Original Article

A study of thyroid profile among the first trimester pregnant women attending tertiary care hospital, Vijayanagara Institute of Medical Sciences, Ballari

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ABSTRACT

Background: As the thyroid dysfunctions are common endocrinal disorders seen during pregnancy, it may go unnoticed due to nonspecific symptoms. The maternal thyroid dysfunction has an adverse impact on both maternal and fetal outcome. Therefore, the evaluation of thyroid functioning during the first trimester avoids complications both in mother and fetus. **Objectives:** The present study was conducted to assess the maternal thyroid functions (triiodothyronine [T3], thyroxine [T4], and thyroid stimulating hormone [TSH]) during the first trimester of pregnancy and also to determine the proportion of thyroid dysfunction in these subjects. **Materials and Methods:** 80 apparently normal the first trimester pregnant women were randomly selected and were aged between 18 and 35 years from the outpatient department of Obstetrics and Gynaecology, Vijayanagara Institute of Medical Sciences, Ballari. The T3, T4, and TSH levels were estimated using chemiluminescent immunoassay method. **Results:** The mean total T3 and T4 levels were significantly increased during 10-12 weeks of gestation as compared to 6-9 weeks with *P* value of 0.03 and 0.02, respectively. Based on American Thyroid Association guidelines for TSH values during the first trimester of pregnancy, the proportion of thyroid dysfunction was found to be high, of which 16.3% were in hypothyroid range, and 2.5% were in hyperthyroid range. **Conclusion:** A high proportion of thyroid dysfunctions (16.3% in hypothyroid range and 2.5% in hyperthyroid range) was observed during the first trimester of pregnancy, and hence a routine antenatal screening is suggested, to diagnose the thyroid dysfunction at the earliest.

Key words: First trimester pregnancy, Triiodothyronine, Thyroid stimulating hormone, Thyroxine

INTRODUCTION

Pregnancy increases demand on the maternal thyroid gland. Failure to cope up with increased demands leads to thyroid dysfunction resulting in maternal and fetal complications. Maternal complications include hypo (subclinical: 2-3%, overt: 0.3-0.5%) and hyperthyroidism (0.2-0.4%).[1]

Fetal complications involve impaired neuropsychomotor development, reduced intelligence quotient, neonatal hypo, or hyperthyroidism depending on maternal thyroid status.[2]

Hence, this study intends to evaluate thyroid status in the apparently normal first trimester of pregnant women during the first trimester to determine abnormalities associated with thyroid functioning at the earliest and to initiate measures that help in preventing both maternal and fetal adverse outcomes.

MATERIALS AND METHODS

A sample of 80 first trimester pregnant women attending the outpatient department of Obstetrics and Gynecology were randomly selected from January 2012 to January 2013.

After taking a brief history, a detailed clinical examination was done for these subjects and the gestational age was confirmed. Informed written consent

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was taken. Then, 2 ml of venous blood sample was collected from antecubital vein, and it was sent to a laboratory for measurement of triiodothyronine [T3], thyroxine [T4], and thyroid stimulating hormone (TSH) levels by chemiluminescent immunoassay method.

Inclusion criteria

1. Apparently healthy first trimester pregnant women including both primigravida and multigravida.
2. First trimester pregnant women in the age group of 18-35 years.

Exclusion criteria

1. Pregnant women diagnosed with thyroid dysfunction.
2. Pregnant women with associated medical illness such as cardiac diseases, diabetes mellitus, respiratory disorders, autoimmune disorders, and psychological disorders,
3. Pregnant women not willing to give consent.
4. Non co-operative subjects.

Chemiluminescence immune assay

Chemiluminescence involves the generation of electromagnetic radiation as light by the release of energy from a chemical reaction. The light so generated from these chemical reactions can be emitted in ultraviolet, visible, infrared region, but the most common the light will be in the visible wavelength range.

Principle

In chemiluminescent immunoassay, the chemiluminescence is used as a label to detect the analyte. The reaction takes place in following steps.

1. The antigens (in the patient sample, i.e., the analyte and the antigen in the reagent) and the antibodies, which are labeled with chemiluminescent label or tag and they are allowed to react with each other and form antigen-antibody complex
2. The next step involves the separation of bound and free reactants. This separation depends on the type of separation system used. The bound form that is retained at the end of separation step contains the antigen that is bound to antibody labeled with the chemiluminescence tag
3. To this antigen bound to chemiluminescent substance, some substrate is added in order to initiate the chemiluminescence reaction. In some assays, the chemiluminescence is achieved by changing the nature of reaction mixture
4. The chemiluminescence that is emitted is measured by means of photomultiplier tube and luminometer. On the basis of chemiluminescence, the concentration of the analyte is estimated.

This antibody-based system provides target specificity and versatility. On the other hand enzyme component provides signal amplification. This feature enhances the detection sensitivity of chemiluminescent immunoassay.[3]

RESULTS

Study design

A descriptive case series study conducted on 80 first trimester pregnant females, to evaluate the thyroid status (T3, T4 and TSH) in them and also to determine any thyroid abnormalities associated with it. The data were tabulated and statistically analyzed.

Statistical tests used are

Mean: Measure of central tendency.
Median: Measure of dispersion.
Independent *t*-test: This was used to compare quantitative variables such as T3, T4, and TSH between any two groups or characteristics or variables.
ANOVA test: This was used to compare quantitative variables such as T3, T4, and TSH between any more than two groups or characteristics or variables.

Table 1 shows the anthropometric details of all the subjects. The mean weight and height of the subjects are 51.20 kg and 154.13 cm, respectively.

Table 2 represents the distribution of the subjects according to their age.

Subjects who were in the age group of 18-24 years constituted 71.2%, those in the age group of

Table 1: Anthropometric measurements of the subjects

Statistics	Weight (Kg)	Height (cm)
Frequency	80	80
Mean	51.20	154.13
SD	2.66	3.91
Minimum	47	146
Maximum	62	164

SD: Standard deviation

Table 2: Age wise distribution of subjects

Age group (years)	Frequency	Percentage
18-24	57	71.2
25-29	20	25.0
30 and above	03	03.8
Total	80	100

25-29 years constituted 25% of the sample and 3.8% of the sample were 30 years and above.

From the Table 2, it is evident that majority of subjects were in the age group of 18-24 years.

Table 3 shows the mean and standard deviation of the thyroid profile of the study subjects, it is evident that mean T4 is 11.452 μg/dl, the mean T3 is about 125.93 ng/dl, and the mean TSH is 1.576 μIU/ml respectively in the study subjects.

This is similar to study done by Mansurian *et al*.,[4] where the mean TSH levels in the study population were 1.31 μIU/ml and the lower limit and upper limit of serum TSH were 0.1 and 6.2 μIU/ml.

Table 4 shows the comparison of mean T4, T3, and TSH levels of subjects between the 6-9 weeks and 10-12 weeks of gestation. From the Table 4 it is obvious that the comparison of T3 and T4 levels between the gestational age of 6-9 weeks and 10-12 weeks are significant, and the *P* values are 0.03 and 0.02 respectively; but the comparison of TSH levels between the 6-9 weeks and 10-12 weeks does not show significance with a *P* value of 0.23.

These observations were similar to studies conducted by Jabber *et al*.,[5] Zarghami *et al*.,[6] Pasupathi *et al*.,[7] Kumar *et al*.,[8] which showed an increase in T3, T4 levels during first trimester of pregnancy.

Table 5 shows the categorization of study subjects based on TSH values as per American Thyroid Association (ATA) guidelines for TSH values for first trimester of pregnancy. It was observed that 81.3% were euthyroid, 16.3% were in hypothyroid range, and 2.5% were in hyperthyroid range.

The present study is in agreement with the study conducted by Dhanwal *et al*.,[9] wherein the incidence of hypothyroidism was found to be 14.3% during first trimester of pregnancy.

The observations of the present study are similar to the study conducted by Nambiar *et al*.,[10] who reported the prevalence of hypothyroidism and thyroid autoimmunity as 4.8% and 12.8%, respectively.

This study is also in favor of study conducted by Sahasrabuddhe *et al*.[11] who reported the prevalence of hypothyroidism as >10%.

A study done by Mukhopadhyay *et al*.[12] reported the incidence of hypothyroidism in pregnancy about 3.69% unlike the observations found in the present study.

A study by Goel *et al*.[13] reported the prevalence of hypothyroidism of about 6.3% which is in favor of the findings of the present study.

A study done by Shah *et al*.[14] reported the prevalence of hypothyroid in 4.4% and overt hyperthyroidism in 0.6% in their study subjects which is quite less compared to the observations of the present study.

Table 3: The thyroid profile of study subjects

Statistics	TSH (ulU/ml)	T3 (ng/dl)	T4 (ug/dl)
Frequency	80	80	80
Mean	1.576	125.93	11.452
SD	1.070	32.04	2.423
Minimum	0.01	71	6.7
Maximum	5.31	206	17.9

SD: Standard deviation, TSH: Thyroid stimulating hormone, T3: Triiodothyronine, T4: Thyroxine

Table 4: Comparison of thyroid profile across gestational age

Thyroid profile	Mean±SD		*P* value*
	GA of 6-9 weeks	GA of 10-12 weeks	
TSH (ulU/ml)	1.77±1.24	1.47±0.96	0.23 (not significant)
T3 (ng/dl)	115.61±26.36	131.48±33.66	0.03 (significant)
T4 (ug/dl)	10.59±1.87	11.91±2.57	0.02 (significant)

SD: Standard deviation, TSH: Thyroid stimulating hormone, T3: Triiodothyronine, T4: Thyroxine

Table 5: Thyroid profile based on TSH levels

Thyroid status	Frequency	Percentage
Hyperthyroidism	02	02.5
Normal	65	81.3
Hypothyroidism	13	16.3
Total	80	100

TSH: Thyroid stimulating hormone

DISCUSSION

Pregnancy can be viewed as a state, in which a combination of events occurs to modify the thyroid economy.[10] There occurs changes in thyroid hormones, TSH levels and even in thyroid binding globulin levels during normal pregnancy.

The thyroid dysfunction can be overlooked in pregnancy because of nonspecific symptoms and hypermetabolic state. Maternal thyroid dysfunction is associated with complications during pregnancy and can affect both the maternal and fetal outcome.[15] Therefore, it is important to identify the thyroid disorders, early in pregnancy, so that appropriate measures can be initiated.

The mean weight and height of the subjects were 51.20 kg and 154.13 cm respectively. The majority of the subjects were in the age group of 18-24 years (71.2%).

The comparison of mean T3 and T4 levels between the gestational ages of 6-9 weeks and 10-12 weeks were significant, with the *P* values are 0.03 and

0.02 respectively. i.e., mean T3 and T4 values were significantly high during 10-12 weeks in comparison to 6-9 weeks of gestational age. Whereas the comparison of TSH levels between 6-9 weeks and 10-12 weeks did not show a significant difference ($P = 0.23$).

The increase in thyroid hormone levels can be attributed to several mechanisms. During pregnancy, there is an increased concentration of estrogen, which influences the increase in the synthesis of hepatic thyroxine binding globulin (TBGs). It also prolongs the half-life of thyroid binding globulins from 15 min to 3 days because of estrogen-induced sialylation. Hence, there is decreased hepatic clearance resulting in an increase in total T3 and total T4 levels. During pregnancy TBG levels begin to increase after 6-8 weeks of gestation[16] and reaches a plateau around mid-gestation and remains high of about 2-3 times of preconception levels until term. Hence the levels of total T4 increase sharply between 6 and 12 weeks of gestation, and progress more slowly thereafter and stabilize around mid-gestation. Moreover, the changes in albumin and free fatty acid.

Concentration facilitates the binding of T4 and T3 to carrier proteins and lowers the concentration of free thyroid hormones levels. This leads to further stimulation of T4 and T3 synthesis.[15,17] The placenta secretes human chorionic gonadotropin (hCG), a glycoprotein hormone, sharing a common α subunit with TSH but having unique β subunit, which confers specificity. hCG or a molecular variant, acts as a TSH agonist, having thyrotrophic activity leads to elevated levels of thyroid hormones in first trimester which contribute to the cause of gestational transient hyperthyroxinaemia, seen in about 0.3% of pregnancies. This is commonly seen in hyperemesis gravidarum, multiple pregnancy, and molar pregnancy.[18]

T4 is a precursor of T3, which is the major active form of thyroid hormone. T4 gets deiodinated to T3 and hence there is an increased turnover of T4. This leads to relative hypothyroxinemia and an increase in the production of T4 due to increased demand. About 80% of T3 produced in the body is derived extrathyroidally from T4 deiodination. T4 level is equilibrated in circulation on a manufacture and expenditure basis. Levels of thyroid hormones are determined not only by synthesis/secretion but also by their metabolism. The variations in T3 and T4 levels seems to be need based.[5]

The enzyme Type III deiodinase, produced by placenta, converts T4 to reverse triiodothyronine and T3 to diiodotyrosine, and it has extremely high activity during fetal life. During fetal life as there is increased demand for T4 and T3 hormones by the fetus, and as it mainly depends on maternal thyroid hormones in early pregnancy until 12 and 14 weeks; it causes an increased production of these hormones which ultimately leads to increase in circulating concentrations of the same hormones.[6,7]

In this study out of 80 pregnant women, the 67 (83.7%) subjects had TSH values of <2.5 μIU/ml, 9 (11%) subjects had TSH values between 2.5 and 4 μIU/ml and 4 (5%) subjects had TSH values >4 μIU/ml. The mean TSH values during 6-9 weeks and 10-12 weeks were 1.77±1.24 μIU/ml and 1.47 ± 0.96 μIU/ml respectively. From these observations, it can be made out that there was decreased TSH levels at a gestational age of 10-12 weeks as compared to 6-9 weeks which was not statistically significant ($P = 0.23$).

This variation in TSH values can be explained by the following mechanism: Thyroid economy differs between the healthy pregnant women and healthy nonpregnant women. Compared with preconceptional levels, TSH concentration is lower throughout the pregnancy. TSH is lowest in the first trimester of pregnancy.[15]

The decrease in TSH level could be attributed to the thyrotrophic action of hCG, which is a thyroid regulator in normal pregnancy, because of hormone specific β subunits and extracellular receptor binding domains of hCG and TSH share multiple similarities.[19]

In normal pregnancy, the placenta produces hCG in the 1st week of conception and levels peak at week 10, before decreasing and reaching a plateau by week 20.

Between 8 and 14 weeks of gestation, the changes in hCG and TSH are mirror images of each other, with significant negative correlation between the two.[15]

The structural homology between hCG and TSH, where they contain a common α subunit and the hormonespecific beta subunits share 85% sequence homology in first 114 amino acid and 12 cysteine residues at the highly conserved position, hence their tertiary structures are very similar.[20]

Therefore during first trimester of pregnancy the elevated hCG levels leads to transient increase in thyroid hormone levels and in turn causes partial suppression of TSH secretion,[17,21] but not high enough to induce overt hyperthyroidism.[20]

But according to ATA guidelines, the upper limit of TSH for first trimester of pregnancy is considered as

2.5 μIU/ml. Applying the same guidelines to our study population revealed the proportion of euthyroid subjects as 81.5%, 16.3% as hypothyroid (subjects had TSH values > 2.5 μIU/ml), and 2.5% (subjects had TSH values < 0.04 μIU/ml), as hyperthyroid. There has been a wide geographic variation in prevalence of hypothyroidism during pregnancy. It varies from 2.5% in west to 11% in India; It seems that prevalence of hypothyroidism is more in Asian countries as compared to west.[22] The subjects in hyperthyroid state could be due to gestational transient thyrotoxicosis which occurs in 1-3% of pregnancies, due to elevated hCG levels or due to overt hyperthyroidism which occurs in 0.4-0.7% of pregnancies. This is in support of the fact that there is a high prevalence of gestational thyrotoxicosis in Asian women during 8-11 weeks of gestation than during 12-14 weeks.[23]

Limitations of the study

In this study, as free T3 and free T4 levels were not estimated. Hence, the categorization of thyroid dysfunction (subclinical/overt hypothyroidism or hyperthyroidism) could not be confirmed.

The Larger sample size is required to get a better idea about the incidence/prevalence of thyroid dysfunction in the Indian population, unlike this study which has a sample size of 80.

As the ATA guidelines have been framed for the western population, the estimation of thyroid abnormalities based on these guidelines in this present study might have been overestimated or underestimated.

CONCLUSION

So to conclude, a significant increase in total T3 and total T4 levels indicate the physiological adaptations which occur during first trimester of pregnancy. The thyroid dysfunction determined based on TSH values (as per ATA guidelines) is quite high. This indicates the proportion of thyroid dysfunction present in the local population.

Further studies are required in this regard in a larger population so that gestational age specific reference intervals can also be established for a local population of a particular geographic area to avoid misinterpretation of thyroid function tests during first trimester of pregnancy.

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