Subclinical Hypothyroidism and Autoimmune Thyroiditis in Pregnancy - A Study in South Indian Subjects

R Gayathri, S Lavanya, K Raghavan

Abstract

Objective: To analyse the prevalence of subclinical hypothyroidism among pregnant women attending Government hospitals in South India. It is also aimed to identify the prevalence of thyroid autoimmunity in euthyroid pregnant women.

Materials and methods: Five hundred pregnant women attending two government Obstetric and Gynecology hospitals in Chennai during a period of 5 months in 2007, were studied. Excluding subjects with known thyroid diseases, 495 subjects were examined. Detailed physical examination was done and details of pregnancy were recorded. All were subjected to blood tests for Free T<sub>4</sub>, TSH and TPO antibodies.

Results: Subclinical hypothyroidism was detected in 2.8%, among them TPO antibodies positivity was seen in 57.1% whereas euthyroid women had significantly lower positivity (7%). No association was seen between hypothyroidism or TPO antibody positivity with gestational age or parity. Hypothyroidism diagnosed by elevated TSH value (≥5.0 mg/l) was significantly associated with increasing gestational age (Trend c<sup>2</sup> = 6.02, p=0.014).

Conclusions: Prevalence of subclinical hypothyroidism among pregnant women is fairly high among Indians and they have high rates of TPO antibody positivity. Screening for hypothyroidism has to be included as a routine screening test to improve maternal and foetal outcomes.

Introduction

Thyroid disorders are commonly encountered in pregnancy. Overt thyroid dysfunction is known to have an adverse impact on pregnancy. Early studies reported up to 20% incidence of perinatal mortality and congenital malformations associated with maternal hypothyroxinemia with up to 60% of surviving children having evidence of impaired mental and physical development. Untreated or inadequately treated overtly hypothyroid women experience about 40% incidence of anemia, preeclampsia, placental abruption and post partum hemorrhage, 30% of neonates were small for gestation and 10% incidence of perinatal mortality and congenital abnormalities were noted. Women with untreated subclinical hypothyroidism (elevated TSH only) had approximately one third the incidence of this problem and in both groups the maternal and fetal outcomes improved with thyroxine therapy. A recent population survey identified 2.5% of pregnant women as having compensated hypothyroidism based on elevated TSH levels. Thyroid microsomal and peroxidase antibodies (TPO antibodies) were positive in all hypothyroid patients as against 11% of controls. Serum TSH positively correlated with thyroid antibody titres and maternal age. A similar prevalence of hypothyroidism and autoimmunity has been found in previous studies in pregnancy. The prevalence of thyroid autoimmunity was 19.6. A meta-analysis of 10 prospective studies of euthyroid women revealed that women with antithyroid antibodies were more than twice likely to experience a miscarriage (Odds ratio 2.30, 95% CI 1.80 -2.95). The importance of identifying subclinical hypothyroidism and thyroid autoimmunity in early pregnancy is thus obvious as it is likely to have a profound influence on the outcome of pregnancy. However, in many developing countries routine assessment of thyroid status is not being done in all pregnant women. Furthermore, the incidence of subclinical hypothyroidism or autoimmune status in this population of women, especially women in South Asia or India is not known as we do not have any published data. Hence this study has been undertaken among pregnant women attending government hospitals of Chennai, Tamil Nadu, South India.

The objectives were

1) to find out the prevalence of subclinical hypothyroidism in pregnant women and 2) to identify the prevalence of thyroid autoimmunity in pregnant women in euthyroid state.

Material and Methods

The study was conducted in the Institute of Obstetrics and Gynaecology, Egmore, affiliated to Madras Medical College, Chennai, India and in the RSRM hospital, affiliated to Stanley Medical College, Chennai, India.

This was a clinic based, cross sectional study of 5 months' duration (January – May 2007). The study had ethical clearance from the institutional ethics committee.

From the outpatient clinics, 500 pregnant women upto gestational age of 36 weeks were selected during the study period. Exclusion criteria included, women with already known thyroid disease, patients already on levothyroxine therapy, patients with TSH>10 mU/L, and patients with subclinical hyperthyroidism.

Subclinical hypothyroidism is defined as an asymptomatic state in which reduction in thyroid activity is compensated...
by elevated TSH to maintain a euthyroid state. Presence of compensated hypothyroidism is associated with normal  \( T_R \),  \( T_U \) Free  \( T_R \) (all by competitive chemiluminescent assay) or FTH index and elevated TSH (ultra sensitive sandwich chemiluminescent assay) (<10 mU/L). General physical examination was done for all. Pelvic examination and ultrasound examination were done. Details of pregnancy regarding gestational age, weight gain and menstrual history were recorded. Features suggestive of hypothyroidism such as family history of thyroid disorders, previously diagnosed thyroid disease, presence of thyroid therapy, skin changes associated with hypothyroidism (cold skin, coarse skin), presence of goiter, slow movements, peri-orbital puffiness and delayed ankle reflex were looked for.

Blood tests included haemoglobin, urea, creatinine, random blood glucose, free  \( T_R \), TSH and TPO antibodies (haem agglutination assay) positive-titre more than 1 : 10². Routine urine examination was also done. Subclinical hypothyroidism was diagnosed if the TSH values were 5-10 mU/L.

### Results

The mean (±SD) age of women was 23.8 ± 3.7 years.

Five women had subclinical hyperthyroidism (normal serum thyroxine with suppressed serum TSH levels) were excluded from the study. The remaining 495 women were tested for thyroid functions. Out of 495 pregnant women in the study group, 50 (10.1%) were in 1st trimester, 291 (58.8%) in 2nd trimester and 154 (31.1%) in 3rd trimester. 234 (47.3%) were primi and 261 (52.7%) were multigravida.

Prevalence of subclinical hypothyroidism was 2.8% (14/495) and it was not associated with the gestational age (Table 1). TPO antibodies were positive in a total of 42(8.5%) of the study group. Among the 14 women with hypothyroidism, 8 (57.1%) were TPO antibody positive, and among the euthyroid women (n=481), 34 (7.1%) had the antibody positivity. The prevalence was significantly higher in the former group (p=0.012). Table 2 shows that the antibody positivity in euthyroid women was not dependent on the gestational age (Trend \( c^2=1.98, p=0.159 \)). It did not show an association with parity also (47.1% in primi and 52.9% in multipara, \( c^2=0.009, p=0.92 \)). Prevalence of hypothyroidism increased in relation to increasing gestational age (\( c^2 = 6.02, p=0.014 \)).

### Discussion

In this study, the prevalence of subclinical hypothyroidism in asymptomatic pregnant women attending outpatient department, was 2.8% which corroborated with that of western literature (2.5%). Raised anti TPO antibodies suggesting thyroid autoimmunity in women with subclinical hypothyroidism was seen in 57.1% while western literature reported prevalence of autoantibodies ranging from 60% to 90%. The mild variation in prevalence of thyroid autoimmunity could probably be because anti thyroglobulin antibodies were not measured in our study.

Western literature reports prevalence of autoimmunity in euthyroid pregnant women as high as 19.6%. According to data from the third National Health and Nutrition Examination Survey (NHANES-III) TPO positivity and anti-thyroglobulin antibodies were found in 12.6% and 13.6% of euthyroid women respectively. We noted that the prevalence of thyroid autoimmunity was independent of gestational age and parity. The reason for the decreased prevalence of autoimmunity in our population needs to be studied. Just as the influence of thyroid function in pregnancy is being increasingly recognized, thyroid physiology may also be altered during pregnancy. In pregnancy the requirement of thyroid hormone is increased because of increased thyroid binding protein (TBG) level due to estrogen activity, increased renal clearance of iodine and placental deiodinase activity.

A prospective study of women with untreated subclinical hypothyroidism found that compared to euthyroid women they were three times more likely to develop placental abruption and 1.8 times more likely to experience preterm labour. Gestational hypertension occurs not only in overt hypothyroid (36.1%) but also in subclinical disease compared to the general population. The incidence of low birth weight is markedly increased in case of overt as well as subclinical hypothyroidism. Fetal neurological development and cognitive function can be influenced by the thyroid status of the mother. Further, adequate thyroxine replacement for women with mild or overt hypothyroidism in early pregnancy results in term delivery in 90% but failure to achieve normal TSH during pregnancy has been associated with term delivery in only 20%. Women in euthyroid state but with thyroid autoimmunity are twice likely to experience spontaneous miscarriage, as it probably represents a generalized activation of immune system, or there is an increased risk of progression to subclinical hypothyroidism or probably due to transplacental transfer of thyroid receptor blocking antibodies. Three randomized controlled trials have studied the effects of Levothyroxine replacement in early pregnancy in women with euthyroid state but with positive TPO-antibodies, which showed marked reduction in miscarriage rate. Furthermore, studies have shown that the target TSH level in pregnancy is ≤ 2.5 mU/L. When the criteria was applied to our study, the prevalence of subclinical hypothyroidism is increased markedly 18.98% (94 out of 495). It is highlighted that as the gestational age increases, the percentage of women with subclinical hypothyroidism is doubled. Hence there is a need for screening subclinical hypothyroidism and thyroid autoimmunity in pregnancy, especially in the 1st trimester when the fetal thyroid tissue is not functional. The role of routine screening becomes all the more relevant in these patients as they are asymptomatic and symptoms if any are ascribed to pregnancy itself. In a country like India where the pregnancy rate is very high because of sheer magnitude of the population and where majority of women seek antenatal care at government institutions, such simple screening

### Table 1: Hypothyroidism Vs gestational age in euthyroid women

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Hypothyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 13 WKS</td>
<td>50</td>
</tr>
<tr>
<td>13 – 28 WKS</td>
<td>291</td>
</tr>
<tr>
<td>&gt; 28 WKS</td>
<td>154</td>
</tr>
<tr>
<td>Total</td>
<td>495</td>
</tr>
</tbody>
</table>

Trend Chi-square= 0.19, p=0.667

### Table 2: Anti TPO antibodies Vs gestational age in euthyroid women

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Number of euthyroid women</th>
<th>Number of AB +VE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;13 WKS</td>
<td>48</td>
<td>1</td>
</tr>
<tr>
<td>13-28 WKS</td>
<td>283</td>
<td>20</td>
</tr>
<tr>
<td>&gt;28 WKS</td>
<td>150</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>481</td>
<td>34</td>
</tr>
</tbody>
</table>

Trend Chi-square = 1.98, p=0.159
procedures could have profound implications on the health of the nation.

Acknowledgement

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References


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