

Original article

“Prevalence of Thyroid Hormone Disorder in Pregnant Females at a Tertiary Care Hospital in the Rural Area of Mandhana-Kanpur”

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Abstract:

Pregnancy is associated with significant but reversible changes in thyroid function which are a result of normal physiologic state and hormonal changes that alter thyroid function. Thyroid function is frequently assessed during pregnancy, both to evaluate suspected thyroid abnormalities and to monitor the status of pre-existing thyroid disease. Thus the laboratory tests of thyroid function must be interpreted with caution during pregnancy. Uncontrolled hyperthyroidism and hypothyroidism are associated with serious maternal, fetal, and neonatal morbidity, and mortality. With this background the present study was planned to investigate the status of thyroid functions in 50 pregnant women of different age groups, with different period of gestation and having different number of pregnancies over a period of one year. From the results and observations of our study we infer that the majority of pregnant women were Euthyroid which is 80%, Hypothyroidism was observed in 8 % of our study population and Subclinical hypothyroidism in 12%. No case of Hyperthyroidism was recorded. The assessment of thyroid function in pregnant women will draw the attention of physicians to deal properly with the thyroid problems during pregnancy and will be useful in adopting strategies which may be applied for pregnant women of this region.

Keywords: fT3, fT4, Hyperthyroid, Hypothyroid, Pregnant women, Subclinical hypothyroid, Thyroid Function Tests, TSH.

Intoduction

Pregnancy is associated with significant but reversible changes in thyroid function which are a result of normal physiologic state and hormonal changes that alter thyroid function^[1]. These changes mean that laboratory tests of thyroid function must be

interpreted with caution during pregnancy^[2]. Thyroid function changes during pregnancy due to the influence of two main hormones; first being the human chorionic gonadotropin (hCG), the hormone that is measured in the pregnancy test and estrogen being the second hormone, which is the main female hormone. TBG levels

around 20 weeks, leading to increases in serum thyroxine levels^[3]. Estrogen increases the amount of thyroid hormone binding proteins in the serum which increases the total thyroid hormone levels in the blood since >99% of the thyroid hormones in the blood are bound to these proteins^[4]. However, measurements of “Free” hormone (that is not bound to protein, representing the active form of the hormone) usually remain normal^[5]. The thyroid is functioning normally if the TSH, free thyroxine (T4) and free triiodothyronine (T3) are all normal throughout pregnancy. Therefore, thyroid function is frequently assessed during pregnancy, both to evaluate suspected thyroid abnormalities, and to monitor the status of pre-existing thyroid disease^[6]. As thyroid disorders are the most common endocrinology disorders of childbearing age^[7]. Moreover, thyroid disorders may affect both the pregnant woman and the developing fetus; where thyroid hormones having important role in embryogenesis and fetal development^[8]. The fetus is completely dependent on the mother for thyroid hormone^[9]. Disorders of the thyroid include both overt and mild/subclinical hypothyroidism and hyperthyroidism and goitre.

Hypothyroidism is estimated to occur in 0.3-0.5% of pregnancies^[10]. Subclinical hypothyroidism appears to occur in 2-3%.^[11] Hyperthyroidism during gestation, usually caused by Graves disease, is rare (0.2%).^[12] Uncontrolled hyperthyroidism and hypothyroidism are associated with serious maternal, fetal, and neonatal morbidity, and mortality. Maternal complications include miscarriage,

pregnancy-induced hypertension, preterm labor, placental abruption, heart failure, and thyroid storm. Fetal and neonatal complications include stillbirth, low birth weight, goiter, hyperthyroidism, and hypothyroidism^[13,14,15]

Problem statement

Checking routinely (screening) for possible thyroid problems was not considered important in pregnant women, where pregnant women with thyroid disease do not always develop symptoms, and when they do, these symptoms can sometimes be attributed to the pregnancy itself. It is only considered important when pregnant women had the typical symptoms of hypothyroidism or hyperthyroidism. Lack of early diagnosis increase the risk of pre-term birth, placental abruption, fetal death, and impaired neurological development in the child. For these reasons, it is important to ensure optimal maternal thyroid function during pregnancy so accurate laboratory assessment of maternal thyroid function is important. Mandhana Kanpur has been described as an iodine deficient region, hence this study is planned to assess the thyroid hormone status in the primigravida females of this region. Moreover, no such study in this region has been carried out before. The assessment of thyroid function in pregnant women will draw the attention of physicians to deal properly with this problem including screening of thyroid hormones during pregnancy.

Materials and Methods

The current study was a hospital based cross sectional study; carried out in the

department of Physiology in collaboration with the department of Biochemistry and the department of Obstetrics and Gynaecology, Rama Medical College Hospital & Research Centre, Kanpur; after due approval from the Institutional Medical Ethics Committee. The study was conducted over a period of one year, from June 2014 to May 2015. This study was carried out on 50 pregnant females aged between 18-35 years. Informed written consent was taken from all the patients included in the study. Pregnant women already diagnosed with twin pregnancy, previous history of thyroid disorder, positive family history of thyroid disorder, eclampsia and pregnancy complicated with any chronic illness (heart disease, renal disease, diabetes mellitus, hypertension and liver disease) were excluded from the study.

The primary aim of this study was to assess the thyroid hormone status fT3, fT4 and TSH in the pregnant women. Under all aseptic guidelines; blood samples were taken from the subjects and Thyroid hormone profile including TSH, fT3 and fT4; was done by the Electrochemiluminescence method on Roche Elecsys 2010 instrument.^[16]

Statistical analysis

Data were computer analyzed using SPSS/PC. Results were expressed as a mean \pm SD. For comparison of the obtained variables between the study periods, we performed the Kruskal–Wallis rank test and χ^2 -test. Spearman's analysis was used to calculate the correlation coefficients. One way ANOVA test was used. P value < 0.05 was marked as statistically significant.

Results

Of total 50 cases were observed, in which 40 patients (80%) were Euthyroid; 6 patients (12%) were Sub-clinical hypothyroid and finally 4 patients (8%) were Hypothyroid. No case of Hyperthyroidism was recorded [Fig-1]. Table-2 reflects that the mean value of fT3 was 3.61 ± 0.70 , 3.33 ± 0.39 , 0.31 ± 0.13 and 0 in Euthyroid, Subclinical hypothyroid, Hypothyroid and Hyperthyroid groups respectively. The mean value of fT4 was 14.86 ± 1.28 , 14.54 ± 0.86 , 3.39 ± 1.29 and 0 in Euthyroid, Subclinical hypothyroid, Hypothyroid and Hyperthyroid groups respectively. The mean TSH value was 3.18 ± 1.22 , 7.49 ± 0.78 , 57.57 ± 25.78 and 0 in Euthyroid, Subclinical hypothyroid, Hypothyroid and Hyperthyroid respectively.

Fig -1: Sample distribution as a function of thyroid hormone status.

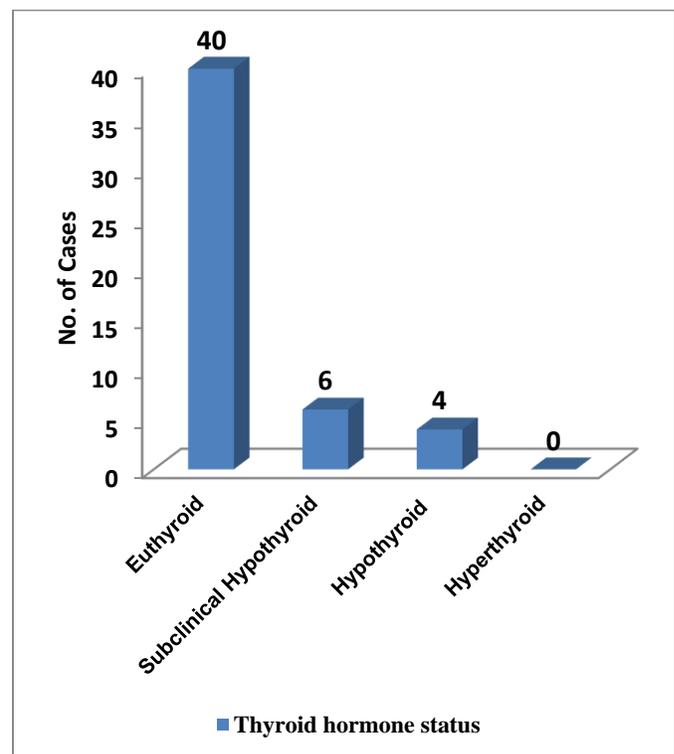


Table -1: Thyroid profile of the study population.

| Thyroid status | No. of cases | ft3 | ft4 | TSH |
|-------------------------|--------------|-------------------|--------------------|--------------------|
| Euthyroid | 40 | 3.61±0.70 | 14.86 ±1.28 | 3.18±1.22 |
| Subclinical Hypothyroid | 6 | 3.33±0.39 | 14.54 ±0.86 | 7.49 ±0.78 |
| Hypothyroid | 4 | 0.31 ±0.13 | 3.39 ±1.29 | 57.57 ±25.78 |
| Hyperthyroid | 0 | 0 | 0 | 0 |
| Total | 50 | 3.31 ±1.09 | 13.91 ±3.32 | 8.05 ±16.01 |

and psychomotor development in infants^[19]. Better and easier measurements of T4 and ft4 during early pregnancy would

Discussion

Specific reference intervals for ft4, T4, T3 in addition to TSH during pregnancy may be particularly important for several reasons. First, it would be important to know what the ft4 levels are in the first trimester as they are higher than in other trimesters in a euthyroid pregnancy; as this is time when the foetus is wholly dependent on T4 from the mother. Accurate reference intervals for T4 and ft4 would then provide the ability to detect a deficiency at this critical time and provide a subtle indication of maternal hypothyroidism. Such hypothyroxinemia may be masked during the first trimester if that determination relied solely on an elevated TSH because of the stimulatory effect of high hCG levels on the thyroid gland. It is possible that high, sustained estrogen levels during this time are associated with transient lowering of serum TSH^[17]; thus curtailing its rising above the normal non pregnant range. Second maintenance of normal maternal thyroid hormone levels is known to be a determinant of adequate foetal thyroid hormone levels early in pregnancy^[18] and adequate mental

thyroid deficiency at this critical time for the foetus. Mild maternal hypothyroidism (subclinical hypothyroidism) has been implicated as the cause of neuro-psychointellectual deficit in offspring^[20]. Accurate reference intervals in early pregnancy would make it possible to better define this condition. In cases of overt hypothyroidism the foetal consequences can be extreme^[21]. However, it appears that the maternal level and delivery of ft4 and not T3 to the foetus is critical for the neuropsychological development of the foetus. A deficiency may not be reflected by the degree of TSH elevation. It is imperative for normal intervals of thyroid hormones to be established for pregnant women especially it should be determined in early pregnancy and particularly T4 level which can be used to screen the foetus and pregnancy risk.

With this background the present study was planned to investigate the status of thyroid functions in pregnant women. This could be useful in adopting strategies which may be applied for pregnant women of this region as this is the first study carried out in this area. Data presented in this study dealt with 50

pregnant women of different age groups, with different period of gestation and having different number of pregnancies. From the results and observations of our study we infer that the majority of pregnant women were Euthyroid which is 80% (**Fig-1**). Hypothyroidism was observed in 8 % of our study population and Subclinical hypothyroidism in 12%. No case of Hyperthyroidism was recorded. The prevalence in North Indian pregnant women is reported to be 14.7%^[22]. Our results are higher than those reported for pregnant women in **European, American and Tunisian** pregnant women where the prevalence was 2.2%, 2.5% and 3.2% respectively^[23-28]. In a study in **United States** where a total of 10,990 patients had first- and second-trimester serum assayed for TSH, free T4, and antithyroglobulin and antithyroid peroxidase antibodies. Subclinical hypothyroidism was documented in 2.2% (240 of 10,990) in the first trimester. Hypothyroxinemia was documented in 2.1% (232 of 10,990) in the first trimester. Subclinical hypothyroidism was not associated with adverse outcomes. Hypothyroxinemia was associated with preterm labor^[29]. **Casey et al (2005)** in their study found subclinical hypothyroidism in his normal pregnant women^[25].

The thyroid hormone profile (**Table-1**) of the pregnant females in our study revealed; the mean value of fT3 as 3.61 ± 0.70 , 3.33 ± 0.39 , $0.310 \pm .13$ and 0 in Euthyroid, Subclinical hypothyroid, Hypothyroid and Hyperthyroid groups respectively. The mean value of fT4 was 14.86 ± 1.28 , 14.54 ± 0.86 , 3.39 ± 1.29 and 0 in Euthyroid, Subclinical hypothyroid, Hypothyroid and Hyperthyroid

groups respectively. The mean TSH value were 3.18 ± 1.22 , 7.49 ± 0.78 , 57.57 ± 25.78 and 0 in Euthyroid, Subclinical hypothyroid, Hypothyroid and Hyperthyroid respectively. While comparing the two groups (Euthyroid versus Hypothyroid) having different parameters, fT3 is significant at $t = 4.88$, $p < 0.05$; fT4 is highly significant at $t = 8.95$, $p < 0.001$; and TSH is also significant at $t = 7.87$, $p < 0.001$. When we compared the two other groups (Euthyroid versus Subclinical hypothyroid) having different parameters, only TSH group is significant having $t = 3.65$ at $p < 0.05$. We also compared the group (Subclinical hypothyroid versus Hypothyroid) having different parameters, fT3 is highly significant at $t = 9.48$ $p < 0.001$; fT4 is highly significant at $t = 3.16$ $p < 0.05$.

In a study similar to ours; five hundred and forty-one apparently healthy Indian pregnant women with uncomplicated single intrauterine gestation reporting to **Armed Forces Clinic** in any trimester were consecutively recruited. Of the 541 consecutive pregnant women in different trimesters enrolled for the study 210 were excluded. The composition of reference population comprising 331 women was 107 in first trimester, 137 in second trimester and 87 in third trimester. The 5th and the 95th percentile values were used to determine the reference ranges for fT3, fT4 and TSH. The trimester wise values in the first, second and third trimester were fT3 1.92-5.86, 3.2-5.73, 3.3-5.18 pm/L FT4 12.0-19.0, 9.48-19.58, 11.32-17.7 & TSH 0.60-5.0, 0.44-5.78, 0.74-5.7 respectively. Analysis of mean, median values for fT3, fT4 and TSH between each trimester showed no significant differences in fT3 and TSH values (95% CL). However

fT4 showed significant variation between each trimester with values decreasing with advancing gestational age (P value first versus second = 0.015, first versus third = 0.003 and second versus third = not significant).

In another study to evaluate serum level of TSH in 124 pregnant women; healthy young primigravidas consecutively attending the antenatal clinic; were included in the study. Mean TSH levels was 1.20 microIU/ml. Three asymptomatic pregnant women (2.5%) were found to have abnormal TSH the values with normal T3 and T4 levels where normal obstetric outcome was good^[30].

In a screening study for 4800 **Chinese** women during the first half of pregnancy; the women were screened for thyrotropin, free thyroxine and thyroid peroxidase antibody. Two different series of reference intervals for TSH and fT4, were calculated, the gestational age – specific reference intervals (S1) and non-pregnant population reference intervals (S2) were used to diagnose thyroid dysfunction. The S2 of serum TSH was 0.3-4.8 mIU/L, fT4 was 10.3 – 24.5 pmol/L. Hormone deficiency as the prevalence of subclinical hypothyroidism at 4,8 and 12 weeks of gestation was 4.59%, 6.15%, 4.68%, respectively, and the prevalence of hypothyroxinaemia was 3.69%, 1.11% 2.92% respectively^[31].

To study the influence of pregnancy on the results of free thyroxine measurement; thirty-eight healthy pregnant women were enrolled in the study. Serial TSH, free thyroid

hormone, total thyroid hCG and thyroid autoantibody levels. Data of 19 individuals were analyzed. An increase of Total T3 and T4 levels was observed parallel with changes of TBG concentration during the first 4 months of gestation. Serum TSH time –curve showed a transient fall in the first trimester, thereafter it returned to the non-pregnant values. Curves of serum TSH and hCG created clear mirror images. Free T4 concentrations elevated in line with the hCG peak at the beginning of gestation, thereafter it clearly followed the course of serum TSH. Free T3 levels gradually decreased throughout pregnancy. The negative correlation between hCG and TSH levels, and the clear identity of the hCG + TSH and free T4 curves^[32].

In a study of 118 healthy pregnant women living in an iodine-sufficient area with the mean age 30.9 ± 4.1 years; TSH levels were measured. It was observed that TSH concentration was significantly higher in the third trimester than in the first trimester ($P = 0.007$)^[33].

To investigate the relationship between TSH and fT4, a study on 5520 women during the first trimester of pregnancy was carried out. The reference interval for TSH was determined to be 0.06–3.67 mU/l. The suppression of TSH was found in 2.93% of the women; a raised concentration of TSH was found in 4.48% of the women. fT4 was determined only for women ($n=697$) with TSH lower than 0.1, for fT4 reference interval of 9.8–23.1 pmol/l for all populations. There were 30 (4.3%) women with fT4 under and 18 (2.5%) women with fT4 over the reference interval^[34].

Galinoer et al (1994) and **Klein et al (1991)** also got high levels of TSH and low levels of T3, T4 in their studies ^[26,27] our results are in agreement of these studies.

The major cause of Hypothyroidism could be attributed to the iodine deficiency in some of these women in our study. While the Kanpur region is considered as marginally iodine sufficient region, the increase of iodine requirement during pregnancy may cause substantial iodine deficit that induces thyroid insufficiency. This further may be due to the use of non iodized salt in low socio-economic groups in the study population.

The higher prevalence of hypothyroidism in advanced gestation suggests that iodine deficiency is probably a key contributor of hypothyroidism in our pregnant women. Hypothyroidism might also be caused by defect in iodine metabolism. However, following iodine metabolism in the study group was beyond the objectives of this research. Also the economic situation in the country does not allow the presence of system with balanced food for pregnant women. This system should provide protection to pregnant women of any malnutrition during pregnancy. Kanpur being an agricultural land; the contamination of water and soil may have negative impact on the thyroid function due to misuse of pesticides by farmers; which leads to contamination of vegetables and fruits affecting the human health ^[35].

Hyperthyroidism was observed in 0.0 % of our pregnant women, it was more or less similar to that reported in **Tunisia** (1.3%).

As our study population was small and the prevalence of hyperthyroidism being low; the reported cases of hyperthyroidism were nil in our study ^[23].

Data revealed that there is no significant difference between those who had abnormal thyroid hormones and those who had normal hormone levels. The group who had abnormal thyroid function had elevated TSH but normal fT3 and fT4. This means that they had subclinical hypothyroidism also known as mild hypothyroidism that has not progressed^[36]. Usually TSH in these cases has not exceeded 10 mIU/ml. The mean TSH in these cases was 7.49 ± 0.78 , mean fT3 was 3.33 ± 0.39 and mean fT4 was 14.54 ± 0.86 . Those cases where TSH is increased and fT3 & fT4 is decreased were grouped under clinical hypothyroidism. In these cases TSH was usually higher. The mean TSH in these cases was 57.57 ± 25.78 , mean fT3 was 0.31 ± 0.13 and mean fT4 was 3.39 ± 1.29 .

Recommendations

Thyroid function testing or only TSH or fT4 studies prior to conception or in early pregnancy are recommended. Pregnant women in the following categories should have thyroid function assessed either at diagnosis or at antenatal booking, or even before conception if feasible: type-1 diabetes, previous history of thyroid disease, current thyroid disease, family history of thyroid disease, goitre, symptoms of hypothyroidism. It is also recommended to launch a program aiming at determination of normal levels of thyroid hormones during the three phases of pregnancy.

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