CLINICAL IMPORTANCE OF THYROID PEROXIDASE AUTOANTIBODIES (TPO–Ab) DETERMINATION IN PREGNANCY

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SUMMARY

Pregnant women with positive thyroid peroxidase autoantibodies (TPO–Ab) run an increased risk for developing postpartum thyroiditis (PPT). Eight clinically healthy pregnant women in third trimester were screened for TPO–Ab titres by radioimmunoassay (RIA) technique and were followed 3–4 months postpartum. During pregnancy TPO–Ab seropositivity was seen in 17.5% cases. Serum thyroxine (T₄) and thyroid stimulating hormone (TSH) levels done only in seropositive cases were with in normal limits. After follow up 21.25% cases showed TPO–Ab seropositivity 3–4 months postpartum. The rise in TPO–Ab titre was very significant in 23.5% of seropositive case (5% of the total) who developed mild thyrotoxic phase of PPT. Serum T₄ levels were increased above normal limits while serum TSH levels were decreased in them along with the clinical findings. Twenty nonpregnant women were included in the study as controls who were all seronegative for TPO–Ab showing significantly high prevalence of TPO–Ab during pregnancy (P<0.001).

INTRODUCTION

Postpartum thyroiditis (PPT) is a syndrome of thyroid dysfunction that occurs in the first year after parturition. It is characterized by transient painless thyrotoxicosis (1–3 months duration) accompanied by a low thyroid radioactive iodine (RAI) uptake followed by a transient hypothyroid phase (1–3 months duration) in women who remained euthyroid during pregnancy in a typical biphasic pattern. Transient uniphasic patterns, either having thyrotoxic phase alone or hypothyroidism only are also observed in some cases.

Spontaneous recovery is generally anticipated but recurrence during future pregnancies is common. Thyroid peroxidase antigen (TPO–Ag) is a membrane bound haem containing glycoprotein with a prosthetic group that plays a key role in biosynthesis of thyroid hormones by catalyzing both the iodination and coupling of tyrosine residues in thyroglobulin molecule.

PPT occur in 50% of TPO–Ab seropositive women. Almost our of the blue it has been realised that around 4–6% of apparently healthy women have transient thyroid dysfunction in first year after delivery due to exacerbation of pre-existing silent autoimmune thyroiditis.

Clinically patient may show any of symptoms and signs normally associated with thyroid dysfunction. This study was undertaken in healthy pregnant women to find out TPO–Ab titres for evaluation of its clinical usefulness. It may give the clinician a clue regarding appropriate time for TPO–Ab estimation so as the include it in routine antenatal screening programme of pregnant
TABLE – I
COMPARISON OF MEAN TPO–AB TITRE (AU/ML) IN SEROPOSITIVE SUBJECTS IN
GROUP–I VS GROUP–II AND PHASE–I VS PHASE–II
(VALUES ARE EXPRESSED AS MEAN ± SD)

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Item</th>
<th>Group–I (Pregnant women)</th>
<th>Group–II (Controls)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Phase–I</td>
<td>Phase–II</td>
</tr>
<tr>
<td>1.</td>
<td>Mean TPO–Ab titre</td>
<td>542.15±193.15</td>
<td>535.69±249.30</td>
</tr>
</tbody>
</table>

Group–I vs Group–II = Very highly significant (p<0.001)
Phase–I vs Phase–II = Non-significant (p>0.05)

ladies for prediction of impending postpartum thyroiditis and may provided an early warning for future hypothyroidism.

MATERIAL AND METHODS
The study included group–I subject consisting of eighty clinically healthy pregnant women in third trimester irrespective of their age, parity and socioeconomic status attending different antenatal hospitals of Lahore. Group–II consisted of twenty age and socioeconomically matched married women at least one year after their last delivery as controls.

In phase–I (third trimester of pregnancy) serum TPO–Ab titres were done in all the cases while T and TSH estimation were done only in the seropositive cases.

![Figure 1. Thyroid Peroxidase Auto-Antibody Seropositivity in Phase – I](image_url)
TABLE – II
COMPARISON OF MEAN LEVELS OF RAISED T₄ AND LOW TSH IN PHASE–II WITH THE VALUES OF SAME SUBJECTS IN PHASE–I
(VALUES ARE EXPRESSED AS MEAN ± SD)

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Item</th>
<th>Phase–I</th>
<th>Phase–II</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>T₄ Titre</td>
<td>144.0±10</td>
<td>178.0±14.54</td>
<td>VHS</td>
</tr>
<tr>
<td>2.</td>
<td>TSH titre</td>
<td>0.77±0.08</td>
<td>0.21±0.05</td>
<td>S</td>
</tr>
</tbody>
</table>

In phase–II all the subjects were reassessed clinically as well as biochemically for TPO–Ab, 3–4 months after parturition. T and TSH levels were estimated only in seropositive women as before.

TPO–Ab titres were measured by RIA technique (AB–TPO Sor in Biomedical Diagnostics, Italy). The assay principle for TPO–AB is based on the competition between TPO–Ab contained in standard or specimen to be assayed and solid phase Fab to TPO (fixed on antibody coated tube walls) for the fixed and limited number of labelled TPO binding sites.

All the samples were diluted with sample diluent (10 ul sample and 500ul diluent), 100 ul of standard/diluted samples were pipetted in to corresponding polystyrene tubes. In each tube 50 ul tracer (1²⁵ labelled TPO) was poured. After mixing all tubes were covered and incubated for 18–22 hours at room temperature. The incubation mixture was aspirated carefully and washed twice with wash buffer. Radioactivity of each tubes was measured by Gamma counter (Cap RIA Germany). The percent value of each standard versus the anti–TPO amounts (AU/ml) were plotted to obtain a standard curve. Percent value of each sample was calculated and plotted directly on the standard curve to find the concentration of TPO–Ab in the sample expressed as AU/ml (AU is arbitrary value). Reference range of TPO–Ab is 0–10.5 AU/ml.

Clinical and laboratory data were analyzed using student’s ‘t’ test (all p values are two tailed).

RESULTS

In phase–I out of 80 subjects only 14 (17.5%) were seropositive for TPO–Ab Fig–I and had a mean titre of 542.15±193.15 AU/ml while there was no seropositive lady in controls having a mean titre of TPO–Ab 4.73±1.88 AU/ml. In phase–II the same 80 subjects were reassessed for TPO–Ab 3–4 months after parturition. 17 women (21.25%) showed TPO–Ab seropositivity Fig–II having mean titre of 535.69±249.30 AU/ml. The mean TPO–Ab titre value in phase–I and phase–II when compared with the mean TPO–Ab titre of controls, the difference was very highly significant statistically (P<0.001). But when the mean TPO–Ab values of phase–I were compared with phase–II, the difference was not significant statistically (P>0.05) table–I.

T₄ estimation was done only in those subjects who were seropositive for TPO–Ab. In T₄ estimation was performed on 14 seropositive subjects and was found within normal limits while in phase–II, T₄ titre were found to be marginally raised in 5 (29.4%) out of 17 seropositive subjects. The subjects in which T₄ titre were found higher than the normal limits in phase II, the mean value of serum T was calculated to be 178.0+14.54 nmol/L, which was very highly
significant statistically when compared with mean T value of the same five subjects in phase.\(^1\) (P<0.001) (table 2).

TSH determination was also done only in TPO–Ab seropositive cases. In phase–I TSH levels were estimated in 14 seropositive cases and were found to be within normal reference range. In phase–II TSH estimation was found to be marginally decreased in 4 (23.52\%) out of 17 seropositive women. Mean levels of decreased TSH levels are shown in table 2.

These 4 women with rising titres of TPO–Ab, increased T levels and decreased TSH levels in phase II developed mild signs and symptoms of thyrotoxic phase of PPT showing that 4 (23.5\%) cases developed mild PPT both clinically and biochemically. These women complained of one or more usual symptoms of hyperthyroidism 3–4 months after parturition e.g. palpitation, excessive sweating, increased appetite, preference to cold, nervousness, weight loss of variable degree.

**DISCUSSION**

The present study showed that TPO–Ab seropositivity was 17.5\% in healthy pregnant women during third trimester of pregnancy and 21.25\% in the same subjects 3–4 months after parturition. this result is in congruence with the findings of Mariotti\(^16\) who reported 16.5\% TPO–Ab seropositivity during pregnancy and 20% TPO–Ab seropositive cases in postpartum period. On the contrary Sakata\(^17\) reported that TPO–Ab seropositivity was seen only in 8.4\% pregnant women. The high percentage of seropositivity for TPO–Ab in healthy pregnant women signifies the presence of some autoimmune process involving the thyroid gland. Scherbaum\(^18\) suggested that the detection of thyroid autoantibodies in apparently healthy individuals indicates the incipient thyroid disease.

In the present study all control subjects were seronegative for TOP–Ab. While Mariotti\(^19\) studied the TPO–Ab in normal healthy subjects and found its prevalence to
be 8.4%. The difference in TOP-Ab seropositivity observed by various workers may be due to various factors including racial and ethnic differences of subjects, methods of their estimation and arbitrarily set limits of positivity by various laboratories.\textsuperscript{20}

The presence of TPO-Ab in healthy pregnant women indicate that these autoantibodies have primary importance in the pathogenesis of postpartum thyroid as other workers have also reported the same.\textsuperscript{21-22}

In the present study, 5% of women developed thyrotoxic phase of PPT 3–4 months postpartum. All these women were TPO-Ab seropositive in phase I and had rising titres of these autoantibodies in phase II. The incidence of PPT found in this study correlates with the findings of Gerstein\textsuperscript{25} who reported that incidence rate of PPT ranged between 3.7–6.9% with an average of 5%.

In contrast to our findings the incidence rates of 2% and 16.7% have been reported respectively\textsuperscript{24-25}. The reports on the prevalence of PPT vary reflecting a variety of factors including study design, frequency and duration of sampling, definition of the normal hormone and antibody ranges and different methods for their measurement and the ethnic origin of the patients.\textsuperscript{26}

In the present study, 23.5% of TPO-Ab seropositive women developed PPT while Rieu\textsuperscript{7} reported that PPT occurred in 50% TPO-Ab seropositive cases.

REFERENCES


