Original Article

A study of autoimmune thyroid disease in pregnant women and its effect on fetal and maternal outcome

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Abstract

Introduction: Anti-thyroid antibodies not only cause thyroid dysfunction but have independent adverse outcomes in the fetus and mother during pregnancy and after birth. Chronic lymphocytic thyroiditis as a presentation of immune system deregulation may be associated with a generalized activation of the immune system at the fetus–maternal unit, the placenta. This interference could be associated with pregnancy morbidities in m o t h e r a n d fetus. This study was done to find out the frequency of autoimmune thyroid disease and its effect on maternal and fetal outcomes in a tertiary care facility in Jharkhand. **Method:** This is an Observational Prospective Study done during an 18-month period on 254 pregnant women in their second trimester who came to the antenatal clinic (ANC) clinic with singleton pregnancy at RIMS Ranchi. **Result:** 222 (87.4%) out of the 254 pregnant women had anti- TPO antibodies less than 35 IU/ml. Anti-thyroid peroxidase (anti-TPO) antibody positivity with values greater than 35 IU/ml was found in 32 patients (12.6%). Anti-TPO antibody mean value was 22.54 ± 19.67 IU/ml. Among the 222 individuals who tested negative for the anti-TPO antibody, 7 (3.3%) had miscarriages, 182 (88.3%) gave birth vaginally, and 33 (14.9%) underwent a cesarean section. Of the 32 individuals who tested positive for the anti-TPO antibody, 2 (6.3%) had miscarriages, 24 (75.0%) had vaginal deliveries, and 6 (18.8%) had cesarean sections. Using the Chi-square test, a *P* value of 0.549 was calculated, indicating statistical insignificance (Pearson Chi-square test value = 0.200[a]). **Conclusion:** Anti-TPO antibody positivity was significantly related to miscarriage and anemia. Other complications like preterm delivery, pre-eclampsia, and low birth weight were higher in anti-TPO antibody-positive patients as compared to anti-TPO antibody-negative patients. However, these findings were not statistically significant.

Keywords: Anemia, Anti-TPO antibody, autoimmune thyroid disease, miscarriage, pregnancy, thyroid dysfunction

Introduction

Autoimmune disorders frequently manifest before or during the reproductive years and are strongly connected with female predominance.[1] The semi-allogeneic fetus poses a challenge to the mother's immune system during pregnancy, one that must be sustained without endangering the health of the fetus or the mother.[2]

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Pregnancy significantly impacts thyroid function through hormonal fluctuations and increased metabolic demands. Key events include increased serum levels of thyroxine-binding globulin, a decrease in free hormone concentrations, a slight increase in basal thyrotropin (TSH), elevated levels of human chorionic gonadotropin (HCG), and modifications to the mother's thyroid hormones' peripheral metabolism. These metabolic alterations represent a transitional phase between preconception and pregnancy, necessitating enhanced hormonal output by the maternal thyroid gland.[3]

The thyroid gland grows by 10% in nations with plenty of iodine but by 20% to 40% in regions without iodine. Together with a corresponding 50% rise in the daily iodine requirement,

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there is a nearly 50% increase in the production of the thyroid hormones triiodothyronine (T3) and thyroxine (T4). While these physiological alterations occur naturally in healthy women, pathogenic mechanisms can induce thyroid dysfunction in many pregnant women.[4]

Five to twenty percent of women who are of childbearing age have thyroid autoimmune disease. Thyroid autoimmunity is linked to a higher risk of unfavorable pregnancy outcomes and impaired fetal neurodevelopment even in the absence of overt maternal thyroid dysfunction. According to available data, thyroid autoimmunity increases the risk of premature birth and miscarriage.[5] Recent research on thyroid disorders in pregnant women in India found that 5.6% of subjects had subclinical hypothyroidism, 3.5 percent had overt hypothyroidism, and 1.5% had subclinical hyperthyroidism.[6,7]

Immune system problems are linked to thyroid disease in a significant number of cases.[8] Anti-thyroperoxidase antibodies (TPOAbs) target thyroid mitochondrial peroxidase and are linked to psychiatric issues and postpartum thyroiditis. Anti-thyroglobulin antibodies (TGAbs) are useful indicators for thyroid cancer and goiter. Anti-thyroid stimulating hormone (TSH) receptor antibodies (TRAb) can cause hyperthyroidism and hypothyroidism. A third class of neutral anti-TSH receptor antibodies is now available.[9,10] Nearly half of pregnant women with subclinical hypothyroidism and over 80% of those with severe hypothyroidism have anti-thyroid antibodies found in them.[11] Nonetheless, some research indicates that they might exist in individuals with normal thyroid hormone and TSH levels.[12] Conversely, anti-peroxidase or anti-thyroglobulin antibodies have been documented in pregnancy, but they have not been linked to overt thyroid illness or subclinical hypothyroidism. Reports differ according to the various authors, with percentages varying from 2 to 20%.[11,13]

Anti-thyroid antibodies have separate negative effects on the mother and fetus during pregnancy and after delivery in addition to causing thyroid dysfunction. An all-over immune system activation in the placenta, the fetus-maternal unit, may be linked to chronic lymphocytic thyroiditis, a manifestation of immune system dysregulation. The mother and fetus's morbidities during pregnancy may be linked to this interference.[14]

Maternal problems such as miscarriage, anemia, pre-eclampsia, prenatal hypertension, placental abruption, premature delivery, and postpartum hemorrhage can be influenced by delivery methods. Thyroid dysfunction can lead to preterm birth, low birth weight, neonatal respiratory distress syndrome, perinatal morbidity, increased neonatal intensive care unit (NICU) admission, and neuropsychological and cognitive impairment. If untreated, children with congenital hypothyroidism may experience severe cognitive, neurological, and developmental issues.[15] This study aims to determine the frequency and impact of autoimmune thyroid disease on maternal and fetal outcomes in a tertiary care facility in Jharkhand. This study would aid in informed clinical decisions, improving pregnancy management for practitioners, and raising awareness among patients.

Materials and Method

An Observational Prospective Study was carried out with consecutive sampling. The duration of the study was 18 months. About 300 pregnant women were enrolled. According to the 2017 Guidelines for The American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and Postpartum, the prevalence of anti-TPOAb was taken as 17%. The sample size was determined by the formula 4PQ/d2, where Prevalence (P) = 17, Q = 100-P, i.e. 100 – 17 = 83, and Allowable error (d) = 5. Therefore, the sample size was 225.76. To increase the power of the study, the sample size was taken as 300. However, 46 patients were lost to follow-up so the final sample size was 254. The place of study was Rajendra Institute of Medical Sciences, Ranchi. Ethical clearance memo no. 92 IEC RIMS Dated-17.08.22.

Inclusion Criteria—Pregnant women in the second trimester. Exclusion Criteria—Women with multiple pregnancies, thyroid disorder, chronic diseases like diabetes mellitus, tuberculosis, chronic cardiac failure, chronic kidney disease, rheumatoid arthritis, etc., Routine testing of hematological parameters and estimation of FreeT3 (FT3), FreeT4 (FT4), TSH, and anti-TPOAbs were conducted. Patients were subsequently assessed for maternal and fetal complications.

Reference ranges used were those indicated by the 2017 guidelines of the American Thyroid Association: Normal TSH = 0.3500–4.9400 uIU/ml. Normal freeT4 level = 0.70–1.48 ng/dl. Normal freeT3 level = 1.58–3.91 pg/ml. Anti-TPO antibody was taken to be positive if the level was >35 IU/ml and negative if it was <35 IU/ml.

Statistical analysis was done by IBM SPSS Statistics for Windows, Version 26.0. Qualitative data was expressed in percentage and proportion using the Chi-square test and quantitative data was expressed by mean, median, and standard deviation, and appropriate tests of significance were used for further analysis.

Results

Out of the 254 patients who participated in this study, 87.4% of patients were anti-TPO antibody negative. 12.6% of patients were anti-TPO antibody positive [Table 1 and Figure 1].

Among anti-TPOAb negatives, 27.02% were urban and 72.98% were rural. Among anti-TPOAb positives, 21.87% were urban residents and 78.13% were rural residents [Table 2 and Figure 2].

Among anti-TPOAb negative patients, 71.17% were non-tribal and 28.83% were tribal. Among anti-TPOAb positives, 84.38% were non-tribal and 15.62% were tribal [Table 3 and Figure 3].

Most of the patients in both antibody-negative and antibody-positive groups were of the age group of 20 to 30 years. The earlier observations were statistically non-significant [Table 4 and Figure 4].

Patients from both antibody-positive and antibody-negative groups had a height of more than or equal to 1.45 m. The earlier finding was statistically non-significant [Table 5 and Figure 5].

Among antibody-negative patients, 32.43% were underweight, 67.57% had normal weight, and none were overweight. Among anti-TPOAb positives, 21.88% were underweight, 75% were of normal weight, and 3.13% were overweight. The earlier observations were statistically significant [Table 6 and Figure 6].

Among both anti-TPOAb positive and negative groups, the majority had TSH levels within the normal range and some had TSH levels above normal. The earlier observations were statistically non-significant [Table 7 and Figure 7].

Among anti-TPOAb negatives, 6.31% had FT3 levels below normal, 90.99% had levels within normal, and 2.70% had levels above normal. Among anti-TPOAb positives, 6.25% had FT3 values below normal, 90.62% had levels within normal,

Table 1: Frequency of anti-TPO antibody positivity within the sample

Variable	Number of patients (frequency)	Percentage	Mean±SD
Anti-TPO antibody levels (in IU/ml)			
Negative <35 IU/ml	222	87.4%	22.54±19.67
Positive >35 IU/ml	32	12.6%	
Total	254	100%	

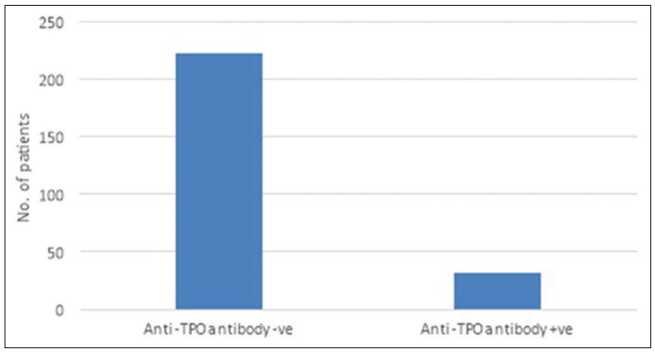

Figure 1: Frequency of anti-TPO antibody positivity within the sample

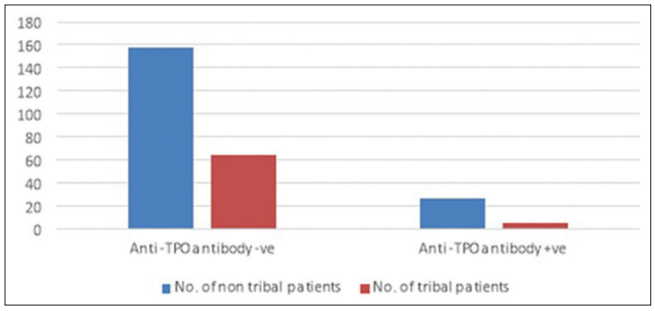

Figure 3: Distribution of the ethnicity of the patients with respect to their anti-TPO antibody status

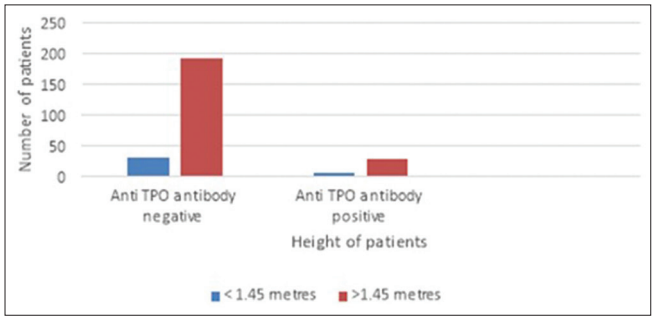

Figure 5: Distribution of the height of patients with respect to their anti-TPO antibody status

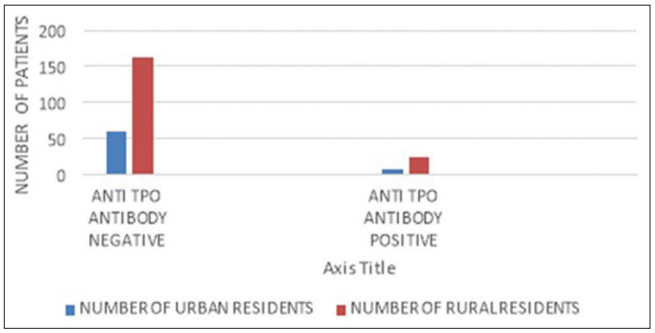

Figure 2: Distribution of rural and urban residents with respect to their anti-TPO antibody status

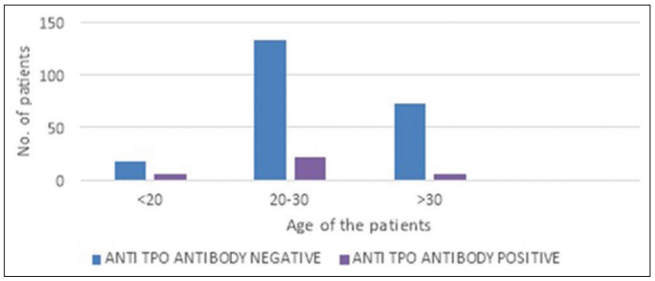

Figure 4: Distribution of the age of patients with respect to their anti-TPO antibody status

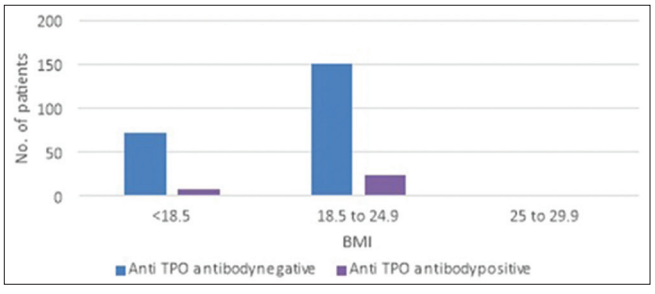

Figure 6: Distribution of the BMI of patients with respect to their anti-TPO antibody status

and 3.12% had levels above normal. The earlier findings were statistically non-significant [Table 8 and Figure 8].

Among anti-TPO antibody negatives, 6.31% had FT4 levels below normal, 91.89% had levels within normal, and 1.80% had levels above normal. Among anti-TPOAb negatives, 12.5% had FT4 levels below normal, 11.7% had levels within normal, and 84.38% had levels above normal. These observations were not statistically significant [Table 9 and Figure 9].

Among anti-TPOAb negatives, 4.50% had pre-eclampsia and 95.49% did not. Among anti-TPOAb positives, 6.25% had pre-eclampsia and 93.75% did not have pre-eclampsia. The earlier observations were statistically non-significant [Table 10 and Figure 10].

Among anti-TPOAb negatives, 96.85% did not have miscarriages and 3.15% had miscarriages. Among positives, 87.5% did not have a miscarriage and 12.5% had a miscarriage. The earlier observations were statistically significant, *P* value = 0.015 [Table 11 and Figure 11].

Among anti-TPO antibody negatives, 24.7% had newborns with birth weight <2.5 kg and 74.8% had normal birth weight (2.5–4.0 kg). Among anti-TPOAb positives, 31.3% had newborns with birth weight <2.5 kg and 65.6% had normal birth weight. The earlier observations were not significant [Table 12 and Figure 12].

Table 2: Distribution of rural and urban residents with respect to their anti-TPO antibody status

Variable	Anti-TPO antibody status	
	Negative	Positive
Number of urban Resident patients	60	7
Percentage (%)	27.02%	21.87%
Number of rural Resident patients	162	25
Percentage (%)	72.98%	78.13%
Total number of Patients	222	32
Percentage (%)	100%	100%

Table 3: Distribution of the ethnicity of the patients with respect to their anti-TPO antibody status

Variable	Anti-TPO antibody status	
	Negative	Positive
Number of non-tribal Patients	158	27
Percentage (%)	71.17%	84.38%
Number of tribal Patients	64	5
Percentage (%)	28.83%	15.62%
Total number of Patients	222	32
Percentage (%)	100%	100%

Table 4: Distribution of the age of patients with respect to their anti-TPO antibody status

Variable	Anti-TPO Status Antibody		Mean±SD
	Negative	Positive	
AGE (in years)			
<20			
Number of Patients	18	5	27.22±4.78
Percentage (%)	8.11%	15.62%	
20-30			
Number of Patients	132	22	
Percentage (%)	59.46%	68.75%	
>30			
Number of Patients	72	5	
Percentage (%)	32.43%	15.62%	
Total			
Number of Patients	222	32	
Percentage (%)	100%	100%	
χ^2=0.772[a]	*P*=0.380		

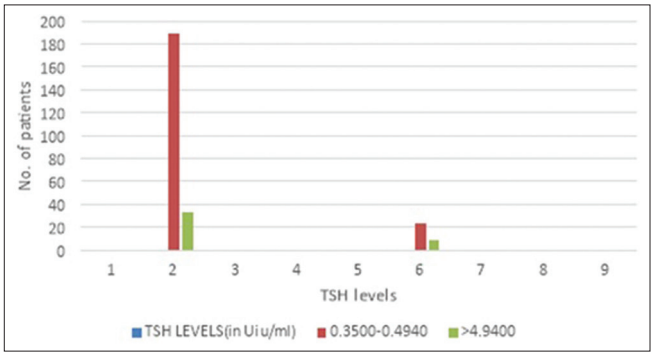

Figure 7: Distribution of the TSH levels with respect to anti-TPO antibody status of the patients

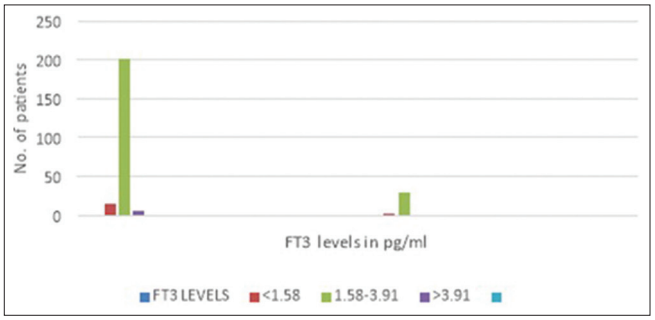

Figure 8: Distribution of the FT3 levels with respect to the anti-TPO antibody status of the patients

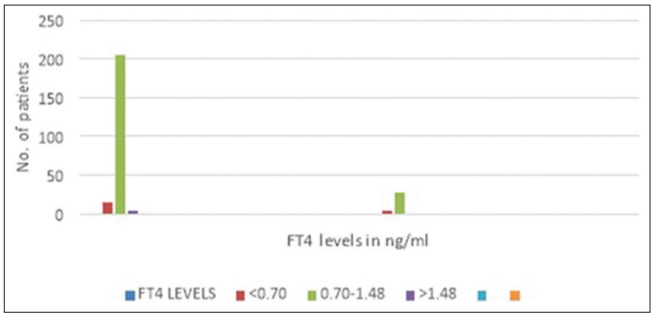

Figure 9: Distribution of the FT4 levels with respect to the anti-TPO antibody status of the patients

Among anti-TPOAb negatives, 31.5% had preterm births and 68.5% were term. Antibody positives had 31.3% preterm births and 68.8% term. The earlier observations were non-significant [Table 13 and Figure 13].

Among anti-TPOAb negatives, 16.7% had hemoglobin levels ≥11 g/dl and 83.3% had hemoglobin <11 g/dl. Among antibody positives, 50.0% had hemoglobin ≥11 g/dl and 50.0% had hemoglobin levels <11 g/dl. The earlier observation was very significant (*P* value = 0.00) [Table 14 and Figure 14].

Among antibody negatives, 3.3% had miscarriages, 88.3% had normal vaginal delivery, and 14.9% had cesarean section done. Among antibody positives, 6.3% had miscarriages, 75.0% had normal vaginal delivery, and 18.8% had cesarean section done. The earlier observations were statistically insignificant [Table 15 and Figure 15].

Discussion

In the present study, the frequency of anti-TPO antibody positivity was 32 (12.6%) among the study population. About 222 (87.4%) patients were anti-TPO antibody negative. Similar to the present study, Forough Saki *et al.*[16] in their prospective study on 600 pregnant women published in 2015 found that the prevalence of anti-TPO positivity is 12.8%.

In the Indian context, M.P.A. Sailakshmi *et al.*[17] stated in 2014 that their study group included 1000 pregnant women in Karnataka, India, and out of them, 126 women had hypothyroidism. Anti-TPO antibodies were positive in 26 women. Prevalence of autoimmunity was 12.8%. Raghunath Bhattacharyya *et al.*,[18] in their study published in 2015, found that 11.5% of the subjects were positive for anti-TPO-Ab. According to the 2017 Guidelines for The American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and Postpartum, the prevalence of anti-TPO antibodies in pregnancy is 2% to 17%.

Table 5: Distribution of the height of patients with respect to their anti-TPO antibody status

Variable	Anti-TPO Antibody status		Mean±SD
	Negative	Positive	
Height of the Patients (in meters)			
<1.45			
Number of Patients	30	4	
Percentage (%)	13.51%	12.5%	
>1.45			
Number of Patients	192	28	1.52±0.051
Percentage (%)	86.49%	87.5%	
Total			
Number of Patients	222	32	
Percentage (%)	100%	100%	
χ^2=0.0.025	*P*=0.875		

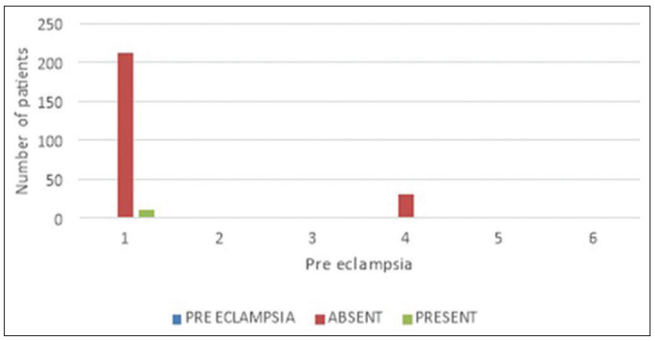

Figure 10: The occurrence of pre eclampsia in the patients with respect to their anti-TPO antibody status

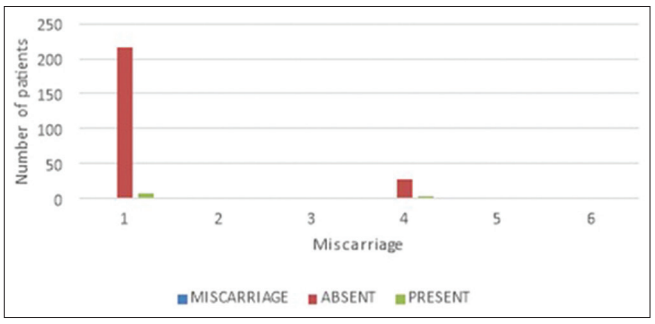

Figure 11: Distribution of the occurrence of miscarriage in the patients with respect to their anti-TPO antibody status

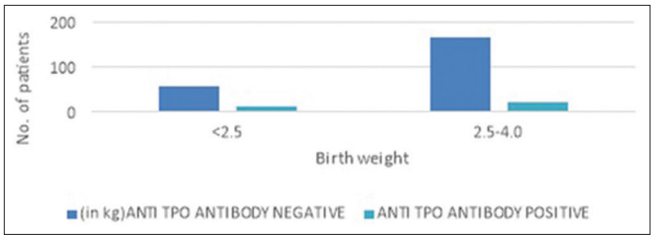

Figure 12: Distribution of the birth weight of the newborns with respect to the anti-TPO antibody status of the patients

Table 6: Distribution of the BMI of patients with respect to their anti-TPO antibody status

Variable	Anti-TPO Antibody Status				Mean±SD
	Negative	Percentage (%)	Positive	Percentage (%)	
BMI in kg/m^2					
<18.5	72	32.43%	7	21.88%	19.54±1.86
18.5-24.9	150	67.57	24	75%	
25.0-29.9	0	0%	1	3.13%	
Total number of Patients	222	100%	32	100%	
	χ^2=8.165[a]	*P*=0.017			

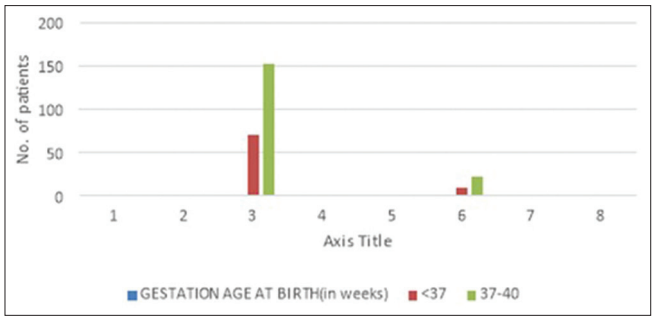

Figure 13: Distribution of the gestational age of newborns at delivery with respect to the anti-TPO antibody status of the patients

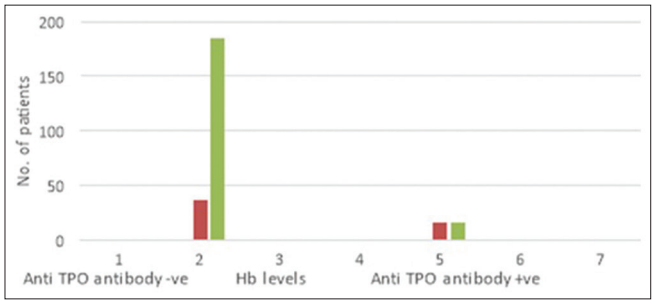

Figure 14: Distribution of the hemoglobin levels of the patients with respect to their anti-TPO antibody status

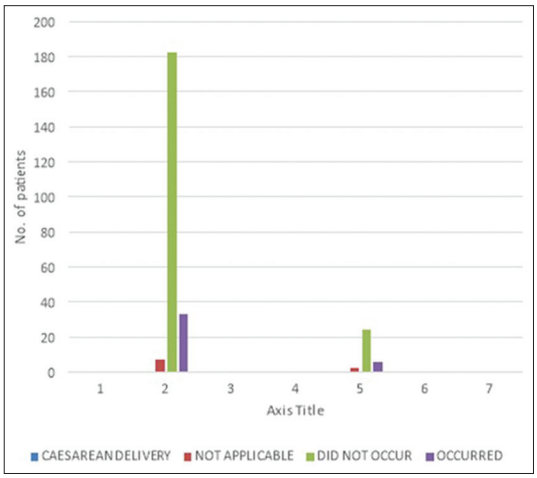

Figure 15: Distribution of cesarean delivery with respect to anti-TPO antibody status

According to Ratan Chandra Mandal *et al.*,[19] of their 510 subjects, 168 had TSH value >2.5 μIU/ml (32.94%) with normal FT4 and they were diagnosed as subclinical hypothyroidism. TSH level >4.5 μIU/ml was estimated in 13.92% of the subjects. TPO Ab was positive in 57 (33.93%) of subclinical hypothyroid and 5 (1.47%) of normal subjects.

In the present study, of the 222 patients who were anti-TPO antibody negative, 18 (8.11%) were less than 20 years old, 132 (59.46%) were 20–30 years old, and 72 (32.43%) were more than 30 years old. Of the 32 patients who were anti-TPO antibody positive, 5 (15.62%) were less than 20 years old, 22 (68.75%) were 20–30 years old, and 5 (15.62%) were more than 30 years old. Most of the patients in both antibody-negative and antibody-positive groups were of the age group of 20 to 30 years.

Table 7: Distribution of the TSH levels with respect to anti-TPO antibody status of the patients

Variable	Anti-TPO status Antibody		Mean±SD
	Negative	Positive	
TSH (in uIU/ml) levels (Uiu/ml)			
0.3500-4.9400			
Number of Patients	189	23	
Percentage (%)	85.13%	71.88%	
>4.9400			
Number of Patients	33	9	2.41±1.73
Percentage (%)	14.86%	28.13%	
Total			
Number of Patients	222	32	
Percentage (%)	100%	100%	
χ^2=3.563[a]		*P*=0.059	

Table 8: Distribution of the FT3 levels with respect to the anti-TPO antibody status of the patients

Variable	Anti-TPO status Antibody		Mean±SD
	Negative	Positive	
FT3 (pg/ml) levels (in pg/ml)			
<1.58			
Number of Patients	14	2	
Percentage (%)	6.31%	6.25%	
1.58–3.91			
Number of Patients	202	29	
Percentage (%)	90.99%	90.62%	
>3.91			
Number of Patients	6	1	2.49±4.24
Percentage (%)	2.70%	3.12%	
Total			
Number of Patients	222	32	
Percentage (%)	100%	100%	
χ^2=0.019[a]		*P*=0.991	

Table 9: Distribution of the FT4 levels with respect to the anti-TPO antibody status of the patients

Variable	Anti-TPO status Antibody		Mean±SD
	Negative	Positive	
FT4 levels (in ng/ml)			
<0.70			
Number of cases	14	4	
Percentage (%)	6.31%	12.5%	0.98±0.26
0.70–1.48			
Number of cases	204	27	
Percentage (%)	91.89%	11.7%	
>1.48			
Number of cases	4	1	
Percentage (%)	1.80%	84.38%	
Total			
Number of cases	222	32	
Percentage (%)	100%	100%	
χ^2=1.937[a]		*P*=0.380	

Table 10: Distribution of the occurrence of pre eclampsia in the patients with respect to their anti-TPO antibody status

Variable	Anti-TPO antibody status	
	Negative	Positive
PRE-eclampsia		
Absent		
Number of patients	212	30
Percentage (%)	95.49%	93.75%
Present		
Number of patients	10	2
Percentage (%)	4.50%	6.25%
Total		
Number of patients	222	32
Percentage (%)	100%	100%
χ^2=0.189[a]	*P*=0.663	

Table 11: Distribution of the occurrence of miscarriage in the patients with respect to their anti-TPO antibody status

Variable	Anti-TPO antibody status	
	Negative	Positive
Miscarriage		
Absent		
Number of patients	215	28
Percentage (%)	96.85%	87.5%
Present		
Number of patients	7	4
Percentage (%)	3.15%	12.5%
Total		
Number of patients	222	32
Percentage (%)	100%	100%
χ^2=5.898[a]	*P*=0.015	

Table 12: Distribution of the birth weight of the newborns with respect to the anti-TPO antibody status of the patients

Variables	Anti-antibody TPO Status		Mean±SD
	Negative	Positive	
Birth weight (in kg)			
<2.5			
Number of Patients	55	10	
Percentage (%)	24.7%	31.3%	2.96±2.05
2.5-4.0			
Number of patients	166	21	
Percentage (%)	74.8%	65.6%	
Total			
Number of patients	222	32	
Percentage (%)	100%	100%	
χ^2=5.898[a]	*P*=0.386		

Table 13: Distribution of the gestational age of newborns at delivery with respect to the anti-TPO antibody status of the patients

Variable	Anti-TPO antibody status	
	Negative	Positive
BIRTH (in		
<37 (preterm)		
Number of patients	70	10
Percentage (%)	31.5%	31.3%
37–40 (term)		
Number of patients	152	22
Percentage (%)	68.5%	68.8%
Total		
Number of patients	222	32
Percentage (%)	100%	100%
χ^2=0.001[a]	*P*=0.97	

Table 14: Distribution of the hemoglobin levels of the patients with respect to their anti-TPO antibody status

Variable	Anti-TPO antibody status		Mean±SD
	Negative	Positive	
Hemoglo Bin Levels (in G/dl)			
≥11			
Number of Patients	37	16	
Percentage (%)	16.7%	50.0%	
<11			
Number of Patients	185	16	10.59±1.66
Percentage (%)	83.3%	50.0%	
Total			
Number of Patients	222	32	
Percentage (%)	100%	100%	
χ^2=18.820[a]	*P*=0.00		

Table 15: Distribution of cesarean delivery with respect to anti-TPO antibody status

Variable	Anti-TPO status Antibody	
	Negative	Positive
Cesarean delivery		
Not applicable		
Number of patients	7	2
Percentage (%)	3.3%	6.3%
Did not occur		
Number of patients	182	24
Percentage (%)	88.3%	75.0%
Occurred		
Number of patients	33	6
Percentage (%)	14.9%	18.8%
Total		
Number of Patients (*n*=254)	222	32
Percentage (%)	100%	100%
χ^2=0.200[a]	*P*=0.549	

The mean age of all cases was 27.22 ± 4.78 years. The earlier observations were statistically non-significant (*P* value = 0.380).

Similar to the present study, Lata K *et al.*,[20] published a study in 2013 that they did in PGIMER Chandigarh. Pregnant and non-pregnant women between 21 and 35 years of age with a history of two or more consecutive miscarriages were included in the study. A third group comprising 100 pregnant women with a history of miscarriage was taken as healthy controls. Thyroid

autoimmunity was found (anti-TPO antibody positive) in 31% of the cases.

In the present study, of the 222 patients who were anti-TPO antibody negative, 189 had TSH levels within the normal ranges and 33 had TSH levels more than the normal range. Of the 32 patients who were anti-TPO antibody positive, 23 had TSH levels within the normal range and 9 had TSH levels above the normal range. Mean TSH levels for all patients was 2.41 ± 1.71, i.e. within the normal range. The earlier observations were statistically non-significant with a *P* value = 0.059. Of the 222 patients who were anti-TPO antibody negative, 14 (6.31%) had FT3 levels below the normal range, 202 (90.99%) had FT3 levels within the normal range, and 6 (2.70%) had FT3 levels above the normal range. Of the 32 patients who were anti-TPO antibody positive, 2 (6.25%) had FT3 values below the normal range, 29 (90.62%) had FT3 levels within the normal range, and 1 (2.70%) had FT3 levels above the normal range. The mean FT3 levels for all patients was 2.49 ± 4.24. The earlier findings were statistically non-significant with *P* value = 0.991 using the Chi-square test. Of the above 222 patients who were anti-TPO antibody negative, 14 (6.31%) had FT4 levels below the normal range, 204 (91.89%) had FT4 levels within the normal range, and 4 (1.80%) had FT4 levels less than the normal range. Of the 32 patients who were anti-TPO antibody positive, 4 (12.5%) had FT4 levels below the normal range, 27 (84.3%) had FT4 levels within the normal range, and 1 (3.13%) had FT4 levels above the normal range. The mean value of FT4 levels in all patients was 0.98 ± 0.26. The earlier observations were not statistically significant with a *P* value = 0.380 using the Chi-square test. Similar to the present study, Marwaha *et al.*[21] in the year 2008 conducted a study to establish the reference range for thyroid hormones in normal pregnant Indian women; five hundred and forty-one healthy pregnant women with uncomplicated single intrauterine gestations were selected from Armed Forces Clinic in any trimester and used electrochemiluminescence technique for estimation of FT3, FT4, TSH, and anti-thyroid antibodies (anti-thyroperoxidase (anti-TPO) and anti-thyroglobulin (anti-Tg)). Analysis of mean and median values for FT3, FT4, and TSH between each trimester showed no significant difference in FT3 and TSH values. However, in contrast to the present study, FT4 showed significant variation between trimesters with values decreasing with advancing gestational age (*P* value: first versus second = 0.015, first versus third = 0.003, and second versus third = not significant).

Sieiro Netto *et al.*[22] stated in 2004 that in their study on the influence of thyroid autoimmunity and maternal age on the risk of miscarriage, about 534 pregnant women, their ages ranging from 12 to 49 years were selected. Serum for peroxidase antibodies, TSH, and FT4 levels were measured. Of 534 women, 29 (5.4%) were TPO antibody positive. TSH levels were significantly higher in TPO antibody-positive women in contrast to the present study. There were no significant differences in FT4 levels, similar to the present study.

Similar to the present study, Ning Yuan *et al.*,[23] published their study in the year 2020. Nine hundred and thirty-eight pregnant women participated in this prospective cohort study. The euthyroid group included 837 pregnant women and the TPO Ab-positive group included 101 euthyroid pregnant women. Serum TPO Ab, thyroglobulin antibody (TGAb), thyroid-stimulating hormone (TSH), and free thyroxine (FT4) levels were assessed.

Effect of anti-TPO antibody on pregnancy and fetal outcomes included gestational diabetes mellitus, spontaneous abortion, premature rupture of membranes, hypertensive disorders of pregnancy, preterm birth, fetal distress, low birth weight, fetal macrosomia, and small for gestational age infants. Their results showed that TPO-Ab positivity was not associated with an increased risk of poor pregnancy or fetal outcomes in euthyroid women. However, TPO-Ab-positive euthyroid women pregnant with a female fetus were independently associated with preterm births (OR: 4.511, 95% CI: 1.075-18.926) after adjustment for potential confounding factors. They concluded that TPO-Ab positivity was not found to be associated with poor pregnancy-related or fetal outcomes in euthyroid women. Of the 222 patients, 215 (96.85%) did not have miscarriages and 7 (3.15%) had miscarriages. Of the 32 patients, 28 (87.5%) did not have a miscarriage and 4 (12.5%) had a miscarriage. The earlier observations were statistically significant with a *P* value = 0.015. Similar to the present study, R Wilson *et al.*[24] conducted a study published in 1999 on pregnant women in their first trimester who had a history of recurrent miscarriage and who were known to be positive for the thyroid peroxidase antibody. They concluded that at the time of presentation, thyroid peroxidase antibody titer was significantly higher in those women who later miscarried than those who continued to term. In contrast to the present study, A.F. Muller *et al.*,[25] in their prospective study, in the year 2000, measured levels of TPO antibodies and TSH. One hundred seventy-three women were observed, of whom 31% (54/173) became pregnant. Pregnancy occurred in 48% (12/25) of the antibody-positive women and in 28% (42/148) of the antibody-negative women. Among those who became pregnant, miscarriage occurred in 33% (4/12) of TPO antibody-positive women and in 19% (8/42) of TPO antibody-negative women. The TSH level was abnormal (<0.01), and birth weight tended to be lower. This study aimed to investigate the association between TPO-Ab positivity and pregnancy-related and fetal outcomes in euthyroid women. In the present study, of the 222 patients who were anti-TPO antibody negative, 70 (31.5%) had newborns at gestational age <37 (preterm) weeks and of the 32 anti-TPO positive patients, 10 (31.3%) had newborns at gestational age <37 (preterm) weeks. The earlier observations were non-significant with a *P* value = 0.97 using the Chi-square test. In contrast to the present study, Min Li *et al.*[26] studied 32 unique studies for their meta-analysis in 2017. Patients involved were divided into two groups: Group 1 (G1) and Group 2 (G2) comprising Asian and Caucasian populations, respectively. Positive thyroid antibodies were associated with the occurrence of preterm birth in both G1 and G2. They concluded that thyroid autoimmunity

may be a more favorable factor leading to preterm birth among pregnant women of different ethnicities, compared with thyroid dysfunction. Jane Cleary-Goldman *et al.*,[27] in 2006 stated that among 10,990 pregnant women, subclinical hypothyroidism was documented in 2.2% in the first and 2.2% in the second trimester. Hypothyroxinemia was documented in 2.1% in the first and 2.3% in the second trimester. Subclinical hypothyroidism was not associated with adverse outcomes. In the first trimester, hypothyroxinemia was associated with preterm labor. Fifteen percent (1,585 of 10,990) in the first and 14% (1,491 of 10,990) in the second trimester had anti-thyroid antibodies. When anti-TPO antibody was positive in either trimester, there was an increased risk for preterm premature rupture of membranes (P = .002) and P<.001, respectively. In the present study, of the 222 patients, 37 (16.7%) had hemoglobin levels ≥11 gm/dl and 185 (83.3%) had hemoglobin levels <11 gm/dl. Of the 32 patients, 16 (50.0%) had hemoglobin levels ≥11gm /dl and 16 (50.0%) had hemoglobin levels <11 gm/dl. The above observations were found to be significant with a p value= 0.00. Similar to the present study, Meena M *et al.*,[28] in the year 2016 conducted a study to assess the overall prevalence of anti-thyroid Peroxidase (anti-TPO) antibodies in pregnant women and the effect of anti-TPO positivity on the outcome of pregnancy in euthyroid women. One thousand Indian women, in their first trimester, were screened for anti-TPO antibodies to know the prevalence. Of this, euthyroid women who were positive for the presence of anti-TPO antibodies were selected and their obstetric history was recorded. These women were followed up and the incidences of maternal and fetal complications were recorded. The complications were compared with the past obstetric history and outcomes in parity and gestation-matched controls (anti-TPO negative). The conclusion was that anti-TPO positive euthyroid females had a higher prevalence of infertility, anemia as well as preterm delivery. In the present study, of the 222 people who were anti-TPO antibody negative, 7 (3.3%) had miscarriages, 182 (88.3%) had a normal vaginal delivery, and 33 (14.9%) had a cesarean section done. Of the 32 people who were anti-TPO antibody positive, 2 (6.3%) had miscarriages, 24 (75.0%) had a normal vaginal delivery, and 6 (18.8%) had cesarean section done. The earlier observations were statistically insignificant with a P value = 0.549 using the Chi-square test. In contrast to the present study, Forough Saki *et al.*[16] in their prospective study on 600 pregnant women published in 2015 found that cesarean section delivery was significantly higher in thyroid autoantibody-positive patients.

Conclusion

The study found that 12.6% of pregnant women had anti-TPO antibody positivity, which was significantly related to miscarriage and anemia. Other complications like preterm delivery, pre-eclampsia, and low birth weight were higher in anti-TPO antibody-positive patients. TSH levels were higher in anti-TPO antibody-positive women, but not statistically significant. FT3 and FT4 levels were mostly within the reference range. Further research is needed to understand the impact of anti-TPO positivity on feto-maternal outcomes and the need for regular screenings.

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Conflicts of interest

There are no conflicts of interest.

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