Original Article

Prevalence of Thyroid Peroxidase Antibody and Pregnancy Outcome in Euthyroid Autoimmune Positive Pregnant Women from a Tertiary Care Center in Haryana

Rajesh Rajput, Tekchand Yadav, Shashi Seth[1], Smiti Nanda[2]

Departments of Endocrinology and Medicine Unit V, [1]Biochemistry and [2]Obstertrics and Gynaecology, Pt. B. D. Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India

Abstract

Objective: To study the prevalence of thyroid peroxidase autoantibody in euthyroid pregnant women and to evaluate the association between thyroid peroxidase autoantibody and pregnancy outcomes. **Materials and Methods:** One thousand thirty consecutive pregnant women attending the antenatal clinic over a period of 1 year and were carrying a healthy singleton uncomplicated intrauterine pregnancy and consuming iodized salt were recruited for the study. Outcomes of the pregnancy was compared between TPO antibody positive euthyroid women (group 1) and TPO antibody negative euthyroid women (group 2). **Results:** Out of 1030 women, 164 (18.9%) were detected TPO antibody positive with euthyroid status. The mean FT4 and TSH level were significantly different in those who were TPO Ab positive as compared TPO Ab negative euthyroid pregnant women. No correlation was observed between the maternal age, gestational age and gravidity with anti TPO antibody levels. Eighteen (12%) women in Group 1and 5 (3.3%) women in Group 2 had miscarriages and the difference was found to be statistically significant (*P* value of 0.004). Twenty-one (14%) women in Group 1 and 5 (3.3%) women in Group 2 had preterm deliveries, which was also found to be statistically significantly (p value of 0.001). Other pregnancy related complications like Intrauterine death, IUGR, preeclampsia and PIH though are present in comparatively higher number in TPO Ab positive euthyroid pregnant women as compared to TPO Ab negative euthyroid pregnant women but this difference was not found to be statistically significant. **Conclusions:** To conclude with the present study shows that a good number of pregnant women with euthyroid status have TPO Ab positivity and this is associated with some adverse pregnancy outcomes like miscarriage and preterm birth of the baby.

Keywords: Euthyroid, pregnancy outcome, TPO autoantibody

Introduction

Evaluation of thyroid disease in pregnancy is important for maternal health, obstetrical outcome, and subsequent development of the child.[1,2] Thyroid diseases are different from other diseases in terms of their ease of diagnosis, accessibility of medical treatment, and the relative visibility that even a small swelling of thyroid offers to the treating physician. It has been recognized that pregnant women who are euthyroid but who are positive for thyroid peroxidase autoantibody (TPO Ab) are at increased risk of various complications of pregnancy including miscarriage, preterm birth, pregnancy-induced hypertension (PIH), intrauterine death (IUD), and intrauterine growth retardation (IUGR).[3,4] Various reasons cited to explain this association include the fact that the presence of thyroid antibodies may represent a marker of a generalized autoimmune imbalance that is responsible for an increased miscarriage rate, increased chances of these women to develop subclinical, or overt hypothyroidism during pregnancy[5] and finally, these women are often older than those without, so an older age, *per se*, may explain the increased rate of fetal loss.[6,7] Many western studies had confirmed this association; however, little information is available from India and none from Haryana which is supposed to be iodine sufficient.[8-10]

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Address for correspondence: Dr. Rajesh Rajput, Department of Endocrinology and Medicine Unit VI, Pt. B. D. Postgraduate Institute of Medical Sciences, Rohtak - 124 001, Haryana, India. E-mail: drrajeshrajput@outlook.com

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Materials and Methods

This was a cross-sectional study conducted at the Department of Endocrinology and Antenatal Clinic in Department of Obstetrics and Gynecology at Postgraduate Institute of Medical Sciences, Rohtak. A total number of 1030 pregnant women who attend antenatal clinic over a period of 1 year were recruited for the study. After explaining the purpose of the study, informed consent was obtained and Institutional Ethical Review Board approved the study. All women who were carrying a healthy singleton uncomplicated intrauterine pregnancy and consuming iodized salt were recruited. On enrollment of participants, detailed history was enquired. All participants were subjected to relevant general physical examination including the presence or absence of goiter and findings were recorded on a predesigned pro forma. Participants having any history of chronic illness, goiter on physical examination, thyroid illness in the past or present, consuming thyroid medications (current and past), family history of thyroid illness, and poor obstetrics history (3 or more abortions) were excluded from the study. Estimation for free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) was done using the electrochemiluminescence technique using commercially available kits by Advia Centaur CP analyzer system. Immulite 1000 anti-TPO Ab solid phase, enzyme-labeled chemiluminescent sequential immunometric assay was used for the measurement of TPO antibodies. The analytical sensitivities for FT3, FT4, TSH, and anti-TPO were 0.2 pg/mL, 0.1 ng/dL, 0.010 μIU/mL, and 7 IU/mL, respectively. Intraassay coefficients of variation for FT3, FT4, TSH, and anti-TPO were 3.8%, 2.20%, 5.2%, and 5.6%, respectively. Laboratory reference ranges for FT3, FT4, and TSH were 2.3–4.2 pg/mL, 0.89–1.76 ng/dL, and 0.35–5.5 mIU/L, respectively. Normal range for TPO Ab was <35 IU/mL and value greater than or equal to indicate elevated anti-TPO in serum. American Association of Clinical Endocrinologist guidelines were used for the classification of pregnant women thyroid status. Those having TSH level ≤2.5 μIU/mL in first trimester and TSH level ≤3.0 μIU/m in second and third trimester with normal FT4 were considered as euthyroid.[11] Euthyroid pregnant women with TPO Ab positivity were included in Group 1 and were followed until the completion/termination of their pregnancy. The pregnancy outcomes of pregnant women with euthyroid status and positive TPO Ab (Group 1) were compared with euthyroid pregnant women with TPO Ab negative status (Group 2).

According to the aims and objectives of the study, the data were analyzed using appropriate statistical tests in Statistical Package for Social Sciences (SPSS) version 20 (SPSS Inc. Chicago IL). For descriptive statistics, frequencies, percentages, mean with standard deviations, and median of different variables were calculated. To assess difference between categorical variables, "Chi-square test" was used. Independent sample *t*-test was used to compare the means of two separate sets of independent samples. For comparison of means of more than two samples, analysis of variance test was used. The *P* values were two-tailed and probability level of significant difference was set at <0.05.

Results

The present study was conducted on 1030 consecutive pregnant women attending the antenatal clinic over a period of 1 year. Median time of recruitment of study participant was 9 weeks and 3 days with a range of 6–12 weeks. Out of these 1030 women, 164 (18.9%) were detected TPO Ab positive with euthyroid status and they were recruited in our study. Six women were lost to follow-up; eight women did not give their consent to participate in study; hence, various pregnancy outcomes were noted in remaining 150 TPO Ab positive euthyroid pregnant women. TPO Ab positive euthyroid pregnant women (Group 1) were compared with equal number of TPO Ab negative euthyroid pregnant women (Group 2). Mean bodyweight of women in both the groups was comparable (Group 1 was 54.08 ± 8.05 and Group 2 was 52.45 ± 9.0; $P = 0.15$). The baseline thyroid profile of both the groups is shown in Table 1. The mean FT4 and TSH level were significantly different in those who were TPO Ab positive as compared TPO Ab negative euthyroid pregnant women. No correlation was observed between the maternal age, gestational age, and gravidity with anti-TPO Ab levels.

Eighteen (12%) women in Group 1 and 5 (3.3%) women in Group 2 had miscarriages, and the difference was found to be statistically significant ($P = 0.004$). Twenty-one (14%) women in Group 1 and 5 (3.3%) women in Group 2 had preterm deliveries and this difference was statistically significantly ($P = 0.001$). Other pregnancy-related complications such as IUD, IUGR, preeclampsia, and PIH though are present in comparatively higher number in TPO Ab positive euthyroid pregnant women as compared to TPO Ab negative euthyroid pregnant women, this difference was not found to be statistically significant.

Table 1: Baseline thyroid function of euthyroid pregnant women with positive and negative thyroid peroxidase antibody

	Mean±SD		*P*
	Euthyroid with positive TPO Ab Group 1 (*n*=150)	Euthyroid with negative TPO Ab Group 2 (*n*=150)	
FT3 (pg/mL)	3.26±0.76	3.25±0.53	0.9
FT4 (ng/mL)	1.10±0.31	1.26±0.22	0.000
TSH (μIU/mL)	1.69±0.68	1.35±0.70	0.000

TPO Ab: Thyroid peroxidase autoantibody, SD: Standard deviation, TSH: Thyroid-stimulating hormone, FT3: Free triiodothyronine, FT4: Free thyroxine

The pregnancy-related outcomes between two groups are summarized in Table 2**.** During the study period, seven women in Group 1 and six women in Group 2 developed GDM ($P > 0.05$).

Discussion

In the present study, we assessed the prevalence of TPO Ab in euthyroid pregnant women and its relationship with various pregnancy outcomes such as miscarriage, preterm, preeclampsia PIH, IUD, and IUGR. 18.9% pregnant euthyroid women were found to be positive for TPO Ab and significant correlation was observed between TPO Ab positivity and rate of miscarriage and preterm deliveries. Negro *et al*.[12] and Hollowell *et al*.[13] observed the presence of TPO Ab in 11.7% and 14.6% of pregnant euthyroid women in their studies, respectively. A study by Bhattacharya *et al*. observed TPO Ab prevalence of 11.34%.[14] The age of these women in the present study ranged from 17 to 36 years with majority in the age range of 21–25 years and it was not statistical different between TPO Ab positive and TPO Ab negative euthyroid women. The median maternal age in both the Group 1 and 2 was less as compared to Western studies,[15] reflecting early marriage and early conception prevalent in India. No correlation was observed between age and TPO Ab positivity in the present study. Similar observations had been reported from some other studies.[16,17] However, Negro *et al*.[12] observed that TPO Ab positive women were more older than anti-TPO Ab negative women. Stricker *et al*.[16] also found a significant association between anti-TPO and maternal age. Kutteh *et al*.[17] also observed significant relationship between increasing age and recurrent pregnancy loss associated with elevated antibody status. Abbassi-Ghanavati *et al*.[18] reported that women who were TPO Ab positive were older, heavier, and more often multiparous than women with negative antithyroid peroxidase antibodies. No correlation between TPO Ab positivity and parity, period of gestation, or body weight was found in the present study.

Among thyroid function tests, FT4 was significantly lower and TSH levels were significantly higher among the TPO Ab positive euthyroid women as compared to TPO Ab negative women in the present study. 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.[19] Similar results were observed by Negro *et al*.[12] and Prummel and Wiersinga,[20] but Stagnaro-Green *et al*.[6] did not detect any significant difference between TSH levels and FT4 levels in between TPO Ab positive and TPO Ab negative euthyroid women.

Eighteen (12%) women TPO Ab positivity and 5 (3.3%) women with TPO Ab negative status had miscarriages and the difference was statistically significant ($P < 0.004$). This could be due to subtle deficiency of thyroid hormone concentrations or a lower capacity of the thyroid gland to adapt to the demands of pregnancy in euthyroid pregnant women with TPO Ab positivity. These results were consistent with the findings of the studies by Stagnaro-Green *et al*.[6] and Negro *et al*.[12] It was also seen in our study that maximum number of miscarriages occurred in first trimester (12/18, 67%) as compared to second trimester (06/18, 33%) in Group 1 and this difference was statistically significant. In Group 2, no significant difference was observed in the number of miscarriage in first and second trimester. Similar results were also seen by Negro *et al*.[2] and Glinoer[19] and Meena *et al*.[21] in their studies. Preterm deliveries were observed in 21 (14%) women of TPO Ab positive group and 5 (3.3%) women in TPO Ab negative group and this difference was statistically significant ($P = 0.001$). These findings were in agreement with those by Negro *et al*.[2] (22.4% in Group 1 vs. 8.2% in Group 2) and Glinoer[19] (16.1% in Group 1 vs. 7.9% in Group 2), respectively. However, the study by Männistö *et al*.[22] and Ligima *et al*.[7] did not show similar correlation between TPO Ab positive and TPO Ab negative women. The likely reason for higher incidence of preterm deliveries is that the presence of thyroid autoantibodies reflects a generalized activation of the immune system that would have resulted in deregulation of the immune system against the fetal-maternal interface. Although other pregnancy-related complications such as IUD, IUGR, preeclampsia, and PIH were present in higher number of women with TPO Ab positivity, this difference was statistically insignificant ($P > 0.05$). Similar findings were also observed in the study by Negro *et al*.[12] and Männistö *et al*.[22]

Conclusion

The present study shows that a good number of pregnant women with euthyroid status has TPO Ab positivity and this

Table 2: Association of anti-thyroid peroxidase antibody with pregnancy outcome in euthyroid women in study population

Pregnancy outcome	Euthyroid with positive TPO Ab Group 1 (n=150) (%)	Euthyroid with negative TPO Ab Group 2 (n=150) (%)	$P^{\#}$
Miscarriage	18 (12)	5 (3.3)	0.004
PIH	12 (8)	6 (4)	0.5
Preeclampsia	4 (2.6)	3 (2)	0.5
Preterm birth	21 (14)	5 (3.3)	0.001
Intrauterine death	4 (2.6)	3 (2)	0.5
IUGR	15 (10)	8 (5.2)	0.09

$^{\#}P<0.05$ is significant. PIH: Pregnancy-induced hypertension, IUGR: Intrauterine growth retardation, TPO Ab: Thyroid peroxidase autoantibody

was found to be associated with adverse pregnancy outcomes such as miscarriage and preterm birth of the baby. One of the limitations of the present study is that we have not studied the role of levothyroxine treatment in prevention of these obstetrics complications. Therefore, larger studies with bigger sample size and population subsets from different geographical regions of country are needed to establish the relationship between TPO Ab and adverse pregnancy outcomes and whether routine estimation of TPO Ab in pregnancy and its treatment is going to benefit the pregnancy outcomes or not needs to be studied.

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Conflicts of interest

There are no conflicts of interest.

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