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A prospective observational study on maternal thyroid-stimulating hormone and its impact on maternal and perinatal outcome

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ABSTRACT

Background: Numerous hormonal changes and metabolic demands occur during pregnancy, resulting in complex changes in maternal thyroid function. Thyroid disorder is the second most common endocrine disorder found in pregnancy next to the diabetes group. It affects 1–2% of women of reproductive age. Overt hypothyroidism complicates 0.3–0.5% of pregnancies. The incidence of subclinical hypothyroidism in pregnant women is about 2–3%. Hyperthyroidism is present in 0.1–0.4%. **Aims and Objectives:** The aim of the study was to assess the maternal thyroid function test during pregnancy and its effect on maternal and fetal outcomes. **Materials and Methods:** A prospective observational study was conducted in the Department of Obstetrics and Gynaecology at Dhanalakshmi Srinivasan Medical College and Hospital, Tamil Nadu over a period of 1 year February 2019 to January 2020. The study is to screen pregnant women for thyroid disorders based on their serum thyroid stimulating hormone (TSH) at the first antenatal visit and its impact on maternal and perinatal outcomes. **Results:** In our study, overall thyroid abnormality incidence was found to be 5.5%. It is statistically significant ($P<0.001$). Subclinical hypothyroid was found as a major thyroid disorder in the study population (significant $P<0.002$). In the study overt hyperthyroidism: 0.5%, subclinical hypothyroidism: 3.5%, primary hypothyroidism 1.5% was found. More than 54% of the study population had no high-risk factors and were found to have a thyroid disorder. In our study, maternal complications in women with thyroid disorders were analyzed. One woman with overt hypothyroidism, one with subclinical hypothyroidism developed mild preeclampsia. One hypothyroid woman had preterm labor at 32 weeks of gestational age. Maternal complications were less inadequately treated patients resulting in a normal incidence of these complications. In our study birth weight of the babies, <2.5 kg was 18.2%, 2.5–3 kg was 63.6%, and >3 kg was 18.2%. Perinatal outcomes were in terms of preterm, intrauterine growth restriction, low birthweight, and fetal distress. **Conclusion:** All pregnant women irrespective of their low risks or high risks for a thyroid disorder should be screened for serum TSH at the first booking visit to prevent the maternal and perinatal complications of thyroid disorders and close monitoring and effective treatment could be provided to them.

Key words: Subclinical thyroid disorder; Enzyme-linked immune sorbent assay, Thyroid function test; Thyroid-stimulating hormone receptor antibodies

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INTRODUCTION

Thyroid disorder is the second most common endocrine disorder found in pregnancy next to the Diabetes group. It affects 1–2% of women of reproductive age. Overt Hypothyroidism complicates 0.3–0.5% of pregnancies. The incidence of subclinical hypothyroidism in pregnant women is about 2–3%.[1] Hyperthyroidism is present in 0.1–0.4%.[1] Pregnancy may affect the course of thyroid disorders, and conversely, thyroid diseases may affect the course of

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gestation.[2] Normal pregnancy results in some significant physiological and hormonal changes that alter thyroid function, and hence laboratory tests of thyroid function must be interpreted with caution during pregnancy.[3] Policy considerations concerning universal routine thyroid screening before and/or during pregnancy remain controversial. The targeted thyroid function testing of only the high-risk group would miss about one-third of women with overt/subclinical hypothyroidism.[4] Uncontrolled hypo or hyperthyroidism may lead to serious complications such as thyroid storm, heart failure, or myxedema coma during pregnancy.[5] During the first 10–12 weeks of pregnancy, the fetus is entirely dependent on the mother for the production of thyroid hormone. By the end of the first trimester, the fetus's thyroid gland begins to produce thyroid hormone on its own. The fetus, however, remains dependent on the mother for adequate amounts of iodine, which is essential to make the thyroid hormones.[6] The World Health Organization recommends iodine intake of 250 μg/day during pregnancy to maintain adequate thyroid hormone production.[7] Population studies carried out in the 1990s have shown that when women with an iodine intake of <100 μg/d become pregnant, the pregnancies are frequently associated with thyroid function abnormalities (mainly maternal hypothyroxinemia), resulting in excessive thyroidal stimulation and goiter formation in both the mother and offspring.[8] The recommended nutrient intake for iodine during pregnancy and breastfeeding should range between 200 and 300 μg/day, with an average of 250 μg/day.[9] Recently, several studies have been published dealing with the assessment of maternal iodine intake by measurements of urinary iodine excretion (UIE). One study showed that advancing gestation time had an influence on UIE measurements in a mildly iodine-deficient pregnant population.[10]

Aims and objectives

The aim of the study was to assess the maternal thyroid function test during pregnancy and its effect on maternal and fetal outcomes.

MATERIALS AND METHODS

This study was a prospective observational study conducted in the Department of Obstetrics and Gynecology at Dhanalakshmi Srinivasan Medical College and Hospital, Tamil Nadu, over 1 year from February 2019 to January 2020. The study was to screen pregnant women for thyroid disorders based on their serum thyroid-stimulating hormone (TSH) at the first antenatal visit and its effect on the maternal and perinatal condition. Pregnant women (n=200) in the age group of 18–36 years with a period of gestation less than equal to −20 weeks who attended the antenatal clinic were followed throughout their pregnancy period. TSH screening was done by taking a TSH serum sample at first (before 20 weeks) prenatal visit. A blood sample was collected from the patients, allowed to clot, and serum was separated by centrifugation at room temperature. The serum was stored at 2–8°C till its usage. The TSH was estimated by using the ELISA method. If serum TSH was abnormal, freeT4 and freeT3 were estimated. According to the biochemical values, those patients were divided into primary hypothyroidism, subclinical hypothyroidism, hyperthyroidism, and euthyroid. Primary hypothyroidism, subclinical hypothyroidism patients were treated with L-Thyroxine in the dose of 2–2.4 mcg/kg/day (as per the endocrinologist's opinion) to maintain serum TSH near normal. Serum TSH estimation was repeated at 6–8 weeks intervals. TSH concentration is kept to <2.5 mIU/L in the first trimester <3 mIU/L in the second and third trimester. In hyperthyroidism, she was started on antithyroid medications and aimed to maintain the FT4 level in the upper limit of normal to prevent iatrogenic fetal Hypothyroidism. Baby details such as birth weight and Apgar score at 1 min and 5 min, and any other complications were noted.

Inclusion criteria

Primigravida, Multigravida, past obstetrics history of prolonged infertility, miscarriage, preterm labor, and intrauterine death were included in the study.

Exclusion criteria

Known thyroid disorder, known heart disease, known diabetes mellitus, twin pregnancy, known renal disorder, and known liver disorder were excluded from the study. The study was approved by the institutional ethical committee. Written informed consent was obtained from the participants of the study. The data was collected on a preformed pro forma. It included patient details, significant events antepartum and immediately postpartum, and the perinatal outcome.

Statistical analysis

The data were organized by editing and coding, run through The Statistical Package the for Social Sciences software version16 and sigma stat 3.5 version, and analyzed for descriptive and inferential statistics. The Chi-square test was used to calculate the significance of association for continuous variables between groups. P<0.05 was taken as statistically significant. Microsoft Word and Excel were used to generate graphs and tables.

Ethical consideration

The study was approved by the institutional ethics committee Dhanalakshmi Srinivasan Medical College and Hospital under IECHS/IRCHS/NO/140 and written informed consent was obtained from all pregnant women. Data confidentiality was maintained throughout the study.

RESULTS

Shows age of the screened women ranged between 18 and 36 years. The majority of the women belonged to the age group of 21–25 years of age. It is significantly high when compared with other groups P<0.001 Chi-square value = 45.91 (P<0.05 taken as significant) (Table 1).

Many (54.5%) patients with thyroid disorders belonged to the age group of 20–25 years. It is significantly high when compared with other groups. P<0.001 (significant) Chi-square value = 15.3 (Table 2).

Primigravida was more common in the screening population. It is significantly high when compared with other groups. P<0.001, Chi-square value=34.2 (Table 3).

The incidence of thyroid disorder among the studied women was 5.5%, out of which one woman (0.5%) was hyperthyroid, and ten women were hypothyroid (5%). The difference between euthyroid cases and hypothyroid disorder cases out of the total population was statistically (P<0.001) (Table 4).

Normal value: free T3: 1.2–4.4 pg/ml; free T4: 0.8–1.9 ng/dl. Among the hypothyroid patients, three (1.5%) were found to be overt hypothyroid and seven (3.5%) patients were considered to be subclinical hypothyroid. P=0.002 which is significant (Table 5).

Thyroid disorders were more common in primigravida (54.5%). It is significantly high when compared with other gravidae. P<0.001, Chi-square value=16.1. (P<0.05 is taken as significant) (Table 6).

Risk factors were present in 5 women (45.5%) with a thyroid disorder. No risk factors were present in 6 women (54.5%) with a thyroid disorder. Risk factors versus thyroid disorder are not significant (P=0.487) (Table 7).

These risk factors were more prevalent among subclinical hypothyroid women. Among them, the commonest risk factor was the previous history of miscarriages and previous history of preeclampsia (Table 8).

Among the women with thyroid disorder one developed preeclampsia, one had preterm labor, and the other had a postpartum hemorrhage (Table 9).

The majority (72.7%) of the women with thyroid disorder delivered vaginally. It is significantly high when compared with another type of delivery. P<0.001, Chi-square value=13.5. Low birth weight (LBW), intrauterine growth restriction (IUGR). Of those newborns of women with thyroid disorders, one was LBW; one was IUGR (Table 10).

Table 1: Age distribution of screening population

Age group in years	No. of patients	%
≤20	10	5
21–25	112	56
26–30	55	27.5
>30	23	11.5
Total	200	100%

Table 2: Age distribution of thyroid disorder patients

Age group in years	No. of patients	%
≤20	0	0
21–25	6	54.5
26–30	3	27.3
>30	2	18.2
Total	11	100

Table 3: Parity distribution of screening population

Parity	No. of patients (n=200)	%
Primigravida	92	46
G2	70	35
G3	32	16
G4 and above	6	3
Total	200	100

Table 4: Distribution of serum TSH level in a screening population

TSH level mIU/L	No. of patients	%
<0.08	1	0.5
0.08–3	189	94.5
>3	10	5
Total	200	100

Table 5: Distribution of FT3, FT4 level in hypothyroid women

Free T3, T4	Thyroid disorder	No. of patients	%
Decreased	Overt hypothyroid	3	1.5%
Normal	Subclinical hypothyroid	7	3.5%
Total		10	5.0%

Table 6: Parity distribution of thyroid disorders patients

Parity	No of patients	%
Primigravida	6	54.5
G2	2	18.2
G3	3	27.3
G4 and above	0	0
Total	11	100

Table 7: Prevalence of risk factors in pregnant women with thyroid abnormality

Prevalence of risk factors	No of patients	%
With risk factor	5	45.5
Without risk factor	6	54.5
Total	11	100

Table 8: Distribution of risk factors in thyroid disorder patients

Risk factors	Primary Hypothyroidism	Subclinical Hypothyroidism	Hyperthyroidism
Family history	1	-	-
Thyroid nodule	-		
Previous miscarriage	1	2	-
Signs & symptoms thyroid disorder		1	
Previous preeclampsia	1	1	-

The majority of babies (63.6%) had a birth weight between 2.5 and 3.0 kg. Birth weight was normal in thyroid abnormality patients. P<0.001 significant, Chi-square value=29.2 (Table 11).

DISCUSSION

This study was conducted in 200 randomly selected antenatal women at the first visit, between 12 and 20 weeks of gestational age. The age of the patients included in the study group varied from 18 to 36 years, with the majority of women belonging to the age group between 20 and 25 years. When parity is analyzed, most of them were primigravida (46%) and second gravida (35%). In our study, overall thyroid abnormality incidence was found to be 5.5%. It is statistically significant (P<0.001). The impact of hyperthyroidism in our study is 0.5%. As far as the parity is concerned, thyroid abnormality was detected mostly in primigravida (54.5%) and third gravida (27.3%). Various studies relatively showed that when the cut-off value of serum TSH was kept above 4 mIU/L, the incidence of thyroid disorder was found to be less (2.2–2.5%).[11] When the cutoff value of serum TSH was kept above 3 mIU/L, it was found that incidence increased from 2.2% to 3.4%. In our study, the incidence is 5%. After a study done by Lazarus and Premawardhana,[12] they have recently published a "nomogram" for TSH serum changes during pregnancy. Their study claimed that 28% of singleton pregnancies with a serum TSH greater than two standard deviations above the mean would not have been identified when using the non-pregnant serum mIU/L in first and second trimesters and is further reduced to 0.13 mIU/L in the 3rd trimester. Conversely, serum TSH levels above 2.3 mIU/L (1st trimester) and 3.1–3.5 mIU/L (2nd and third trimesters) may already be indicative of a slight thyroid under-function. In 1991, Glienor's study reported a higher incidence of thyroid abnormality (17%), and he attributed low iodine intake as the cause of thyroid abnormalities.[12] When thyroid abnormalities and risk factors were analyzed, 45.5% were associated with risk factors, while 54.5% were not associated with any risk factors. This coincides with LeBeau and Mandel, which showed that targeted thyroid function testing of only the high-risk group would miss about one-third of pregnant women with overt/subclinical hypothyroidism.[13] In our study, maternal complications in women with thyroid disorders were analyzed. One woman with overt hypothyroidism

Table 9: Maternal outcome in thyroid disorders (n=11)

Outcome	No of patients	%
Abortion	-	-
Preeclampsia	1	9.1
Preterm labor	1	9.1
Abruption	-	-
PPH	1	9.1

Table 10: Mode of delivery in women with thyroid disorders

Delivery	No of patients	%
Normal vaginal	8	72.7
Instrumental	0	0
LSCS	3	27.3
Total	11	100

Table 11: Distribution of birth weight of babies

Weight (kg)	No of babies	%
≤2.5	2	18.2
2.51–3	7	63.6
>3	2	18.2
Total	11	100

one with subclinical hypothyroidism developed mild preeclampsia.[14] One hypothyroid woman had preterm labor at 32 weeks of gestational age. Maternal complications were less inadequately treated patients resulting in a normal incidence of these complications. If thyroid disorders were not identified, maternal complications would be more.[15] Pop et al., study showed the incidence of anemia 31%, abruption 19%, and postpartum hemorrhage 19% in the untreated hypothyroid group. In 1993 Leung's study showed the impact of preeclampsia to be around 22%. In our study, the incidence of normal delivery is 72.7%, no Instrumental delivery, and lower segment cesarean section rate is 27.3 %. Lower segment cesarean section was indicated for obstetric reasons. In our study, birth weight of the babies, <2.5 kg was 18.2%, 2.5–3 kg was 63.6%, and >3 kg was 18.2%.[16,17]

CONCLUSION

Pregnancy has profound effects on the regulation of thyroid hormone in healthy women. These effects need to be recognized, precisely assessed, clearly interpreted,

and correctly managed. Maternal alteration of thyroid function (hypothyroidism and subclinical hypothyroidism) due to iodine deficiency has important implications in the maternal and perinatal outcome. In our study incidence of overt hypothyroidism is 1.5%, subclinical hypothyroidism is 3.5%, and primary hyperthyroidism is 0.5%. Pregnant women without risk were found to have more percentage of thyroid disorders. This study concludes that all pregnant women irrespective of their risks for a thyroid disorder should have serum TSH estimated at the first booking visit to prevent the maternal and perinatal complications of thyroid disorders. Thereafter close monitoring and follow-up can be provided for a healthy mother and baby.

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CAK- Has conceptualized the study and played primary role in compiling, analysis, and interpretation of the data. All the drafts were prepared, reviewed, and final draft was approved by **NZ, CAK, PJ**. **NZ, CAK, and PJ-** have contributed in fine tuning of the proposal, contributed in data collection and entry. Reviewed the results and contributed to preparation and review of drafts. All the authors have read and approved final version of the manuscript. All the authors take complete responsibility for the content of the manuscript.

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