- i) Main lacunae of the study is small sample size most probably due to the prevailing COVID 19 situation.

ii) If the parameters especially autoantibodies could have been measured by better method it might have given better result.

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