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Original Research Article

ANTITHYROID PEROXIDASE POSITIVITY IN RECURRENT MISCARRIAGES AND ASSOCIATED OBSTETRIC COMPLICATIONS

K.Manjula[1], T.S.Aarifa Thasleem[2], S. Janani[3]

[1]Consultant, Department of Obstetrics and Gynaecology, Maa Hospital and Motherhood Wellness Clinic, Katpadi, Vellore, Tamilnadu, India.
[2]Assistant Professor, Department of Obstetrics and Gynaecology, Institute of Social Obstetrics and Government Kasthurba Gandhi Hospital, Chennai, Tamilnadu, India.
[3]Assistant Professor, Department of Obstetrics and Gynaecology, Institute Of Social Obstetrics and Government Kasthurba Gandhi Hospital, Chennai, Tamilnadu, India.

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Corresponding Author:
Dr. S. Janani,
Email: janani.sakkarapani7@gmail.com

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ABSTRACT

Background: Recurrent miscarriage, affecting about 1% of couples, is often linked to autoimmune thyroid disease. Anti-thyroid peroxidase antibody (anti-TPO) positivity is increasingly recognised as a significant factor contributing to pregnancy loss and related complications. This study aimed to determine the association between anti-TPO antibody positivity and recurrent miscarriage, and to evaluate obstetric complications such as preeclampsia and preterm labour among affected women. **Materials and Methods:** A case-control observational study was conducted at the Institute of Social Obstetrics, Madras Medical College, Chennai, from March 2017 to March 2018, involving 100 participants: 50 women with a history of recurrent miscarriage (cases) and 50 women without a history of miscarriage (controls). Serum TSH (thyroid-stimulating hormone) and anti-TPO antibody levels were measured using standard immunoassay methods. **Results:** The mean age of cases was 25.92 ± 2.70 years, and controls 24.18 ± 1.38 years. Anti-TPO antibody positivity was significantly higher in cases (28%) than in controls (6%) ($p = 0.006$). Subclinical hypothyroidism was observed in 8% of cases and none of the controls. Maternal complications occurred in 20% of cases, including preeclampsia (12%) and preterm labour (6%), compared to none in controls ($p = 0.011$). Statistical analysis confirmed a significant association between thyroid autoimmunity and recurrent miscarriage ($\chi^2 = 8.575$, $p = 0.003$). **Conclusion:** Anti-thyroid peroxidase antibody positivity is significantly associated with recurrent miscarriage and adverse obstetric outcomes. Routine screening and early management of thyroid autoimmunity may help prevent pregnancy loss and improve maternal health.

INTRODUCTION

The term miscarriage refers to the unplanned termination of a pregnancy before foetal viability. Recurrent miscarriage is defined as the loss of three or more consecutive pregnancies affects about 1% of couples attempting to conceive.[1] Several factors contribute to recurrent pregnancy loss, including genetic, anatomical, endocrine, immune, and environmental causes. Among endocrine disorders, thyroid dysfunction, particularly autoimmune thyroid disease (AITD), has gained significant attention as a possible contributor to pregnancy complications.[2]

The most common cause of hypothyroidism in women of reproductive age is autoimmune thyroid disease, particularly Hashimoto's thyroiditis.[3] Recurrent miscarriages, preeclampsia, preterm labor, and impaired foetal development are adverse pregnancy outcomes associated with thyroid dysfunction and autoimmunity, which are common in this population.[4] Subclinical hypothyroidism, although often asymptomatic, occurs in about 2–3% of pregnancies and may contribute to early pregnancy loss if untreated.[5]

Thyroid hormones play an important role in maintaining normal reproductive and foetal functions.[6] They influence ovulation, implantation, placental development, and foetal brain maturation. During pregnancy, physiological changes such as increased thyroxine-binding globulin, elevated iodine requirements, and stimulation of the thyroid by human chorionic gonadotropin (HCG) impose an additional burden on the maternal thyroid gland.[7] Women with limited thyroidal reserve or subclinical hypothyroidism may therefore experience thyroid insufficiency during gestation, leading to complications.

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Anti-thyroid peroxidase (anti-TPO) antibodies are key markers of autoimmune thyroid disease.[8] Thyroid peroxidase is an enzyme crucial for thyroid hormone synthesis, and the presence of anti-TPO antibodies indicates immune-mediated thyroid injury. These antibodies are detected in 90–95% of individuals with autoimmune thyroiditis and may also appear in euthyroid women. Although not all women with anti-TPO antibodies show overt thyroid dysfunction, their presence has been associated with an increased risk of miscarriage and other obstetric complications.[9]

The mechanism by which anti-TPO positivity contributes to pregnancy loss is not fully understood. It suggested that the antibodies may reflect a generalised immune imbalance affecting implantation and placental development. They may signify a reduced ability of the thyroid gland to meet the increased hormonal demands of pregnancy, even in women with normal baseline thyroid function. Also, maternal thyroid autoantibodies can cross the placenta, potentially influencing foetal thyroid function and development.

Early detection and management of thyroid autoimmunity in women with recurrent pregnancy loss are of clinical importance.[10] Assessing thyroid function and the presence of anti-TPO antibodies before or during early pregnancy may help identify women at risk for miscarriage, preeclampsia, and preterm labour. The present study aims to determine the association between anti-TPO antibody positivity and recurrent miscarriages, and to evaluate the occurrence of obstetric complications such as preeclampsia and preterm labour among affected women.

MATERIALS AND METHODS

This was a case-control observational study comprising 100 eligible participants, which was conducted at the Institute of Social Obstetrics, Madras Medical College, from March 2017 to March 2018. All participants provided written informed consent before enrolment, and the hospital's Institutional Ethics Committee approved the study.

Inclusion and exclusion criteria

The study included women with a history of recurrent miscarriages, defined as more than three consecutive pregnancy losses in the first trimester, who attended the antenatal clinic at Madras Medical College. Women with anatomical uterine abnormalities, overt hypothyroidism, antiphospholipid antibody syndrome, or other autoimmune disorders were excluded from the study.

Methods

The 50 women with a history of recurrent miscarriage were assigned to the case group, and 50 without such a history to the control group. Data collected included serum levels of anti-TPO antibodies and thyroid-stimulating hormone (TSH). 10 ml of venous blood was drawn from each participant using Vacutainer tubes under standard quality control and safety procedures. Serum samples were analysed for TSH using Microparticle Enzyme Immunoassay (MEIA) kits and for anti-TPO antibodies using Chemiluminescent Immunoassay (CLIA) kits. The normal reference range for TSH during pregnancy was 0.35–2.5 µIU/ml, with values above 2.5 µIU/ml considered elevated, while anti-TPO levels above 34 IU/ml were regarded as positive. Cases were assessed for obstetric complications, including preeclampsia and preterm labour.

Statistical Analysis

Data were analysed using IBM SPSS Statistics version 23. Categorical variables were presented as frequencies and percentages, and continuous variables as mean ± standard deviation. Group differences were assessed using the unpaired t-test, chi-square test, or Fisher's Exact test, with $p \leq 0.05$ considered statistically significant.

RESULTS

OThe mean age of the cases was 25.92 ± 2.70 years compared to 24.18 ± 1.38 years among controls. The mean height was 158.50 ± 5.10 cm in cases and 158.72 ± 6.08 cm in controls, while the mean weight was 69.06 ± 8.59 kg and 68.34 ± 4.86 kg, respectively. The mean systolic blood pressure was 113.8 ± 14.6 mmHg in cases and 106.6 ± 6.6 mmHg in controls, with diastolic pressures of 72.1 ± 11.8 mmHg and 71.4 ± 6.4 mmHg, respectively. The mean birth weight was comparable between the groups, at 2.92 ± 0.36 kg in cases and 2.98 ± 0.30 kg in controls. [Table 1]

Table 1: Distribution of general physical and perinatal

Variables	Cases	Controls
Age	25.92 ± 2.70	24.18 ± 1.38
Height (cm)	158.50 ± 5.10	158.72 ± 6.08
Weight (kg)	69.06 ± 8.59	68.34 ± 4.86
SBP (mmHg)	113.8 ± 14.6	106.6 ± 6.6
DBP (mmHg)	72.1 ± 11.8	71.4 ± 6.4
Birth weight (kg)	2.92 ± 0.36	2.98 ± 0.30

More women aged ≥25 years were observed among cases 31 (62%) compared to controls 18 (36%) (p = 0.009). Regarding place of residence, 26 (52%) cases were urban and 24 (48%) rural, while controls were urban 29 (58%) and rural 21 (42%). For socio-economic status, cases were upper lower 27 (54%), low middle 13 (26%), and upper middle 10 (20%), whereas controls were upper lower 21 (42%), low

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middle 17 (34%), and upper middle 12 (24%). [Table 2]

Table 2: Demographic characteristics

Variable	Category	Cases	Controls
Age (years)	< 25	19 (38%)	32 (64%)
	≥ 25	31 (62%)	18 (36%)
Place of residence	Rural	24 (48%)	21 (42%)
	Urban	26 (52%)	29 (58%)
Socio-economic status	Low middle	13 (26%)	17 (34%)
	Upper lower	27 (54%)	21 (42%)
	Upper middle	10 (20%)	12 (24%)

All cases were multigravida (100%) compared to 24 (48%) of controls ($p < 0.001$). A history of three or more abortions was present in all cases and absent in controls ($p < 0.001$). Preterm delivery occurred in 8% of cases and none of the controls, while post-term delivery was higher among controls, 33 (66%) ($p = 0.0005$). Maternal complications were significantly more frequent in case 10 (20%) than in controls (none) ($p = 0.011$). Anti-TPO antibody positivity was higher in case 14 (28%) compared to controls 3 (6%) ($p = 0.006$). [Table 3]

Table 3: Comparison of obstetric, maternal, and thyroid parameters

Variable	Category	Cases	Controls	P value
Obstetric code	Multigravida	50 (100%)	24 (48%)	<0.001
	Primigravida	0	26 (52%)	
Abortion history	None	0	36 (72%)	<0.001
	1	0	10 (20%)	
	2	0	4 (8%)	
	3	48 (96%)	0	
	4	2 (4%)	0	
Gestational age at delivery (weeks)	≤36+6	4 (8%)	0	0.0005
	37–37+6	8 (16%)	0	
	38–38+6	16 (32%)	3 (6%)	
	39–39+6	16 (32%)	14 (28%)	
	≥40	6 (12%)	33 (66%)	
Mode of delivery	Normal vaginal delivery	21 (42%)	20 (40%)	-
	Caesarean section	29 (58%)	30 (60%)	
Urine albumin	Nil	44 (88%)	50 (100%)	-
	1+	2 (4%)	0	
	2+	2 (4%)	0	
	3+	2 (4%)	0	
Comorbidities	None	47 (94%)	50 (100%)	-
	Obesity (BMI >25)	3 (6%)	0	
Maternal complications	None	40 (80%)	50 (100%)	0.011
	Preeclampsia	6 (12%)	0	
	Preterm labour	3 (6%)	0	
	PROM	1 (2%)	0	
Gestational outcome	Preterm (<37 weeks)	4 (8%)	0	0.0005
	Term (≥37 weeks)	46 (92%)	50 (100%)	
TSH status	Normal	46 (92%)	50 (100%)	-
	Subclinical hypothyroidism	4 (8%)	0	
Anti-TPO antibody	Negative	36 (72%)	47 (94%)	0.006
	Positive	14 (28%)	3 (6%)	

DISCUSSION

This study aimed to evaluate the association between anti-TPO antibody positivity and recurrent miscarriage, and to assess related obstetric complications, including preeclampsia, preterm labour, and other adverse pregnancy outcomes, in comparison with healthy controls. Older maternal age, higher gravidity, and a history of multiple abortions were significantly more frequent among women with recurrent miscarriage compared to the control group. Similarly, Jaiswal and Bag found that the mean age of the cases was 24.18 years. Most pregnancy losses occurred between 9 and 14 weeks of gestation.[11] Yan et al. studied 220 women with a known cause of recurrent miscarriage and 496 with unexplained cases. The mean ages were similar (32.7 ± 5.5 years vs. 32.2 ± 5.6 years; $p > 0.05$).[12]

Ali Ghalib et al. studied 120 euthyroid women and found anti-TPO positivity significantly higher in miscarriage cases (19.4%) than controls (6.5%) ($p = 0.03$, OR = 3.48), mostly involving first-trimester losses.[13] Godines-Enriquez et al., the baseline parameters, such as height (1.55 ± 0.06 m), weight (67 ± 12.6 kg), BMI (27.7 ± 4.8 kg/m²), number of gestations (3.4 ± 0.9), and miscarriages (3.1 ± 0.8), showed no significant variation between the groups ($p > 0.05$).[14] In this case, recurrent miscarriage is

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associated with advanced maternal age, increased gravidity, and elevated anti-TPO antibody levels, whereas other baseline characteristics show no significant differences; screening for thyroid autoimmunity is recommended.

In our study, socio-economic status showed no significant difference between cases and controls. Similarly, Meena and Nagar found that about two-thirds of participants were urban residents, with a higher urban representation (66.67% vs. 33.33%), and most belonged to the middle socioeconomic class.[15] Thus, socioeconomic status showed no association with recurrent miscarriage, suggesting that lifestyle or economic factors may not influence its occurrence.

In this study, preterm delivery and maternal complications, including preeclampsia and preterm labour, were significantly higher among cases, while mode of delivery and albuminuria showed no significant differences. Similarly, Meena and Nagar found that no significant association between anti-TPO antibody status and pregnancy complications, including gestational hypertension (8.33% vs. 6.17%), preeclampsia (3.33% vs. 3.61%), or preterm delivery (<34 weeks: 5% vs. 1.8%; 34–37 weeks: 8.33% vs. 3.19%) ($p > 0.05$). Similarly, rates of cesarean delivery (25% vs. 21.59%), premature rupture of membranes (3.33% vs. 3.29%) did not differ significantly between groups.[15] Thus, higher rates of preterm delivery and maternal complications among cases suggest that closer monitoring and early intervention may improve outcomes.

In the present study, thyroid function was comparable between groups, while anti-TPO antibody positivity showed a significant association with recurrent miscarriage. Similarly, Lata et al. found no significant difference in miscarriage rates between antibody-positive women who were hypothyroid and those who were euthyroid ($p = 0.23$). However, live births correlated with FT4 ($R = 0.17$, $p = 0.001$) and TPOAb ($R = 0.17$, $p = 0.01$).16 In Yan et al.'s study of 496 women, TPOAb positivity was found in 9.3%. Live birth rates were 64% in TPOAb-negative, 53% in TPOAb-positive with thyroxine, and 58% without treatment. TPOAb positivity correlated with elevated TSH ($p < 0.001$).[12] Ali Ghalib et al. found anti-TPO antibody positivity in 19.4% of miscarriage cases and 6.5% of controls ($p = 0.03$, OR = 3.48; 95% CI: 1.06–11.48).[13] Therefore, anti-TPO positivity and recurrent miscarriage suggest screening for thyroid autoimmunity in women with pregnancy loss may help identify at-risk individuals and guide early management.

In our study, thyroid antibody positivity was linked to elevated TSH levels among cases, while overall thyroid function and physical parameters remained comparable between cases and controls. Similarly, Godines-Enriquez et al., the TSH level was significantly higher in the TAI-positive group (4.8 ± 3.8 mIU/L) compared to the TAI-negative group (3.1 ± 1.1 mIU/L, $p = 0.0001$), while FT4 (1.17 ± 0.25 mIU/L vs. 1.14 ± 0.22 mIU/L) and TT3 (126.7 ± 39 vs. 126 ± 32 mIU/L) were comparable ($p > 0.05$).[14] This shows that elevated TSH in antibody-positive women suggests mild thyroid dysfunction; routine thyroid screening may aid miscarriage prevention. Also demonstrates a strong association between recurrent miscarriage and anti-TPO antibody positivity. Routine thyroid screening and early management of thyroid autoimmunity may help reduce pregnancy loss and improve obstetric outcomes.

Limitations

The study's small sample size, single-centre setting, and limited assessment of thyroid antibodies may restrict generalisability. Its observational design and lack of long-term follow-up also limit causal inference and comprehensive evaluation of subsequent pregnancy outcomes.

CONCLUSION

A significant association between anti-TPO antibody positivity and recurrent miscarriage, indicating that thyroid autoimmunity may contribute to pregnancy loss even in euthyroid women. Routine screening for anti-TPO antibodies and thyroid function in women with recurrent miscarriage can help identify those at risk and allow timely intervention. Early management of thyroid dysfunction may improve pregnancy outcomes and reduce maternal complications. Future research with larger, multicentre cohorts and long-term follow-up is recommended to further clarify the underlying mechanisms and establish standardised screening and treatment protocols.

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