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Research Article

Impact of Anti-Thyroid Peroxidase Antibody Positivity on Pregnancy Outcomes: A Prospective Observational Study from a Tertiary Care Hospital in North India

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Abstract:

Background: Pregnancy involves significant hormonal changes, and thyroid dysfunction is acommon complication affecting approximately 8.25% of women in India. Anti-Thyroid Peroxidase (Anti-TPO) antibodies are markers of autoimmune thyroid disease and may be associated with adverse outcomes even in euthyroid women.

Methods: A prospective observational study of 219 pregnant women was conducted at JNMC, AMU, Aligarh. Subjects were screened for serum TSH and Anti-TPO antibodies. Maternal and neonatal outcomes were compared between Anti-TPO positive (n=20) and negative (n=199) groups.

Results: The prevalence of Anti-TPO antibodies was 9.1%. Anti-TPO positivity was strongly associated with a 15-fold higher risk of miscarriage (15.0% vs. 1.0%, p<0.001) and elevated TSH levels (15.0% vs. 1.5%, p<0.001). Composite adverse outcomes were significantly higher in the positive group (35.0% vs. 18.6%, p=0.031).

Conclusion: Anti-TPO antibodies are a critical biomarker for early pregnancy loss and thyroid dysfunction progression.

Keywords: anti-thyroid peroxidase antibodies; pregnancy outcomes; tsh; prevalence; critical biomarker

Introduction

Pregnancy is a state of changing metabolic and hormonal physiology where several changes occur in thyroid function. The thyroid glands must boost production of hormones by 40% to 100% to meet maternal and fetal needs. A transient fall in TSH is noted during the first trimester due to structural homology with human chorionic gonadotrophin (hCG), which stimulates the thyroid gland. Failure to adapt to these gestational physiological changes results in thyroid dysfunction, posing a significant risk to maternal and fetal outcomes. The management of thyroid disease during pregnancy is heavily guided by the American Thyroid Association (ATA). According to ATA (American Thyroid Association) guideline trimester specific range of serum TSH are as follows: [1,2] 1st trimester-0.1-2.5 mIU/L, 2nd trimester-0.2-3 mIU/L, 3rd trimester-0.3 -3 mIU/L. Despite the general belief that autoimmune activity decreases during pregnancy due to immune suppression, thyroid antibodies are still frequently detected, even in women with normal thyroid function. [2-4].

As high as 10-20% of women during pregnancy in their first trimester are found to have thyroid peroxidase (TPO) antibody positive and also euthyroid. Among these women, 16% will develop a high TSH level beyond 4.0 mIU/L during 3rd trimester and another 33%-50% will develop postpartum thyroiditis.[1] Inability to adjust to the physiological changes of pregnancy can lead to thyroid dysfunction, which may negatively impact both maternal and fetal health, though this remains a subject of ongoing debate. [5–7]. The significance of Anti-Thyroid Peroxidase (Anti-TPO) antibodies in pregnancy is paramount, as they serve as identifying markers for thyroid autoimmunity. These antibodies can lead to thyroid follicular cell destruction via cytokines and antibody-dependent cell-mediated cytotoxicity.

Even in euthyroid women, Anti-TPO antibodies have been suggested to have an independent association with adverse pregnancy outcomes, particularly Recurrent Pregnancy Loss (RPL) and preterm birth. It is speculated that thyroid autoimmunity represents a generalized autoimmune imbalance or an underlying immune dysregulation that adversely affects the maternal-fetal interface. Furthermore, euthyroid women with thyroid antibodies are at increased risk of progressing to subclinical or overt hypothyroidism as pregnancy progresses and demands on the gland increase. Recent clinical investigations have further solidified the role of Anti-TPO antibodies as independent predictors of early gestational wastage, particularly in euthyroid cohorts. [8] Modern evidence suggests that the presence of these antibodies

significantly elevates the risk of subsequent pregnancy loss and hypothyroidism during pregnancy, even in women with previously unexplained recurrent pregnancy loss. This growing body of literature emphasizes that Anti-TPO positivity likely reflects a localized inflammatory environment at the decidual-placental interface, which can impair implantation and placentation independently of biochemical thyroid status

Materials and Methods

The present study was an observational prospective cross-sectional study conducted from 2023-2025 at the Department of Obstetrics and Gynecology in collaboration with the Department of Endocrinology, J.N.M.C.H., AMU Aligarh. Ethical clearance for the study protocol was obtained from the Institutional Ethics Committee (Ref No: IECJNMC/1165) and participants were enrolled from antenatal and Endocrinology OPD after written consent

Inclusion Criteria: Singleton pregnant women without existing medical or surgical complications.

Exclusion Criteria: Women with known thyroid disorders, autoimmune diseases, or history of uterine malformations.

Investigations: Serum TSH and Anti-TPO antibody levels were measured using

Chemiluminescence Immunoassay (CLIA) on the Beckman Coulter Access 2 system. Blood samples were collected across trimesters to monitor progression

Variables	Anti-TPO+ (n=20)	Anti-TPO– (n=199)	p-value
Mean Age (years ±SD)	25.9 ± 4.6	25.9 ± 3.7	0.648
Mean BMI (kg/m²±SD)	25.02 ± 2.14	25.62 ± 2.76	0.311
Primigravidas (%)	30.0(6)	32.2(64)	0.884
Anti-TPO Status	9.1	90.9	-

Table 1: Demographic Profile

TSH Levels	Anti-TPO positive (n=20)		Anti-TPO negative (n=199)		p-value
	n	%	n	%	
Normal (≤3)	17	85.0	196	98.5	<0.001
Elevated (>3).	3	15.0	3	1.5	<0.001

Table 2: TSH Levels by Anti-TPO Status

Outcome	Anti-TPO+ % (n=20)	Anti-TPO– %(n=199)	p-value
Recurrent Pregnancy Loss	5.0% (1)	4.0% (8)	**<0.001**
Gestational Hypertension	5.0% (1)	15.1% (30)	1.000
Gestational Diabetes	20.0% (4)	25.1% (50)	0.488
Preterm PROM	10.0% (2)	4.0% (8)	0.248
Postpartum Haemorrhage	10.0% (2)	4.0% (8)	0.772
≥1 Complication	7(35.0%)	37(18.6%)	0.031
No Complications	13(65.0%)	162(81.4%)	

Table 3: Adverse Maternal Outcomes

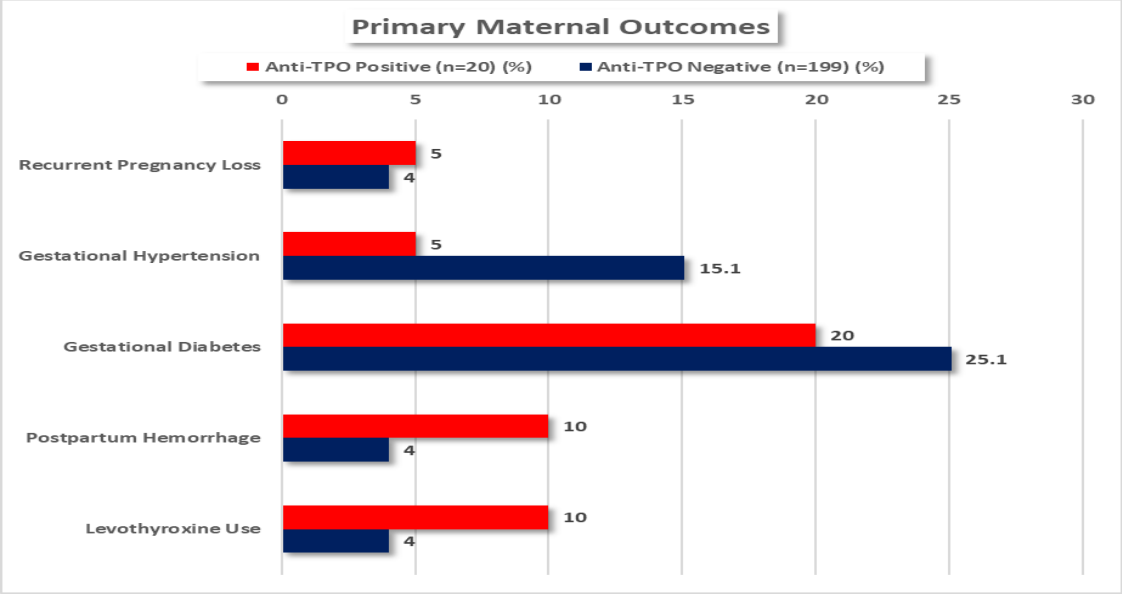

Figure 1A: Adverse Maternal Outcomes

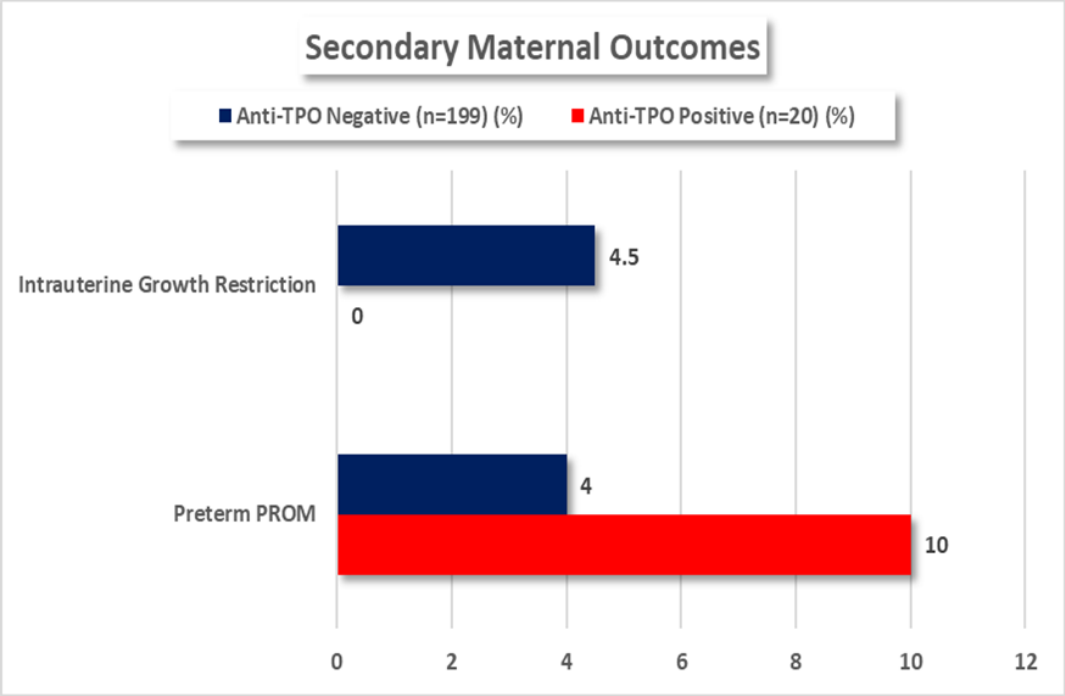

Figure 1B: Adverse Maternal Outcomes

Mode of Delivery	Anti-TPO+(n=20)		Anti-TPO-(n=199)		p-value
	n	%	n	%	
Vaginal	12	60.0	101	50.8	0.246
C-Section	5	25.0	56	28.1	
Assisted	3	15.0	42	21.1	

Table 4: Mode of Delivery

Progression	Anti-TPO+ (n=20)		Anti-TPO- (n=199)		p-value
	n	%	n	%	
Developed	2	10.0	2	1.0	0.001
Maintained	18	90.0	197	99.0	

Table 5: Thyroid Dysfunction Progression

Discussion:

This study highlights a 9.1% prevalence of thyroid autoimmunity in our cohort, aligning with regional Indian studies. In the present study, the prevalence of anti-thyroid peroxidase (anti-TPO) antibodies among pregnant women was found to be 9%, aligning well with the global prevalence estimates reported in previous studies, which range from 5% to 15% depending on population demographics, iodine status, and assay sensitivity. Anti-TPO antibodies are critical markers, as antibody-positive women show higher mean TSH levels and an increased risk of progression to overt disease. Our results reveal a 15-fold higher risk of miscarriage in Anti-TPO positive women ($p<0.001$).

Our results indicates that the TSH level and frequency of hypothyroidism in positive TPO Ab women was significantly higher than the negative TPO Ab group. This rise of thyroid-stimulating hormone concentrations in euthyroid TPO Ab positive women could be due to autoimmune-mediated inflammation of thyroid gland that leads to reduction in the functional reserve of the thyroid gland and is associated with reduced adaptation of thyroid gland to the physiological changes of pregnancy.

Increased TSH levels in positive TPO Ab women may be due to immune-mediated inflammation in the thyroid gland, leading to reduced thyroid function, related to decreased thyroid adaptation to physiological changes in pregnancy. Similar results were observed by Negro et al. [7] and Prummel and Wiersinga[9], on the contrary Stagnaro-Green et al[10] did not detect any significant difference between TSH levels in TPO Ab positive and TPO Ab negative women.

This finding was consistent with the study done by Shahbazian et al [11], which showed the mean TSH level was significantly different in women with negative TPOAb than those with positive TPO-Ab (Mean (SD): 2.25(1.47) vs. 4.82(9.38), $P<0.0001$). In the research done by Rajput, Yadav [12], the TSH levels in positive TPO Ab pregnant women were significantly higher than that in the negative TPO Ab group. Yuan, Sun [13] also showed that TSH levels were significantly higher in the positive anti TPO Ab group than the negative anti-TPO Ab group. Dhillon-Smith et al [14] reported higher TPO Ab positive rates were found in women with a BMI >34.9 kg/m2 and with increasing TSH concentrations

Based on the results of Bhat S [15]and Cakmak BD, [16] studies, a statistically significant relationship has been reported between thyroid disorders in pregnancy and its poor pregnancy outcomes

The association with Recurrent Pregnancy Loss was also statistically highly significant ($p<0.001$). This suggests that thyroid autoimmunity increases early pregnancy wastage, potentially through immune-mediated placental disruption or a reduced ability of the thyroid gland to adapt to pregnancy. Reinforcing these findings, contemporary research notes that Anti-TPO positivity remains a formidable risk factor for miscarriage even when euthyroid status is maintained through treatment. High-quality meta-analyses suggest that while levothyroxine may stabilize TSH, it might not

fully mitigate the risk of pregnancy loss in Anti-TPO positive women with RPL, pointing toward a need for multidisciplinary immunomodulatory research. In a research done by Mohammad Ali [17] and Abbassi-Ghanavati, Casey [18] a threefold enhancement in miscarriage was related in the positive anti-TPO Ab group in comparison to the negative anti-TPO Ab group (1% vs. 0.3%). Thus, the results suggest that anti-TPO Ab can be one of the markers of increased miscarriage. Lata et al [19]. found no significant difference in miscarriage rates between antibody-positive women who were hypothyroid and those who were euthyroid (p = 0.23) Furthermore, data indicates a significant correlation between higher Anti- TPO titers and an increased odds of recurrent loss, strongly advocating for titer-based risk stratification in clinical practice. In our study, Anti-TPO positivity was the primary driver of adverse outcomes, with the highest riskobserved when combined with elevated TSH (33.7%). Anti-TPO positive women were 10 times more likely to develop thyroid dysfunction during pregnancy (10.0% vs 1.0%, P=0.001). This emphasizes that these antibodies reduce functional reserve, leading to a reduced adaptation to thephysiological changes of pregnancy. The higher treatment rate with levothyroxine in the positive group (10% vs 4%,p<0.001) reflects proactive management guided by these markers. Interestingly, Anti-TPO status did not significantly influence GDM, gestational hypertension, or PPH in this cohort. Neonatal outcomes, including low birth weight and NICU admission, also showed no significant differences between groups (p>0.05). This confirms that thyroid autoimmunity specifically threatens early pregnancy viability without necessarily elevating late-gestation or immediate neonatal risks.

Our findings suggest that anti-TPO antibody status does not significantly influence the likelihood of vaginal, caesarean, or assisted delivery in this study population. The distribution of delivery methods is relatively similar regardless of anti-TPO status, and there is no evidence from this data to suggest that thyroid autoimmunity affects the choice or necessity of delivery mode and postpartum hemorrhage risk in this study population. No statistically significant difference between the two groups. This finding correlated with the study of Netra et al [20].

Conclusion:

There is a high prevalence of Anti-TPO antibodies in antenatal women, which is significantly associated with adverse outcomes, particularly miscarriage and Recurrent Pregnancy loss. Close monitoring and timely treatment of thyroid dysfunction (including subclinical hypothyroidism) in anti-TPO+ women may help reduce the risk of miscarriage and other complications. High TPOAb titers warrant intensified prenatal surveillance and possibly earlier intervention.

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Conflict Of Interest: None

Contribution To Authorship: Dr Yashasvi Bajpai prepared the original draft, collected and prepared the data and Muhammmad Uwais Ashraf played a role in the analysis and interpretation of data. Dr Nasreen Noor and Dr Hamid Ashraf had a signicant contribution to the conception and design of the study, protocol formulation, analysis and interpretation of data and preparing the writeup.

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