Thyroid Disorders in Pregnancy- Experience from North East India

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ABSTRACT

Aims: Thyroid dysfunction is commonly encountered in pregnancy and can affect maternal and Fetal outcomes. Limited data are available from north east India on the prevalence of various thyroid disorders in pregnancy. The present study was hence conducted to evaluate the prevalence of thyroid disorders in a large government hospital in Assam.

Study Design: Prospective cohort study.

Place and Duration of Study: Sample: Department of endocrinology and department of obstetrics, Gauhati medical college, Guwahati between may 2011 to April 2013.

Methodology: Pregnant women irrespective of gestational age attending the antenatal clinic of Gauhati medical college were screened for thyroid dysfunction by estimation of serum free t34 (FT4), TSH and thyroid peroxidase antibodies (TPOAB). Subjects with known thyroid disorders, chronic illness or on medications known to affect thyroid status were excluded from the study. Results were interpreted as per the American thyroid association (ATA) 2011 guidelines.

Results: A total of 542 pregnant women were enrolled for this prospective cohort study. The mean age was 23.85±4.04 yrs. Of the 542 women screened, 69.18% were Euthyroid, 21.58% had subclinical hypothyroidism (SCH), 5.35% had overt hypothyroidism (OH), hyperthyroidism was...
observed in 2.39% and 1.47% had gestational Thyrotoxicosis. TPOAB were positive in 18.08% of women.

**Conclusion:** A high prevalence of thyroid disorders specially hypothyroidism were seen in this study using the newer ATA diagnostic criteria emphasizing the need for screening of all women during pregnancy.

**Keywords:** Pregnancy; thyroid disorders; north east India; hypothyroidism; subclinical hypothyroidism; TPO antibody.

**1. INTRODUCTION**

Thyroid dysfunction during pregnancy has long been known to have adverse effects on the mother and fetus. Taking into account the physiological changes in thyroid status during pregnancy, the American thyroid association [1] and endocrine society [2] published new pregnancy specific ranges and guidelines for the diagnosis and management of thyroid disorders in pregnancy. Recent studies have also highlighted the effect of maternal hypothyroidism on cognitive function in childhood [3]. The presence of TPOAB is also being recognized as a risk factor for progression to hypothyroidism, miscarriage, premature delivery [4,5] and perinatal death [6]. However the question of universal screening during pregnancy remains a matter of debate with the Indian thyroid society (ITS) recommending screening of all women for thyroid dysfunction in the first antenatal visit [7]. However, endocrine society [2] recommends screening for thyroid dysfunction only in high risk groups.

Studies from north east India on the prevalence of thyroid disorders in pregnancy are sparse [8]. In a recent study from north India hypothyroidism was the most common abnormality described seen in 14.3% [9] while thyroid insufficiency has been reported in 18% in a cross sectional study from south India [10]. The present study was hence undertaken to assess the prevalence of thyroid disorders in pregnancy among women attending a public hospital in Assam, India.

**2. MATERIALS AND METHODS**

Pregnant women irrespective of gestational age attending the antenatal clinic of Gauhati medical college, Assam were enrolled for this prospective cohort study. Subjects with known thyroid disorders who were on medications for their thyroid related disease, a history of diabetes mellitus, hypertension, any chronic illness or on medications known to affect thyroid status were excluded from the study.

Informed consent was taken from the patients and thorough clinical evaluation was done to look for features of thyroid dysfunction if any, including presence of goitre. The gestational age and expected date of delivery was noted. Ethical clearance was obtained from the institutional ethical committee of Gauhati medical college.

Five milliliters (ml) of blood was collected and analyzed for TSH, free T4, and anti TPO antibody in their first visit. As patients were enrolled in the clinic at different stages of gestation, gestational age differed among subjects. TSH and free T4 was planned to be repeated at necessary intervals if required according to the results of thyroid function tests in the first visit. TSH and free T4 were estimated by chemiluminescence using immulite 1000. A third generation TSH assay was used with a normal range of 0.4-4.0 mIU/L. The lower detection limit was 0.004 mIU/L. The intra assay coefficient of variation was 4.5% and inter assay coefficient of variation was 8%. Free T4 was estimated by immulite 1000 with a normal range of 0.89-1.76 ng/dL. The intra assay coefficient of variation was 4.5% and inter assay coefficient of variation was 8%. Anti tpo antibody was done by chemiluminescence method (immulite 1000). The lower detection limit is 7 IU/mL. Anti TPO > 150 IU/mL was taken as positive. The intra assay coefficient of variation was 4.3% and inter assay coefficient of variation was 10.5% (Table 1).

According to the american thyroid association (ATA) guidelines 2011 the normal pregnancy specific reference range for TSH is 0.1-2.5 mIU/L in the first trimester, 0.2-3.0 mIU/L in the second and 0.3-3.0 mIU/L in the third trimester (Table 2). Based on this recommendation subjects were diagnosed to have overt hypothyroidism (OH) if fT4 was low along with an elevated TSH of more than 2.5 mIU/L in the first trimester or more than 3.0 mIU/L in the 2nd and 3rd trimesters or a TSH >10 mIU/L irrespective of fT4 levels. Subclinical hypothyroidism (SCH) was defined as a normal fT4 with an elevated TSH of 2.5/3.0-10.0 mIU/L (trimester specific range).
Table 1. Lab ranges

| Test    | Normal range | Intra assay coefficient of variation | Inter assay coefficient of variation |
|---------|--------------|-------------------------------------|-------------------------------------|
| TSH     | 0.4-4.0 mIU/L| 4.5%                                | 8%                                  |
| Free T4 | 0.89-1.76 ng/dL | 4.5%                               | 8%                                  |
| Anti TPO| 7-150 IU/mL  | 4.3%                                | 10.5%                               |

Hyperthyroidism was defined as a suppressed tsh < 0.1 mIU/L with normal or elevated FT4. Gestational thyrotoxicosis (GTT) was diagnosed in women in first trimester with suppressed TSH with subsequent normalization and no clinical signs of graves’ disease.

Data were expressed as mean, median and standard deviation or number (%) unless specified. Data analysis was done using ms excel (windows 8) and SPSS software.

Table 2. Trimester specific normal values TSH

| Tsh   |
|-------|
| First trimester | 0.1-2.5 mIU/L |
| Second trimester | 0.2-3.0 mIU/L |
| Third trimester | 0.3-3.0 mIU/L |

3. RESULTS

Five hundred and forty two subjects at various gestational ages attending the antenatal OPD were recruited for the study. Of these, 313 (58.61%) subjects were primigravida and 229 (42.25%) were multigravida. We had one twin pregnancy and the remaining were singleton pregnancies. The mean age of the subjects was 23.85±4.04 years. Out of 542 patients at screening, 92 (16.97%) were in first trimester, 162 (29.88%) were in second trimester and the rest (53.13%) were in third trimester. The prevalence of subclinical hypothyroidism (SCH) was 21.58%, overt hypothyroidism (OH) was 5.35%, hyperthyroidism 2.39% and that of gestational thyrotoxicosis (GTT) was 1.47% (Fig. 1). The patients were divided in the following groups according to their thyroid function tests with respect to thyroid autoimmunity (Table 3). Goiter was present in 24 (4.43%) subjects.

The overall prevalence of TPO ab was 18.08%. TPO ab was positive in 16.8% of euthyroid women, 23.93% of women with SCH, 17.24% of women with OH. (Fig. 2) among the women with hyperthyroidism, two had graves’ disease and TPO ab were positive in both of them. Eleven women had subclinical hyperthyroidism and all were TPO negative.

Symptoms suggestive of thyroid dysfunction were present in 13(11.11%) of patients with subclinical hypothyroidism, 7(24.1%) with overt hypothyroidism and 2(15.3%) with hyperthyroidism. One patient with gestational thyrotoxicosis had hyperemesis which resolved.

4. DISCUSSION

Recognition of thyroid dysfunction during pregnancy is important in view of the adverse effects on maternal and fetal health as well as long term cognitive effects in the offspring. The recent changes in the normal levels of serum TSH in pregnancy has resulted in an increase in women being diagnosed with thyroid disorders specially hypothyroidism. Using an upper limit for serum TSH of 2.5 mIU/L in the first trimester and

Table 3. Distribution of patients according to their thyroid function status

| Thyroid status  | Patient groups          | Number (%) |
|-----------------|-------------------------|------------|
| Normal (n=375, 69.18%) | Group 1 (normal TSH, with TAI) | 63 (16.8) |
|                 | Group 2 (normal TSH, without TAI) | 312 (83.2) |
| SCH (n=117, 21.58%) | Group 3 (subclinical hypo, with TAI) | 28 (23.93) |
|                 | Group 4 (subclinical hypo, without TAI) | 89 (76.06) |
| OH (n=29, 5.35%) | Group 5 (overt hypo, with TAI) | 5 (17.24) |
|                 | Group 6 (overt hypo, without TAI) | 24 (82.75) |
| Hyperthyroidism (n=13, 2.39%) | Group 7 (hyper, with TAI) | 2 (15.38) |
|                 | Group 8 (hyper, without TAI) | 11 (84.61) |
| GTT (n=8, 1.47%) | Group 9 (GTT) | 8 (1.47) |

***TAI: thyroid autoimmunity***

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Fig. 1. Distribution of patients according to their thyroid function status

![Pie chart showing distribution of thyroid function status]

Fig. 2. Distribution of thyroid autoimmunity in various gestational groups (%)

![Bar chart showing distribution of thyroid autoimmunity]

Table 4. Symptoms and signs of thyroid dysfunction

| Symptoms and signs | Normal N=375 | SCH N=117 | OH N=29 | Hyperthyroidism N=17 | GTT N=8 |
|--------------------|-------------|-----------|---------|----------------------|--------|
| Dry skin           | -           | 3 (2.56)  | 4 (13.7)| -                    | -      |
| Cold intolerance   | -           | 4 (3.41)  | 5 (17.2)| -                    | -      |
| Puffiness          | -           | 3 (3.41)  | 3 (10.3)| -                    | -      |
| Paresthesias       | -           | -         | 3 (10.3)| -                    | -      |
| Weight loss        | -           | -         | -       | 2 (11.7)             | -      |
| Constipation       | -           | 5 (4.27)  | 4 (13.7)| -                    | -      |
| Goitre             | 10 (2.56)   | 10 (8.54) | 2 (6.89)| 2 (11.76)            | -      |
| Hyperemesis        | -           | -         | -       | -                    | 1 (12.5)|
| Ophthalmopathy     | -           | -         | -       | -                    | -      |
3.0 mIU/L in the second and third trimesters, the present study shows a prevalence of SCH of 21.58% and OH of 5.35%. Dhanwal et al. [9] in their study of 1000 women from north India in their first trimester found a prevalence of hypothyroidism of 14.3% using a TSH cut off of 4.5 mIU/L and a TPO ab prevalence of 6.8%. In a recently published cross sectional study from south India [10] of 334 pregnant women of ≤14wks gestation using a TSH cut off of 2.5 mIU/L, thyroid insufficiency was seen in 18%, 3.7% had OH, 9.2% had SCH and 5.2% had hypothyroxinemia. In another study conducted in New Delhi among 400 pregnant women between 13-26 wks of gestation, the prevalence of hypothyroidism was 12% and hyperthyroidism was 1.25% [11]. In a large Chinese survey of 4800 pregnant women [12], the prevalence of SCH was 27.8% using a diagnostic cut off of TSH>2.5 mIU/L and 4.0% using a reference interval derived in their laboratory (0.14-4.87). They concluded that TSH in the first trimester was much higher than 2.5 mIU/L in Chinese pregnant women. Some Indian studies have also attempted to establish reference ranges in an Indian population. Marwaha et al. [13] in a reference population of 331 pregnant women used the 5th and 95th percentile to determine reference ranges for fT3, fT4 and TSH. The trimester wise values in first, second and third trimesters were: fT4 (12-19.45, 9.48-19.58, 11.32- 17.7 pm/l) and TSH (0.6-5.0, 0.44-5.7 and 0.74-5.7µiu/ml). In another study by Maji et al [14] from Kolkata, references ranges were determined in 402 healthy pregnant women using the 2.5th and 97.5th percentile. TSH levels were 0.25-3.35 µiu/ml in 1st, 0.78-4.96 in 2nd and 0.89-4.6 in 3rd trimester. Corresponding ranges for fT4 were 0.64-2.0, 0.53-2.12 and 0.64-1.98 ng/dL in 1st, 2nd and 3rd trimesters respectively. Recent study conducted by Rajput et al [15] from Rohtak, Haryana in 461 pregnant women during first trimester, the prevalence of subclinical hypothyroidism was 21.5%, overt hypothyroidism was 0.4%, subclinical hyperthyroidism was 3.3% and anti TPO was elevated in 27.8%.

In developing countries the most frequent cause of hypothyroidism is represented by severe iodine deficiency while in developed countries it is caused by chronic autoimmune thyroiditis [16]. Thyroid autoantibodies have been detected in up to 50% of women with SCH and 80% of women with OH [17]. The present study shows relatively lower TPO antibody positivity in women with hypothyroidism. As the iodine status of these women was not estimated we cannot specify the cause of thyroid dysfunction in them. Higher prevalence of hypothyroidism in our study population could probably be due to location of Assam in sub-Himalayan region, which is known as an iodine deficient area, presence of goitrogens in diet or micronutrient deficiency such as selenium or iron deficiency [18]. Nambiar et al [19] in their study of 483 pregnant women in the first trimester found a prevalence of TPO ab of 12.4%. Hypothyroidism was seen in 4.8% using a TSH level of >4.0 mIU/L. In another study from south India among 500 pregnant women, TPO positivity was seen in 2.8% of euthyroid women and 5.7% of women with SCH [20]. Our study however shows a higher prevalence of TPO antibodies in 16.8% of euthyroid women. In another large study by Negro et al [21] of 984 euthyroid pregnant women, TPO ab was positive in 11.7%. As presence of thyroid autoimmunity is a risk factor for progression to hypothyroidism these women are to be followed up at regular intervals.

Our study hence shows a relatively high prevalence of hypothyroidism with symptoms of thyroid dysfunction being present in only a minority stressing the need for screening of all pregnant women. The increased prevalence of TPO antibodies also underscores the need for following up these women.

5. CONCLUSION

Thyroid dysfunction was diagnosed in a high proportion of women being screened at an antenatal clinic in a public hospital in Assam. Keeping in mind the known effects of thyroid dysfunction on maternal and fetal well being, screening of all pregnant women should be recommended for optimal pregnancy outcome.

ETHICAL APPROVAL

Institutional ethical committee approval was taken before starting the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.
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