ORIGINAL RESEARCH PAPER

Gynaecology

A STUDY ON PREVALENCE OF THYROID PEROXIDASE ANTIBODIES PRETERM DELIVERIES, IUD AND RECURRENT PREGNANCY LOSS AT A TERTIARY CARE HOSPITAL, TAMILNDU, INDIA

KEY WORDS: Prevalence, TPO-Ab, IUD

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ABSTRACT

Background:
Thyroid peroxidase antibody (TPO-Ab) is associated with increased risk of adverse pregnancy outcomes. The present study was aimed to find out the prevalence of thyroid peroxidise antibodies (TPO-Ab) in the study population

Methods:
This cross sectional prevalence study was conducted on a total of 130 patients who had preterm deliveries, intra uterine deaths and miscarriages were included in the study for the period 8 months at a tertiary care hospital.

Results:
The prevalence of high TPO-Ab in the study population was 5.4%. The proportion of High TPO Ab was seen in women with preterm births followed by miscarriages and IUD of the study population.

Conclusions:
The association of TPOAb and TSH is strong and significant at p value is <0.000297 and it leads to developing hypothyroidism during pregnancy. The screening of TSH and TPOAb is essential during pregnancy to avoid complications related pregnancy.

INTRODUCTION:

Pregnancy has a profound impact on the thyroid gland and thyroid function. The gland increases 10% in size during pregnancy in iodine-replete countries and by 20% – 40% in areas of iodine deficiency. Production of thyroxine (T4) and triiodothyronine (T3) increases by 50%, along with a 50% increase in the daily iodine requirement. These physiological changes may result in hypothyroidism in the later stages of pregnancy in iodine-deficient women who were euthyroid in the first trimester. The range of thyrotropin (TSH), under the impact of placental human chorionic gonadotropin (hCG), is decreased throughout pregnancy with the lower normal TSH level in the first trimester being poorly defined and an upper limit of 2.5 mIU/L. Ten percent to 20% of all pregnant women in the first trimester of pregnancy are thyroid peroxidase (TPO) or thyroglobulin (Tg) antibody positive and euthyroid. Sixteen percent of the women who are euthyroid and positive for TPO or Tg antibody in the first trimester will develop a TSH that exceeds 4.0 mIU/L by the third trimester, and 33%–50% of women who are positive for TPO or Tg antibody in the first trimester will develop postpartum thyroiditis. In essence, pregnancy is a stress test for the thyroid, resulting in hypothyroidism in women with limited thyroidal reserve or iodine deficiency, and postpartum thyroiditis in women with underlying Hashimoto's disease who were euthyroid prior to conception. Thyroid peroxidase antibodies (TPO-Ab) are known to be associated with adverse pregnancy outcomes1,2. Although most pregnant women with elevated serum levels of TPO-Ab are clinically and biochemically euthyroid, they may be at increased risk for spontaneous abortion, preterm delivery, and placental abruption1-3. The exact mechanism of this association of adverse outcome with TPO-Ab positivity is unknown. TPO-Ab positivity is found in 5-10% of pregnant women and is associated with increased risk of developing thyroid dysfunction during pregnancy, after childbirth and in the postpartum period1-5. The, Indian Thyroid Association (ITA) recommends routine screening for thyroid dysfunction and thyroid antibodies ideally in preconception period but definitively during early pregnancy6. The present study was designed to find out the prevalence of thyroid peroxidise antibodies (TPO-Ab) in the preterm deliveries, IUD and miscarriage and to assess the co-morbidities associated with the presence of TPOAb in mothers with abnormal outcomes and to find out the association between TPOAB and mode of delivery that labour natural and C-section.

METHODS:

This was a cross sectional prevalence study, conducted in the Labour Ward & Post Natal Ward, Department of Obstetrics and Gynaecology, in collaboration with the Department of Endocrinology at a tertiary care hospital in Chennai. After taking informed written consent, all the 130 patients who had preterm deliveries, IUD, miscarriages irrespective of gestational age were recruited to study the prevalence of TPOAb positivity for a period of six months from January 2017 to August 2017. The sample size was calculated taking an anticipated prevalence of TPO-Ab as 9.3% and absolute margin of error as 5%, with 95% level of confidence. Before starting the study, clearance was taken from the Institutional Ethical Committee. All the subject pregnant women underwent T3, T4, serum TSH, serum TPO-Ab testing at term delivery. The serum TSH and TPO-Ab testing was done using ELISA technique. The TSH reference range taken in this study was 0.5-6μIU/ml, the T3 reference range taken in this study was 80-180ng/dl, the T4 reference range taken in this study was 4.6-12 ug/dl and TPO-Ab reference range taken was 7.6-27.6IU/ml. This was done by reducing 0.1mIU/L from the lower and 1.0mIU/L from the upper reference range of standard hospital reference laboratory values as per recommendation of American Thyroid Association (ATA) Guidelines (2011), and the higher pregnancy specific ranges reported in the Indian population7,8. A detailed history and examination was performed using a semi structured questionnaire with special regards to maternal age, gestational age, parity, gravida, height, weight and BMI etc. and routine blood investigation, thyroid profile and thyroid peroxidase antibodies

were also done for the study population.\

Inclusion Criteria:
Pregnant women of all ages, Both primi and multigravida,Both euthyroid and hypothyroid,Patients with preterm deliveries,Post Natal and postabortal women,First trimester abortions and recurrent pregnancy losses and Preterm and term IUD's.

Exclusion Criteria:
Preeclampsia,Diabetes,PROM, Antepartum haemorrhage, Infections, Incompetent cervix, and Uterine anomalies.

Statistical Analysis;
With the prevalence of TPOAb in pregnant women of 9.3% with an absolute margin of error as 5% at 95% confidence level, the prevalence of TPOAb among the preterm deliveries, IUD's miscarriages were analysed. And the associated co-morbidities were also analysed.

RESULTS:

Table 1: Age group wise study cases

AGE GROUP	FREQUENCY	%
15-19	13	10.0
20-24	73	56.2
25-29	35	26.9
30-34	5	3.8
35-39	4	3.1
40-44	0	0.0
TOTAL	130	100.0

The table 1 shows the age group wise study subjects. The mean age of the study population was 23.9 years. Most of the cases (56.2%) were in the age group between 20-24 years. 10% of the teenage pregnancy was noted among the study cases. 6.9% of preterm birth occurred in the age of more than 30 years in the study subject.

Table 2: Obstetric Score of the study cases

OBST.SCORE	FREQUENCY	%
G1P0	85	65.4
G2P1	1	0.8
G2P1L1	34	26.2
G2A1	1	0.8
G3A2	1	0.8
G3P1L1A1	3	2.3
G3P2L2	5	3.8
TOTAL	130	100.0

The table 2 shows the Obstetric scores of the study cases. Of the 130 cases,85 (65.4%) were primi , 37 cases (28.5%) were had one child, 5 cases (3.8%) were had two living children. Similarly, most of them (65.4%) were in gravida 1 followed by 27.7% in gravdia 2 and rest 6.9% were in gravida 3 was noted.

Table 3: Out Come of Pregnancy / Mode of delivery

Out Come of Pregnancy / Mode of delivery	Nos.	%
Labour Natural	80	61.5
C- Section (LSCS)	11	8.5
Abortion	19	14.6
IUD	20	15.4
Total	130	100.0

The table 3 shows the outcome pregnancy / mode of delivery. Out of 130 cases 80 were labour natural, 11 were LSCS, 19 were abortions and 20 were IUD.

Table 4: Serum Blood Results of the study cases

GROUP	CATEGORY				Total
	T3	T4	TSH	TPOAb	
HIGH	25 (19.2%)	4 (31.5%)	17 (13.1%)	7 (5.4%)	90
LOW	2 (1.5%)	4 (3.1%)	13 (10.0%)	118 (90.7%)	137
NORMAL	103	85	100	5	293
TOTAL	130	130	130	130	520

The chi-square statistic is 389.8972. The p-value is < 0.00001. The result is significant at p < .05 & .01.The table value for chi-square at 0.05 and 0.01 and d.f. = 6 is 12.59 and 16.81

The table 4 shows the blood results of T3, T4, TSH and TPOAb among the study cases. It revealed that 5.4% were positive cases of thyroid peroxidase antibodies found in the study cases. Similarly, the abnormal results of T3,T4 and TSH were found as 19.2%, 31.5% and 13.1% respectively. There exists a strong association between the results of serum blood that high & low and normal categories of thyroid namely T3,T4,TSH and TPOAb and statistically significant. The p- value is <0.00001.

Table 5: Statistical data of Thyroid hormones and enzymes in study subjects

Variables	N	Min.	Max.	Mean	Std. Deviation	Median
TPOAB	130	0	1000	19.58	124.23	0.37
T3	130	67.24	298.6	144.24	40.11	139.1
T4	130	2.86	18.19	10.41	3.06	9.69
TSH	130	0.08	27.97	3.06	3.85	1.9

Table 6: Association of T3,T4 and TSH in TPOAb.

HORMONES		TPOAB		Test
VARIABLE	RESULT	HIGH	NORMAL	
T3	HIGH	0	25	-
	NORMAL	5	98	
	LOW	2	0	
T4	HIGH	0	41	-
	NORMAL	7	80	
	LOW	0	2	
TSH	HIGH	4 (57.1%)	11	Chi-square test The p-value is 0.000297
	NORMAL	3(42.9%)	99	
	LOW	0	13	-
	Total	7 (100%)	123	

The table 6 shows the results of TPOAB with T3, T4 and TSH among the study subject. We found that there exist a strong association between TSH and TPOAB that High and Normal in the study subject and statistically significant at 5% and 1% level of significance. The p-value is 0.000297.

Table 7: Results of TPOAb and Outcome of pregnancy

Results TPO Ab	Preterm birth	IUD	miscarriages	Total
High	5(3.8%)	1(0.8%)	1 (0.8%)	7(5.4%)
Low and Normal	86	19	18	114
Total	91 (70.0%)	20(15.4%)	19 (14.6%)	130(100.0%)

The table 7 shows the results of TPOAb in foetal outcome that IUD and miscarriages and preterm birth. It revealed that 5.4% was foetal outcome of pregnancy due to the presence of high TPO antibodies in the study subject.

Table 8: Mode of Delivery and TPOAB results

MODE	TPOAB		Total	Chi-Square Test
	HIGH	NORMAL		
LN	4 (5%)	76 (95%)	80 (100%)	p-value 0.000038 at 5% l.o.s.
LSCS	1 (9.1%)	10 (90.9%)	11 (100%)	
ABORTION	1 (5.3%)	18 (94.7%)	19 (100%)	p-value 0.970293 at 5% l.o.s. not significant
IUD	1 (5%)	19 (95%)	20 (100%)	
Total	7 (5.4%)	114 (87.4%)	130 (100%)	

The table 8 shows the mode of delivery, foetal outcome of pregnance and TPOAb results. Out of 130 cases TPOAB results were high in 4 labour natural, 1in LSCS, 1 in abortion and 1 in IUD was noticed. We found that there exist an association between TPOAB and Mode of delivery that Labour natural , C section and statistically significant at 5% level of significance and the p-value is 0.000038.

Table 9 Age Group wise TPOAB Results

AGE GROUP (in years)	TPOAB		Total
	HIGH	NORMAL	
15-19	0	13	13
20-24	1	72	73
25-29	4	31	35
30-34	0	5	5
35-39	2	2	4
40-44	0	0	0
Total	7	123	130

The table 9 shows the results of TPOAB and age group. Out of 130 cases 7 had high TPOAB. There was no high TPOAB in teenage group but two cases were had high TPOAB in (35-39) age group and rest of them was seen in age group (20-29).

DISCUSSION:

The prevalence of High TPO-Ab in pregnant women observed in the present study was 5.4%. This observation is similar to Negro et al and Ghafoor et al who observed a prevalence of 11.7% and 11.2%, in euthyroid pregnant Italian and Pakistani women respectively2,3. Similarly, Gulati K et al who repoted TPO positivity in 11.3% of pregnant euthroid women9 . Similarly, Ijima et al who reported TPO positivity in 10.6% of pregnant euthyroid Japenese women10 Haddow et al also reported TPO positivity in 12.9% euthyroid American pregnant women11. However the observation differs from those reported by Gayathri et al and Ghanavati et al who found a lower prevalence of TPO-Ab positivity in euthyroid pregnant women1,12. In a systematic review and meta-analyses of published literature by Thangaratinam et al the reported prevalence of TPO-Ab in euthyroid pregnant women varied between 5.4% and 31%13. In the present study nearly 4.6% of thyroid peroxidase antibody positive women, the TSH levels at term/delivery had crossed the upper limit of the euthyroid range >5.22µml/l. In Contradiction, in Gulati K et al who repoted 18.61% of thyroid peroxidase antibody positive women, the TSH levels at term/delivery had crossed the upper limit of the euthyriod range (>5.2µml/l) as compared with thyroid peroxidase antibody negative women, the difference was statistically significant, p=0.029. Glinoer et al found that the progression of pregnant women to subclinical hypothyroidism can be predicted by the serum TSH levels and TPO-Ab titres in the first trimester. They also recommended the use of these parameters to identify high risk women and advised for close monitoring of thyroid functions of these women and administration of L-thyroxine to the selected cases14. Negro et al reported development of hypothyroidism at term in 19% of euthyroid TPO-Ab positive women. Their study suggested that the women who are TPO positive and euthyroid in early pregnancy carry a significant risk of developing hypothyroidism with progressing gestation, despite a marked reduction in antibody titres. They found progressive increase in the serum TSH concentration of euthyroid TPO positive women, from a mean of 1.7 mIU/L at 12th week to 3.5 mIU/L at term2. We also observed increased in mean serum TSH level to 3.06 mIU/L at term/delivery. The results of the present study are in accordance with the previous studies and confirm that the requirement of thyroid hormones increase with advancing gestation. We observed that the overall caesarean section rates in the TPO-Ab high and labour natural were 9.1% and 5.0% respectively. However, the overall incidence of foetal distress was found lesser (abortion 1, IUD 1) in the TPOAb high women in the study subject as compared to the normal TPO Ab group (Abortion – 18, IUD - 19). Negro et al reported a higher incidence of miscarriage amongst TPO positive euthyroid women as compared to TPO negative women, 3.8% and 2.4%, respectively, p<0.01. In the present study, the incidence of miscarriage amongst TPO high women (1 of 19) compared to TPOAb normal women (1 of 20) were same to 0.8%. The difference in our observation is probably because of smaller size of the present study. Besides, in the study by Negro et al, all the miscarriages in the TPO positive group and most (19 of 20) in the TPO negative group occurred during the first trimester2. However, in the present study the mean gestational age at presentation to the term delivery was in third trimester, < 37 weeks, in study subjects and by this time most of the miscarriages would had already occurred. Author had one case of IUD in the TPO Ab high group and 19 in the TPO Ab Normal group. There was no case of stillbirth/NND in either of the groups. Ghanavati et al and Negro et al also did not find any association of stillbirth/NND with TPO positivity, whereas Mannisto et al observed 2 to 3 fold greater perinatal mortality in the infants of thyroid autoantibody-positive mothers[1,15,16].

CONCLUSION:

The present study stated the prevalence of TPOAB positivity was 5.4% among the study subjects and the presence of TPOAB high was noticed in the age group (20-29) and (35-39) except in teenage (15-19), (30-34) and (40-44) age groups. It was noticed that the association of TPOAB with TSH was strong and statistically significant and the p value was <0.000297. Besides, it was found that there exists an association between Mode of delivery and TPOAB in the study subject and statistically significant at p-value <0.000038. The TPOAB positivity was noted in the hypothyroid patient, as in previous studies. Therefore, the screening of TSH and TPOAB during pregnancy is important to find the subclinical hypothyroidism and to prevent its complication like preterm birth, IUD, and abortions.

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