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Original Research Article

Study of prevalence of thyroid peroxidase antibodies in preterm deliveries and recurrent pregnancy loss

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ABSTRACT

Background: Evaluation of thyroid disorder in pregnancy is essential for maternal health, obstetrical outcome and neurodevelopment of the child. Euthyroid pregnant women having positive thyroid peroxidase antibodies have an elevated risk of miscarriage, premature birth, gestational hypertension, and intrauterine fetal demise. Thyroid autoimmunity (TAI) and subclinical hypothyroidism (SCH) have been connected with adverse outcomes in pregnancy and foetus. The present aim of the study was to estimate the prevalence of TPO antibodies in recurrent pregnancy losses, first trimester abortions and preterm deliveries.
Methods: This was a hospital-based cross-sectional prevalence study conducted for 18 months. The study consists of 100 women who had preterm deliveries and miscarriages attending to department of obstetrics and gynaecology, Narayana medical college and hospital, Nellore, Andhra Pradesh.
Results: In our study out of 100 cases, 11 had high thyroid peroxidase antibody (TPOAb) levels, of which 9 had preterm deliveries and 2 had miscarriages. Out of 100 cases 5 cases had elevated T_3 levels, 6 cases had elevated T_4 levels and 24 cases had elevated TSH levels.
Conclusions: There was a statistically significant association of thyroid peroxidase antibodies (TPOAb) with T_3, T_4, and, TSH ($P<0.05$) and it leads to developing hypothyroidism during pregnancy. The presence of TPOAb in pregnant women significantly increases the risk of preterm delivery. The screening of TSH and thyroid peroxidase antibodies is essential during pregnancy to avoid complications. So, screening T_3, T_4, TSH and thyroid peroxidase antibodies are essential during pregnancy to avoid complications.

Keywords: Preterm, Recurrent pregnancy loss, Thyroid peroxidase antibodies

INTRODUCTION

Structural and functional changes in thyroid gland are common in pregnancy to reach the requirements of mother and foetus, but they are reversible. Abnormal thyroid hormone levels could give rise to increased placental insufficiency and adverse obstetric outcomes such as fetal brain damage, preterm births, and fetal death.[1]

The most frequent unfavourable event in early pregnancy is a miscarriage. Thyroid autoantibodies have a role in these regions and have been linked to substantial changes in the path of pregnancy that affect the mother, foetus, and newborn.[2]

Anti-TPO antibodies are autoantibodies directed against thyroid peroxidase protein that belong to the IgG immunoglobulin class. These antibodies are found in people who have thyroid malfunction (hypothyroidism or hyperthyroidism), but also noticed in healthy people.[3]

Thyroid antibody positivity has been linked to a variety of negative pregnancy outcomes, that comprises of spontaneous miscarriage, recurrent loss of pregnancy, and premature birth.[4]

Although it is widely acknowledged that overt hypothyroidism is harmful to pregnant woman's health, new research suggests that subclinical hypothyroidism may have an impact on maternal and foetal health. Studies reveal a link with miscarriage and preterm delivery in euthyroid women having anti-thyroglobulin antibodies, anti- peroxidase antibodies.[5]

Evaluation of thyroid disorder in pregnancy is important for maternal health, obstetrical outcome and neuro development of the child. Euthyroid pregnant women having a positive thyroid peroxidase antibody have an elevated risk of miscarriage, premature birth, gestational hypertension, and intrauterine fetal demise.

Thyroid autoimmunity (TAI) and subclinical hypothyroidism (SCH) have been connected with adverse outcome in pregnancy and fetus.[6]

Aims and objectives

The aim of the present study was to estimate the prevalence of TPO antibodies in recurrent pregnancy losses, first trimester abortions and preterm deliveries.

The objectives of the present study were to analyse the abnormal consequences linked with the presence of TPOAb in mothers, to examine the connection between the presence of TPOAb and unfavourable outcome in pregnancy, to understand the association of TPOAb and Overt and subclinical hypothyroidism, the importance of screening of thyroid function during pregnancy and prevent the poor fetomaternal outcomes.

METHODS

This was a hospital based cross-sectional prevalence study conducted for a period of 18 months i.e., from October 2019 to March 2021.

The study consists of 100 women who had preterm deliveries, miscarriages attending outpatient as well as admitted in the antenatal ward and postnatal ward in the department of obstetrics and gynaecology, Narayana Medical College and Hospital.

The study group was comprised of all the pregnant women who had preterm deliveries and miscarriages regardless of the gestational age, that is fulfilling inclusion and exclusion criteria. Written informed consent were taken from all the patients participating in the study. They were subjected to a detailed history and thorough general and clinical examination, lab investigations, thyroid profile, thyroid peroxidase antibody testing (normal range: TPO AB <9 IU/ml), ultra-sonic examination and other clinical work up were done. The study showed that the contribution of thyroid peroxidase antibody testing and its sensitivity determining risk of preterm deliveries and recurrent pregnancy loss.

Inclusion criteria

Both primi and multigravida, both euthyroid and hypothyroid women, patients with preterm deliveries, first trimester abortions and recurrent pregnancy loss.

Exclusion criteria

Patients with premature rupture of membranes, infections, preeclampsia, multiple pregnancy, incompetent cervix, uterine anomalies, antepartum haemorrhage, diabetes.

RESULTS

In a total of 100 patients, the range of age was 19 years to 37 years and the overall mean±SD age (years) was 24.07±3.72 years. According to age group, 7 (7.0%) patients had age less than 20 years, 28 (28.00%) patients had between 20 to 22 years, 38 (38.00%) patients had. age between 23 to 25 years, 19 (19.00%) patients had age between 26 to 28 years, and 8 (8.00%) patients had age more than 28 years (Figure 1).

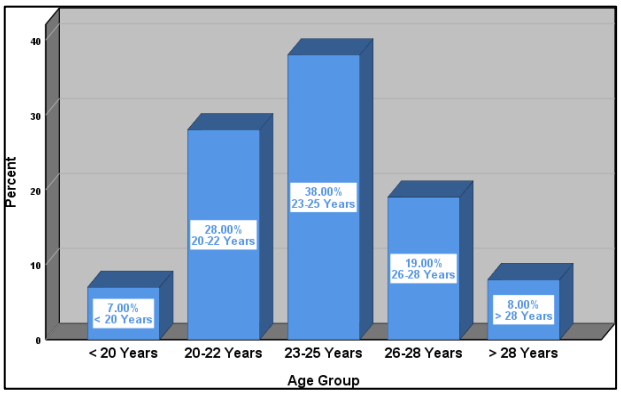

Figure 1: Distribution of age groups in the present study.

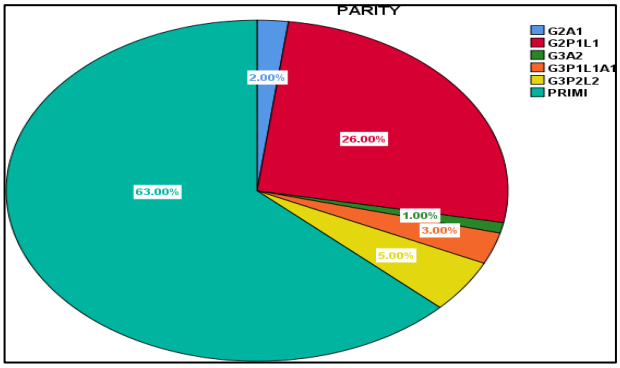

Figure 2: Distribution of parity in the present study.

In a total of 100 patients, 63 (63.00%) patients were primi, 26 (26.00%) patients were $G_2P_1L_1$, 2 (2.0%) patients were G_2A_1, 01 (1.00%) patients were G_3A_2, 03 (3.00%) patients were $G_3P_1L_1A_1$, and 05 (5.00%) patients were $G_3P_2L_2$ respectively (Figure 2).

Out of 100 pregnant women, 63 (63.00%) were primi gravida, 37 (37.00%) were multi gravida. Out of 34 cases of parity, 29 (85.29%) were para-1 and 5 (14.7%) were para-2.

In a total of 100 cases of their mode of delivery, 16 (16.00%) cases had abortions, and 3 (3.00%) were IUD, 62 (62.00%) cases were normal delivery (LN), and 19 (19.00%) were caesarean delivery (LSCS) (Table 1).

Table 1: Mode of delivery in the present study.

Mode of delivery	Number	Percentage
LN	62	62.00
LSCS	19	19.00
Abortion	16	16.00
IUD	3	3.00
Total	100	100.00

The mean of TPO AB was 26.92±141.68, the mean of T_3, T_4 and TSH was 139.17±35.56, 9.78±2.27, and 3.15±3.56 respectively.

Table 2: TPOAB classification in the present study.

TPOAB grade	Number	Percentage
High (>9 IU/ml)	11	11.00
Normal (<9 IU/ml)	89	89.00
Total	100	100.00

According to TPOAB classification (n=100), 11 (11.00%) cases had high TPOAB (+ve), and 89 (89.00%) were normal TPOAB (-ve) (Table 2).

According to T_3 classification (n=100), 5 (5.00%) cases had high in T_3 level, 92 (92.00%) had normal in T_3 level, and 3 (3.00%) cases had low in T_3 level.

According to T_4 classification (n=100), 6 (6.00%) cases had high in T_4 level, 91 (91.00%) had normal in T_3 level, and 3 (3.00%) cases had low in T_4 level.

According to TSH classification (n=100), 24 (24.00%) cases had high in TSH level, 68 (68.00%) had normal in TSH level, and 8 (8.00%) cases had low in TSH level.

Table 3: Mode of deliveries in high TPOAB groups.

Categories	High TPOAB	Total
Preterm deliveries	9	81
IUD	0	3
Miscarriage	2	16
Total	11	100

The mode of deliveries in high in TPOAB (n=11), 6 cases were preterm birth, 3 cases were term deliveries, and 2 cases were miscarriage (abortions) (Table 3).

The association between TPOAB and age group, among the high TPOAB (+ve) cases (n=11), 4 (36.4%) cases had age between 20 to 22 years, one (9.1%) case has age between 23 to 25 years, 5 (45.5%) cases had 26 to 28 years, and one (9.1%) case has age more than 28 years. Whereas in the normal TPOAB (-ve) group (n=89), 7 (7.9%) cases had age less than 20 years, 24 (27.0%) cases had age between 20 to 22 years, 37 (41.6%) cases had age 23 to 25 years, 14 (15.7%) cases had age between 26 to 28 years, and, 7 (7.9%) cases had age more than 28 years. The association between age group and TPOAB was shown statistically not significant (p=0.076).

Among the high TPOAB (+ve) cases (n=11), 5 (45.5%) cases had gravida-1, and, 6 (54.5%) cases had gravida-2. Whereas in the normal TPOAB (-ve) group (n=89), 58 (65.2%) cases had gravida-1, 22 (24.7%) cases had gravida-2, and, 9 (10.1%) cases had gravida-3. The association between TPOAB and gravida was shown statistically not significant (p=0.09).

The association between TPOAB and classification of parity, in a total of 34 cases, among them 6 (17.6%) cases had TPOAB (+ve) cases, and 28 (82.4%) were TPOAB (-ve) cases. Among the high TPOAB (+ve) cases (n=6), 6 (100.00%) cases had parity-1, whereas in the normal TPOAB (-ve) group (n=28), 23 (82.1%) cases had parity-1, and 5 (17.9%) cases had parity-2. The association between TPOAB and classification of parity was shown statistically not significant (p=0.262).

The association between TPOAB and mode of delivery, among the high TPOAB (+ve) cases (n=11), 2 (18.2%) cases had abortions, 7 (63.6%) cases had normal delivery (LN), and, 2 (18.2%) cases had caesarean delivery (LSCS). Whereas in the normal TPOAB (-ve) group (n=89), 14 (15.7%) cases had abortions, 3 (3.4%) cases had IUD, 55 (61.8%) cases had normal delivery (LN), and, 17 (19.1%) cases had caesarean delivery (LSCS). The association between TPOAB and mode of delivery was shown statistically not significant (p=0.937).

The association between TPOAB and T_3 category, among the high TPOAB (+ve) cases (n=11), 8 (72.7%) cases had normal level of T_3, and, 3 (27.3%) cases had low level of T_3. Whereas in the normal TPOAB (-ve) group (n=89), 5 (5.6%) cases had high level of T_3, 84 (94.4%) cases had normal level of T_3. The association between TPOAB and T_3 category was shown statistically significant (p<0.0001).

The association between TPOAB and T_4 category, among the high TPOAB (+ve) cases (n=11), 9 (81.8%) cases had normal level of T_4, and, 2 (18.2%) cases had low level of T_4. Whereas in the normal TPOAB (-ve) group (n=89), 6 (6.7%) cases had high level of T_4, 82 (92.1%) cases had normal level of T_4, and 1 (1.1%) case had low level of T_4. The association between TPOAB and T_4 category was shown statistically significant (p=0.006).

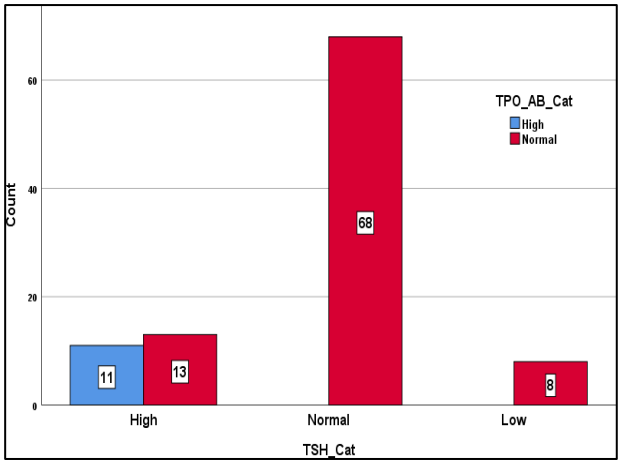

Figure 3: Association between TPOAB and TSH group.

The association between TPOAB and TSH category, among the high TPOAB (+ve) cases (n=11), 11 (100.0%) cases had high level of TSH. Whereas in the normal TPOAB (-ve) group (n=89), 13 (14.6%) cases had high level of TSH, 68 (76.4%) cases had normal level of TSH, and 8 (9.0%) cases had low level of TSH. The association between TPOAB and TSH category was shown statistically significant (p<0.0001) (Figure 3).

The mean difference of age was higher (25.73±4.67 years) in TPOAB (+ve) cases (n=11) that the normal TPOAB (-ve) group (n=89) (23.87±3.56 years). The mean difference between TPOAB group for age was shown statistically not significant (p=0.118).

The mean difference of T_3 was higher (141.94±33.41) in normal TPOAB (n=89) than the high TPOAB group (n=11) (116.79±45.54). The mean difference between TPOAB group for T_3 was shown statistically significant (p=0.026).

The mean difference of T_4 was higher (9.98±2.17) in normal TPOAB (n=89) group than the high TPOAB group (n=11) (8.11±2.47). The mean difference between TPOAB group for T4 was shown statistically significant (p=0.009).

The mean difference of TSH was higher (10.08±5.94) in high TPOAB (n=11) group than the normal TPOAB group (n=89) (2.29±1.87). The mean difference between TPOAB group for TSH was shown statistically significant (P=0.001) (Table 4).

Table 4: Comparison of mean difference between TPOAB groups for TSH.

TPO AB category		N	Mean	SD	Std. error mean	t-value	P value
TSH	High	11	10.08	5.94	1.79	4.321	0.001
	Normal	89	2.29	1.86881	0.199		

DISCUSSION

A high thyroid-stimulating hormone level without indications or symptoms of hypothyroidism and a normal thyroxin level is referred to as subclinical hypothyroidism. Although it is widely acknowledged that overt hypothyroidism is harmful to a pregnant woman's health, new research suggests that subclinical hypothyroidism may have an impact on maternal and foetal health. Studies show a relationship between miscarriage and premature delivery in euthyroid women with anti-peroxidase antibodies and/or anti-thyroglobulin antibodies.[5]

The most common negative consequence in early pregnancy is miscarriage. Thyroid autoantibodies play a role in both of these areas, and they're linked to significant changes in the mother, foetus, and new born during pregnancy.[2]

Thyroid autoantibodies in euthyroid women can lead to miscarriages and pre-eclampsia, among other issues. Women with hypothyroidism have a greater risk of anaemia, infertility, and preterm birth. Women with antithyroid antibodies have been found to suffer spontaneous miscarriages. This can be used as an additional indicator of the mother's immune system failure.[3]

Recurrent miscarriage (RM) and poor pregnancy outcomes have been linked to thyroid hormone insufficiency during pregnancy. Thyroid associated autoimmunity (TAI) is the most common cause of thyroid dysfunction, defined by a significantly higher serum level of thyroid-stimulating hormone (TSH) than in women without thyroid autoimmune. TAI is linked to an increased risk of miscarriage, and the incidence of TAI in women with RM is higher than in women who are normally fertile.[7]

Prevalence

When compared to a pregnant woman in good health control population, the prevalence of thyroid autoimmunity was greater in pregnant women with a history of recurrent abortion.[8]

In our study, in TPOAb (+), 9% of cases had preterm labour.

From the recent study of a meta-analysis which was conducted by Yadav et al, the pooled estimate of the prevalence of hypothyroidism among pregnant women in

India was 11.07%.[9] In the present study, the prevalence of TPO Ab (+ve) cases was 11%.

In a study of Meena et al, the prevalence of anti-TPO positivity was 11%, 13.9% in a retrospective cohort study of Vissenberg et al.[10,11]

From this, it was observed that our study is coincides with the study of Yadav at al.[9]

In a study of Lata et al, in TPOAb (+), 3% of cases the preterm labour.[8]

In a study of Meena and Nagar, 5% of cases had preterm deliveries in in anti-TPO Ab+ women.[12]

In a study of Castillo et al, the prevalence of subclinical hypothyroidism was 9.6%.[5]

Comparison of the current research with other researches

In this study, a total of 100 patients, the range of age was 19 years to 37 years and the overall mean±SD age (years) was 24.07±3.72 years. According to age group, 7 (7.0%) patients had age less than 20 years, 28 (28.00%) patients had between 20 to 22 years, 38 (38.00%) patients had age between 23 to 25 years, 19 (19.00%) patients had age between 26 to 28 years, and 8 (8.00%) patients had age more than 28 years.

In this study, in a total of 100 patients, 63 (63.00%) patients had primi, 26 (26.00%) patients had $G_2P_1L_1$, 2 (2.0%) patients had G2A1, 26 (26.00%) patients had $G_2P_1L_1$, 01 (1.00%) patients had G_3A_2, 03 (3.00%) patients had $G_3P_1L_1A_1$, and 05 (5.00%) patients had $G_3P_2L_2$ respectively.

In this study, out of 100 pregnant women, 63 (63.00%) were primi gravida, 37 (37.00%) were multi gravida.

In this study, out of 34 cases of parity, 29 (85.29%) were para-1 and 5 (14.7%) were para-2.

In this study, in a total of 100 cases of their mode of delivery, 16 (16.00%) cases had abortions, and 3 (3.00%) were IUD, 62 (62.00%) cases were normal delivery (LN), and 19 (19.00%) were caesarean delivery (LSCS).

In this study, according to TPOAB classification, 11 (11.00%) cases had high TPOAB (+ve), and 89 (89.00%) were normal TPOAB (-ve).

In a study of Rajput et al, TPO antibody positive (18.9%) and TPO antibody negative (81.1%).[13]

In this study, according to T_3 classification, 5 (5.00%) cases had high in T_3 level, 92 (92.00%) had normal in T_3 level, and 3 (3.00%) cases had low in T_3 level.

In this study, according to T_4 classification, 6 (6.00%) cases had high in T_4 level, 91 (91.00%) had normal in T_3 level, and 3 (3.00%) cases had low in T_4 level.

In this study, according to TSH classification, 24 (24.00%) cases had high in TSH level, 68 (68.00%) had normal in TSH level, and 8 (8.00%) cases had low in TSH level.

In this study, out of 11 cases of high in TPOAB, 6 cases were preterm deliveries, and, two cases were miscarriage (abortions).

CONCLUSION

Thyroid hormone is crucial for the early development of the placenta during pregnancy. The foetus completely depends on the maternal thyroid hormone for optimal neural and skeletal development, especially during the first twelve weeks of pregnancy.

There was a statistically significant association of TPOAb with T_3, T_4, and, TSH ($P<0.05$) and it leads to hypothyroidism during pregnancy.

The presence of TPO-Ab in pregnant women significantly increases the risk of preterm delivery. The screening of TSH and TPOAb is essential during pregnancy to avoid complications related pregnancy. So, the screening of thyroid and TPOAb is essential during pregnancy to avoid complications related pregnancy.

In patients with recurrent miscarriage and if all the other work up for recurrent pregnancy loss have turned out to be negative then tests for detecting anti TPO should be considered even with normal TSH levels. And if anti TPO antibodies turns out to be positive, treatment with Tablet levothyroxine can be considered.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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