

AUTOIMMUNE THYROIDITIS IN PREGNANCY- A CROSS SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL OF SOUTHERN ODISHA

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ABSTRACT

BACKGROUND

A lot of physiological changes occur during pregnancy due to complex endocrine and immunological alterations. Autoimmune thyroid dysfunction is quite common which is responsible for various fetomaternal complications. There are few Indian studies regarding thyroid autoimmunity. Hence study was taken to assess the prevalence of autoimmune thyroiditis in this part of India.

Aims and Objectives- To know prevalence of autoimmune thyroiditis in pregnancy by estimating TPO Ab, FT4, FT3, S.TSH

Study Design- Cross Sectional Study

MATERIALS AND METHODS

This study was done taking 1000 pregnant women attending antenatal clinic from October 2015 to November 2016 fulfilling inclusion and exclusion criteria, irrespective of gravida and trimester. They were screened for FT3, FT4, S. TSH and TPOAb.

RESULTS

Mean Age of presentation was 25.87 ± 4.06 . 17.3% of the patients were TPOAb positive. TPOAb levels vary from 69 IU/mL to 1300 IU/mL with a mean level of 173.13 ± 145.82 . TPOAb level > 35 IU/mL was taken as positive. Amongst these, majority 12% were euthyroid, 4.7% were hypothyroid, 0.6% were hyperthyroid. There was no significant difference in multi or primigravida. But more patients were in 2nd Trimester of pregnancy.

CONCLUSION

There is a significant prevalence of thyroid autoimmunity in this part of country that is 17.3 % in comparison to western countries where it is 6.5 %. Hence screening of all pregnant women for thyroid autoimmunity is suggested to avoid fetomaternal complications.

KEY WORDS

Autoimmune Thyroiditis, Pregnancy.

HOW TO CITE THIS ARTICLE: George R, Mohanty N, Kurian S. Autoimmune thyroiditis in pregnancy- a cross sectional study in a tertiary care hospital of Southern Odisha. J. Evolution Med. Dent. Sci. 2019;8(02):117-120, DOI: 10.14260/jemds/2019/26

BACKGROUND

Thyroid disorders constitute one of the most common endocrine disorders in pregnancy, resulting from various factors like increase in thyroglobulin, increase in HCG concentration and increase renal loss of iodine as well as increased requirement of iodine. Other factors like increase in metabolism of thyroid hormones and placental modification in iodine transfer¹ also contribute.

Various obstetric complications like abortion, preeclampsia, preterm delivery and fetal complications like prematurity, low birth weight, stillbirth and perinatal death² are encountered. There is increased incidence of neonatal admission and respiratory distress syndrome. Maternal hypothyroidism in first trimester is harmful for fetal brain development and leads to mental retardation and cretinism.

'Financial or Other Competing Interest': None.

Submission 16-08-2018, Peer Review 01-01-2019,

Acceptance 08-01-2019, Published 14-01-2019.

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DOI: 10.14260/jemds/2019/26



Thyroid disorders may be overlooked in pregnancy because of nonspecific symptoms which simulate physiological changes in pregnancy. Presence of thyroid autoimmunity is one of the markers of underlying subtle alteration in thyroid reserve. Increase in TSH concentration in pregnant women with thyroid autoantibodies support their hypothesis,³ suggesting routine screening of all pregnant women for thyroid peroxidase TPOAb along with thyroid function tests.

MATERIALS AND METHODS

1000 consecutive pregnant patients presenting to MKCG Medical College Hospital Brahmapur, during the period of October 2015 to November 2017 were studied. Patients with Gestational trophoblastic disease, any associated medical comorbid conditions like DM/HTN/CKD and patients with bad obstetric history are excluded from the study and the patients are enrolled to study irrespective of their gravida, period of gestation, h/o thyroid dysfunction.

Blood samples are taken and sent for TSH, FT3, FT4, TPOAb levels and are standardized according to different trimesters of pregnancy. TPOAb level > 35 IU/mL was taken as positive. The patients with autoimmune thyroiditis are categorized to hypothyroid, Hyperthyroid and euthyroid based on S. TSH, S. FT3 & S. FT4 values.

Data Collection

Data collection was done in a case record format after taking informed consent from each patient. Demographic data and past medical history, were collected. Baseline S. TSH, FT3, FT4, S. TPOAb are measured and noted. The investigation results included blood tests and FNAC of thyroid if goiter was found. A thorough general physical examination and systemic examination is done before being included in the study.

Statistical Analysis

Statistical analysis was performed using the SPSS 16.0 statistical software package (SPSS Inc., Chicago, IL, USA). The data were analysed with the one-way ANOVA test & Fishers Exact test for quantitative variables and the P-value ≤ 0.05 was considered significant.

RESULTS

Trimester	Mean Age
First TM	25.47 $\pm$ 3.56
Second TM	25.82 $\pm$ 3.96
Third	26.31 $\pm$ 4.18
Mean Age in Total	25.87 $\pm$ 4.06

Table 1. Mean Age of Presentation of Patients at Antenatal Clinic

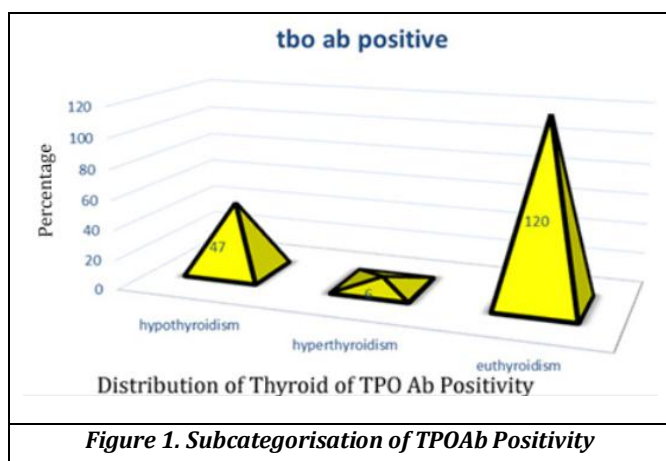
P-value ≤ 0.05 was considered significant.

Out of 1000 pregnant women studied mean age was 25.87 $\pm$ 4.06. According to trimester is among first trimester mean age was 25.47 $\pm$ 3.56 and in second trimester was 25.82 $\pm$ 3.96 and in third trimester was 26.31 $\pm$ 4.18.

	Hypothyroidism		Hyperthyroidism		Euthyroidism	Total Patients with TPOAb Positivity
	Subclinical	Overt	Subclinical	Overt		
Autoimmune Thyroiditis	30 (3%)	17 (1.7%)	3 (0.3%)	3 (0.3%)	120 (12%)	173 (17.3%)

Table 4. Distribution of Thyroid Status in Patients with TPOAb Positivity

P-value ≤ 0.05 was considered significant.



The no of patients detected with TPOAB positivity is 173 patients. Out of that, 47 patients were detected with hypothyroidism, 6 patients were hyperthyroid, 120 patients were euthyroid, which constituted 4.7%, 0.6 %, and 12 % respectively. (p value < 0.002) P value is obtained using (One-way ANOVA) test. So according to our study there is a statistically significant prevalence of thyroid autoimmunity and the majority were euthyroid.

	Mean age in Years
Autoimmune Hypothyroid	26.13 $\pm$ 3.92
Autoimmune Hyperthyroid	26.00 $\pm$ 4.43
Autoimmune Euthyroid	25.55 $\pm$ 4.16

Table 2. Distribution of Average Age Among Women with Thyroid Autoimmunity

P-value ≤ 0.05 was considered significant.

In patients detected with TPOAB positivity the mean age among autoimmune hypothyroidism was 26.13 $\pm$ 3.92 and in patients with autoimmune hyperthyroidism was 26.00 $\pm$ 4.43 and in TPO Antibody positive euthyroid patients was 25.55 $\pm$ 4.16 and the p value obtained shows that there is no significant difference between mean age groups.

TPO Ab	Values (IU/mL)
Mean $\pm$ SD	173.13 $\pm$ 145.82
Minimum	69.4
Maximum	1300

Table 3. Distribution of TPOAb Values in Patients with Antibody Positivity

In our study among the patients diagnosed with autoimmunity the TPOAb level ranged from 69 IU/ml to 1300 IU/ml. The mean TPOAB level obtained was 173.13 $\pm$ 145.82.

	S. TSH	S. FT4	S. FT3
Mean $\pm$ SD	4.60 $\pm$ 5.30	1.42 $\pm$ 1.38	3.37 $\pm$ 0.90
Minimum	0.03	0.02	1.00
Maximum	32.3	15.6	8.2

Table 5. Distribution of Baseline Thyroid Function in Patient with TPOAb Positivity

The results obtained are the upper limit of S. TSH obtained is 32.3 and the lower limit is 0.03 and the mean S. TSH (4.60 $\pm$ 5.30). The upper limit of S. FT4 was 15.6 and the lower limit was 0.02 and the mean S. FT4 (1.42 $\pm$ 1.38). The upper limit of S. FT3 was 8.3 and the lower limit was 1.00 and the mean S. FT3 was (3.37 $\pm$ 0.90).

Parity	Autoimmune Hypothyroidism	Autoimmune Hyperthyroidism	Autoimmune Euthyroidism
Primigravida	16	2	55
Multigravida	31	4	65
Total no	47	6	120

Table 6. Distribution of Parity of Women in This Study Related to Thyroid Autoimmunity

The Fishers Exact Test value = 2.125 and the p value = 0.3456

In our study, out of 47 cases of autoimmune hypothyroidism detected, primigravida constituted 16 patients and multigravida 31 patients. Out of 6 patients detected with hyperthyroid autoimmunity 2 were

primigravida and 4 were multigravida. Out of 120 euthyroid patients with TPOAB positivity 55 patients were primigravida and 65 patients were multigravida. So, our results show that there is no significant effect of parity and risk for thyroid autoimmunity

Trimester	Autoimmune Hypothyroidism	Autoimmune Hyperthyroidism	Autoimmune Euthyroidism
First Trimester n=148	15 (1.5%)	1 (0.1%)	14 (1.4%)
Second Trimester n=552	19 (1.9%)	4 (0.4%)	69 (6.9%)
Third Trimester n=332	13 (1.3%)	1 (0.1%)	37 (3.7%)
Total (n) 1000	47 (4.7%)	6 (0.6%)	120 (12%)

Table 7. Distribution of Cases of Autoimmune Thyroiditis in Various Trimesters

Our results came to be statistically significant which is showing that second trimester being diagnosed with more patients as having thyroid autoimmunity.

DISCUSSION

The effects of Thyroid dysfunction (Both Hypothyroidism and Hyperthyroidism) and autoimmune thyroiditis on fetomaternal outcomes is not a new subject. Pregnancy affects the natural course of thyroid autoimmunity and conversely.

Various studies have been conducted through world to know the prevalence of autoimmune thyroiditis and its effects on foetomaternal outcome. Many of these studies are done in western population, whose generic pattern and standards of living having much impact on the development of thyroid dysfunction and thyroid autoimmunity are quite different from that of Indian population. Very few studies have been conducted in our population. So, this study done is done to assess the prevalence of autoimmune thyroiditis in pregnancy.

Findings and Implications

In our study, out of 1000 pregnant women studied mean age was 25.87 ± 4.06 . According to trimester is among first trimester mean age was 25.47 ± 3.56 and in second trimester was 25.82 ± 3.96 and in third trimester was 26.31 ± 4.18 .

In patients detected with TPOAb positivity the mean age among autoimmune hypothyroidism was 26.13 ± 3.92 and in patients with autoimmune hyperthyroidism was 26.00 ± 4.43 and in TPO Antibody positive euthyroid patients was 25.55 ± 4.16 .

The mean age differences between major groups are compared with chi square test and p value obtained was ($p=0.7066$) indicating that there is no significant age difference between various age groups detected with TPOAb positive

The normal level of TPOAb level is < 35 IU/ml. In our study among the patients diagnosed with autoimmunity the TPOAb level ranged from 69 IU/ml to 1300 IU/ml. The mean TPOAb level obtained was 173.13 ± 145.82 . In a study conducted by Li Y, et al⁴ the max value of TPOAb detected was 1500 IU/ml. Out of the 47 cases of autoimmune

hypothyroidism detected, 30 patients were subclinical hypothyroidism and 17 were overt hypothyroidism. Out of 6 patients diagnosed with autoimmune hyperthyroidism, 3 patients were subclinical hyperthyroidism and 3 patients were overt hyperthyroidism. These findings is comparable with the study of R. GAYATHRI et al⁵ whose studies showed high rates of TPOAb positive in patients with subclinical hypothyroidism.

We have compared the mean level of S. TSH S. FT4 and S. FT3 among patients detected with TPOAB positive.

The results obtained are the upper limit of S. TSH obtained is 32.3 and the lower limit is 0.03 and the mean S. TSH (4.60 ± 5.30). The upper limit of S. FT4 was 15.6 and the lower limit was 0.02 and the mean S. FT4 (1.42 ± 1.38). The upper limit of S. FT3 was 8.3 and the lower limit was 1.00 and the mean S. FT3 was (3.37 ± 0.90). This is partially in contrary to the results obtained by VIDYA et al⁶ showing mean S. TSH level is 1.59 ± 0.84 , mean S. FT4 level = 1.30 ± 0.92 and the mean S. FT3 level = 2.59 ± 1.33 .

Our study also analyzed whether the parity is a risk factor for thyroid autoimmunity. In our study out of 47 autoimmune hypothyroidism detected primigravida constituted 16 patients and multigravida 31 patients. Out of 6 patients detected with hyperthyroid autoimmunity 2 were primigravida and 4 were multigravida. Out of 120 euthyroid patients with TPOAB positivity 55 patients were primigravida and 65 patients were multigravida.

The significance of parity is assessed with chi-square test and Fisher Exact probability Test, and the value are 2.125 and p value is= 0.3456 showing that it is not significant. So our results shows that there is no significant effect of parity and risk for thyroid autoimmunity. These results were consistent with the previous studies like Walsh J et al⁷ p value was ($=0.46$). Another study conducted by Yehuda M et al also conducted a multivariate regression analysis and confirmed the absence of association between thyroid autoimmunity and parity.

Our study also analysed whether the trimester of pregnancy is a risk factor for the development of autoimmune thyroiditis. The results obtained is analysed using the Fishers Exact Test and the values obtained are value is = 10.51 and the p value obtained is 0.0326 and it came to be statistically significant which is showing that second trimester being diagnosed with more patients as having thyroid autoimmunity. This correlates with the studies conducted earlier like Raghunath Bhattacharya et al,⁸ Rajesh Rajput et al⁹ which also showed similar values. This may be explained due to the pregnancy changes like increased thyroglobulin concentration and albumin and transthyretin changes. The increased sample size among second trimester may also be a confounding factor.

Limitation

One limitation is the cross-sectional design. Our study included a single blood sample for hormone assay and no serial measurements are done and the patients are not followed up which would have helped us to know the effect of thyroid autoimmunity on mother and fetal outcomes. As a result, a cause effect relationship cannot be determined between pregnancy and thyroid autoimmunity

Furthermore, this study only measured TPOAb value and did not included other autoantibodies like Antithyroglobulin

antibody, TSH Receptor Antibody in assessing thyroid autoimmunity

One of the limitations of this study is small sample size, which might have interfered with the normal population distribution of thyroid dysfunction and autoimmune thyroiditis. The study on a much larger sample would enable us to understand the exact picture and magnitude of the problem.

CONCLUSION

Several studies in western countries show association of thyroid dysfunction and adverse pregnancy outcome. Prevalence of hypothyroidism is 2.5% in those countries. But our study demonstrates higher prevalence of hypothyroidism that is 9%. This higher prevalence may be due to higher prevalence of thyroid autoimmunity in our country that is 17.3% according to our study versus 6.5 % in western countries. Our study showed a prevalence of 3% subclinical and 1.7% overt autoimmune hypothyroidism; subclinical and overt hyperthyroidism constituted 0.3 % each while the euthyroid patients constituted 12%; so, majority are euthyroid. These euthyroid autoimmune patients should be regularly monitored because there is high chance of developing thyroid dysfunction. So, there is a significant prevalence of autoimmune thyroiditis in pregnancy.

Till now there is no available recommendation for screening of thyroid dysfunction among Indian pregnant women.

American Endocrine Society guidelines do not suggest universal screening but recommends screening of specific subset of subjects like 1) those who are currently on thyroid therapy 2) Family history of thyroid disease 3) goiter 4) history of autoimmune disorder 5) history of high neck radiation 6) history of postpartum thyroid dysfunction 7) precocious delivery of infant with thyroid disease. With this target case finding, there is a high chance of missing a lot of cases of thyroid dysfunction and thyroid autoimmunity.

Our study results suggest screening of all pregnant women in antenatal clinic for thyroid dysfunction and thyroid autoimmunity so that associated maternal and fetal complications can be avoided by supplementing thyroxine and adequate measures.

However more studies taking larger population from different parts of India is required to give an opinion

regarding routine thyroid screening of the pregnant women. So, it is a rising question for future randomized trials to answer.

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