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Prevalence and feto-maternal outcomes of subclinical hypothyroidism in pregnancy among mothers attending a tertiary care hospital of Darjeeling District, West Bengal, India

Tanmoy Das[1], Nilratan Das[2], Sohan Bhowmick[3], Arunava Biswas[4]

[1]RMO cum Clinical Tutor, [2]Assistant Professor, Department of Obstetrics and Gynecology, North Bengal Medical College and Hospital, Darjeeling, [3]Assistant Professor, Department of Obstetrics and Gynecology, Santiniketan Medical College, Bolpur, [4]Associate Professor, Department of Pharmacology, Maharaja Jitendra Narayan Medical College and Hospital, Cooch Behar, West Bengal, India

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ABSTRACT

Background: Pregnancy is a stressful test for the mother's thyroid function. The frequency of hypothyroidism in pregnant women is high. However, there are no adequate studies to evaluate the adverse effects of subclinical hypothyroidism (SCH) during pregnancy. **Aims and Objectives:** This study was carried out to evaluate the prevalence of SCH in pregnancy and its adverse feto-maternal outcomes among mothers attending a tertiary care teaching hospital in Darjeeling district, West Bengal, India. **Materials and Methods:** The present study was an institution-based observational descriptive study with a prospective longitudinal design conducted for 1 year among pregnant women attending the antenatal clinic of the study institution in the first trimester of their pregnancy. The sample size for the present study was calculated to be 200. A consecutive sampling technique was utilized. The enrolled women were evaluated for thyroid status by assessing serum thyroid stimulating hormone and free T4 level. All the enrolled mothers were kept under close follow-up and they were evaluated for the development of any antenatal, intranatal, and postnatal complications. **Results:** The mean age was found to be 23.1 ± 4.2 years, most of the women were nulliparous (60%). Of the women, 74% were euthyroid, while the prevalence of SCH was found to be 16%. On follow-up till the termination of their pregnancies, mothers suffering from SCH had statistically significantly higher incidence of maternal complications such as hypertensive disorders in pregnancy ($P=0.001$), abortion ($P<0.001$), postpartum hemorrhage ($P=0.020$) and also fetal adverse outcomes, such as intrauterine growth restriction ($P=0.018$), fetal premature birth ($P=0.035$), and low birth weight ($P=0.004$) when compared with euthyroid mothers. **Conclusion:** The burden of SCH high in the study population, and it was significantly associated with a number of different maternal as well as fetal complications and adverse outcomes.

Key words: Feto-maternal outcome; Subclinical hypothyroidism; Pregnancy

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INTRODUCTION

Pregnancy influences thyroid function in multiple ways.[1] Not only does the maternal hypothalamic-pituitary-thyroid (HPT) axis undergo a series of adjustments, the fetus develops its own HPT axis and the placenta plays an active role in iodide and T4 transport and metabolism.[2] Thus, an integrated three-compartment thyroid model exists during gestation. The thyroid gland increases by 10% in size during pregnancy in iodine-replete countries and by 20–40% in areas of iodine deficiency. Production of thyroxine (T4) and triiodothyronine (T3) increases by 50%, along with a 50% increase in the daily iodine requirement.[1]

Address for Correspondence:
Dr. Arunava Biswas, Associate Professor, Department of Pharmacology, Maharaja Jitendra Narayan Medical College and Hospital, Coochbehar - 736 101, West Bengal, India. **Mobile:** +91-9674328329. **E-mail:** drabiswas@gmail.com

Research has observed that overt hypothyroidism complicates 2–3 pregnancies/1000, whereas subclinical disease is seen in about 5%.[3] Idris et al., found that in addition to an increased risk of low birth weight, hypothyroidism early and late in pregnancy may also increase the rate of cesarean section.[4] Children born to women who were not treated for thyroid deficiency during pregnancy (as defined by increased serum thyroid-stimulating hormone [TSH]) had average IQ scores at 7–9 years of age that were 7 points lower than those of controls.[5]

There is already a debate among clinicians whether thyroid function tests should be included among routine antenatal tests or not depending on its cost versus benefit effects.[6] Many clinicians believe it is useful. The spectrum of thyroid dysfunction is varied in nature. There are studies which have established the obstetric and fetal complications associated with overt hypothyroidism but there is not an adequate number of studies to evaluate the adverse effects of subclinical hypothyroidism (SCH) during pregnancy.[7,8]

Aims and objectives

This study was carried out to evaluate the prevalence of SCH in pregnancy and its adverse feto-maternal outcomes among mothers attending a tertiary care teaching hospital in Darjeeling district, West Bengal, India.

MATERIALS AND METHODS

A prospective longitudinal observational descriptive study was conducted for a period of 1 year (May 2017–April 2018) after prior approval from the Institutional Ethics Committee (NBMC/IEC 2016–17/01) among pregnant women attending the antenatal clinic of the study institution in their first trimester of pregnancy. Antenatal women with <12 weeks of gestation, singleton uterine pregnancy, and willing to provide written informed consent for the present study were consecutively recruited and those with a positive history of addiction, known history of thyroid disorders before pregnancy, having systemic diseases such as hypertension, diabetes, dyslipidemia, malignancy, autoimmune diseases, and with active infection were excluded from the study.

The sample size for the present study was calculated based on Cochran's formula, considering the prevalence of hypothyroidism among pregnant women to be 13.13%, based on the findings reported by Dhanwal et al.,[9] Assuming an absolute precision of 5%, at 95% confidence level, the minimum sample size calculated was 179. Considering a dropout rate of 10%, the final sample size was calculated as 197, which was further rounded off to 200. A consecutive sampling technique was utilized for the study.

The enrolled women were evaluated by detailed history taking, clinical examination, and routine laboratory and ultrasonographical examination. In addition to routine investigations, they were also evaluated for thyroid status by assessing serum TSH and free T4 levels. All the enrolled mothers were kept under close follow-up and they were evaluated for the development of any antenatal, intranatal, and postnatal complications. Mode of delivery and development of any fetal complications were also noted. Serum TSH of 0.2–2.5 IU/L in the first trimester was taken as a normal value for patients. Those with a TSH concentration more than 2.5 IU/L in the first trimester and serum FT4 within the normal range are considered cases of SCH. Those with TSH levels more than 2.5 IU/L and low FT4 (<0.5 ng/dl) in the first trimester are considered overt hypothyroidism, and those with TSH concentration <0.2 IU/L are considered cases of hyperthyroidism.

Statistical analysis

Data were entered into a Microsoft Excel spreadsheet and then analyzed using statistical software (SPSS, version 20.0) and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for continuous variables and count and percentages for categorical variables. The $P<0.05$ was considered statistically significant.

RESULTS

In the 200 participants that were assessed for the present study, the mean age was found to be 23.1±4.2 years, with the majority being between 18 and 25 years of age (79.5%). Most of the women were nulliparous (60%), followed by prime mothers (31%). The mean body mass index of the mothers was found to be 23.7±0.4 kg/m^2 (Table 1).

On assessment of the thyroid status of the participants, it was observed that 148 of the mothers (74%) were euthyroid, while the prevalence of SCH was found to be 16%. About 7.5% of the mothers were found to be suffering from overt hypothyroidism, while the prevalence of hyperthyroidism was observed to be 2.5% (Table 1).

On follow-up of the mothers till the termination of their pregnancies, it was seen that among the women who were suffering from SCH, anemia in pregnancy was the maternal complication with the highest incidence (31.2%), followed by hypertensive disorders in pregnancy (28.1%). As for adverse maternal outcomes, postpartum hemorrhage had the highest incidence (21.9%) (Table 2).

Regarding adverse fetal outcomes, it was seen that among the mothers with SCH, intrauterine growth restriction

(IUGR) had the highest incidence (21.9%), followed by prematurity (18.8%) (Table 3).

On statistical analysis, it was observed that when compared with euthyroid mothers, mothers suffering from SCH had a statistically significantly higher incidence of maternal complications. These include hypertensive disorders in pregnancy (P=0.001), abortion (P<0.001), antepartum hemorrhage (P=0.017), postpartum hemorrhage (P=0.020), and preterm labor (P=0.002). Requirement for cesarean-section deliveries was also found to be statistically significantly higher in this group as compared to euthyroid patients (P=0.012). Statistical analyses also showed that patients suffering from SCH also had a statistically significantly higher incidence of fetal adverse outcomes, such as IUGR (P=0.018), fetal distress in labor (P=0.018), premature birth (P=0.035), and low birth weight (P=0.004) (Tables 2 and 3).

Table 1: Sociodemographic characteristics of the study participants (n=200)

Parameters	Frequency	Percentage
Age group (years)		
<18	2	1
18–25	159	79.5
25–35	36	18
>35	3	1.5
Parity		
0	120	60
1	62	31
2	14	7
3	4	2
BMI		
<18.5	32	16
18.5–24.9	94	47
25–29.9	68	34
>30	6	3
Thyroid status		
Euthyroid	148	74
Subclinical hypothyroid	32	16
Over hypothyroid	15	7.5
Hyperthyroid	5	2.5

BMI: Body mass index

DISCUSSION

Thyroid disorders, especially hypothyroidism, are persistent and growing problems worldwide.[10] While overt versions of the condition, such as overt hypo- and hyperthyroidism are often detected and managed appropriately, subclinical versions of the condition, due to their non-specific, often silent symptomatology, are often missed by clinicians during assessment.[11] This makes conditions like SCH severely under-diagnosed, especially in areas like sub-Himalayan regions, where there is it already an endemic disease.[12] This, in turn, leads to a lack of data regarding the pathophysiology and the squeal of SCH, particularly among high-risk groups like pregnant women. The present study aimed at filling this gap in knowledge by the assessment of not only the burden of SCH among pregnant women presenting to a tertiary care hospital of northern West Bengal, which served primarily sub-Himalayan communities but also compare and contrast its squeal among these women in terms of feto-maternal complications and outcomes with that of their euthyroid counterparts.

In the present study, the age of the participants ranged from 16 to 38 years, with the mean age being 23.1±4.2 years.

Table 2: Comparison of participants with subclinical hypothyroidism and euthyroid participants with respect to maternal complications (n=200)

Complications	Euthyroid patients (n=148%)	Subclinical hypothyroid patients (n=32%)	P-value
Anemia in pregnancy	2 (14.8)	10 (31.2)	0.098
Cesarean section delivery	26 (17.6)	12 (37.5)	0.012*
Hypertensive disorders in pregnancy	10 (6.8)	9 (28.1)	0.001*
Preterm labor	7 (4.7)	8 (25)	0.002*
Antepartum hemorrhage	6 (4.1)	6 (18.8)	0.017*
Postpartum hemorrhage	10 (6.8)	7 (21.9)	0.020*

*Statistically significant

Table 3: Comparison of participants with subclinical hypothyroidism and euthyroid participants with respect to fetal and neonatal complications (n=200)

Complications	Euthyroid patients (n=148%)	Subclinical hypothyroid patients (n=32%)	P-value
Intrauterine growth restriction	8 (5.4)	7 (21.8)	0.018*
Intrauterine fetal demise	3 (2.1)	2 (6.2%)	0.105
Prematurity	7 (4.8)	6 (18.8)	0.035*
Fetal distress in labor	6 (4.1)	6 (18.8)	0.018*
Low birth weight	8 (5.4)	8 (25)	0.004*

*Statistically significant

Smith and Bold, also reported similar age distribution in their study sample, in whom they examined the effects of SCH.[13]

The prevalence of SCH in the present study was 16%. Sahu et al., showed in their study on overt and subclinical thyroid dysfunction among Indian pregnant women that the prevalence of SCH and overt hypothyroidism in pregnancy were 6.5% and 4.6%, respectively.[14] The comparatively higher prevalence of SCH can be attributed to the study population, which lives in the sub-Himalayan belt, a region well known for being a zone with a high prevalence of iodine deficiency.[15]

In this study, the occurrence of various maternal and fetal complications was evaluated in subclinical hypothyroid group and they were compared to those of the euthyroid group. In the present study, abortion rate was found to be 6.2% in subclinical hypothyroid group as compared to 1.3% in euthyroid group and this difference in the abortion rate was found to be statistically significant ($P<0.001$). Pregnancy loss is a common clinical problem. The leading etiologies associated with pregnancy loss include a variety of causes such as chromosomal abnormalities, endocrine disorders, autoimmune diseases, anatomical abnormalities, and infections. With regard to thyroid status, both hypothyroidism and hyperthyroidism have long been associated with increased fetal loss. The findings of the present study substantiate these assertions and are similar to that reported by Partha et al., and Wolfberg et al.,[16,17] Significantly higher incidence of spontaneous loss of pregnancy in mothers suffering from SCH as compared to euthyroid women has also been reported by Wang et al., in their study.[18]

In this study, 28.1% of mothers of the subclinical hypothyroid group and 6.6% of mothers of the euthyroid group had a hypertensive disorder in pregnancy ($P=0.001$). Wilson et al., found that the incidence of hypertension in pregnancy was 6.2% in subclinical hyperthyroid, 8.5% in euthyroid, and 10.9% in subclinical hypothyroid groups.[19] The association of overt hypothyroidism and hypertensive disorders in pregnancy is not surprising. Hypothyroidism is an accepted cause of reversible hypertension both in the pregnant and in the non-pregnant population.[20] Hypothyroidism can cause vascular smooth muscle contraction both in systemic and renal vessels, which leads to increased diastolic hypertension, peripheral vascular resistance, and decreased tissue perfusion.[21] In this study cesarean section rate was significantly higher in the SCH group as compared to that of the euthyroid group (37.5% vs. 17.57%, $P=0.012$). In a study done by Sahu et al., cesarean section rate was also found to be significantly higher among pregnant hypothyroid women ($P=0.04$).[14]

In this study, preterm labor was found in 25% of cases of subclinical hypothyroid group and 4.7% of cases of the euthyroid group ($P=0.002$). Furthermore, the occurrence of APH was seen in 18.8% of mothers of the subclinical hypothyroid group as compared to 4.1% in the euthyroid group ($P=0.017$). Casey et al., showed in that preterm delivery is almost 2 folds higher in women with SCH (RR=1.8, 95% CI=1.1–2.9) and antepartum hemorrhage was 3 times more likely in women with SCH (RR–3.0, 95% CI 1.1–8.2).[22] The incidence of PPH was found to be 21.9% in the subclinical hypothyroid group and 6.7% in cases of euthyroid group ($P=0.02$). Radha et al., in their study, showed that incidence of PPH was higher in SCH mothers compared to euthyroid mothers (6% vs. 2%, $P=0.014$).[23] They also found significant association between inadequately treated hypothyroidism and other maternal complications, similar to the present study.

Regarding the fetal complications, in the present study, the occurrence of IUGR was significantly higher in the subclinical hypothyroid group as compared to the euthyroid group ($P=0.018$). Saki et al., also found significant association between SCH with IUGR ($P=0.028$).[24] In this study, while the occurrence of IUFD was higher in the SCH group, it was not found to be statistically significant in analysis. This is in contrast to the findings reported by authors such as Ashoor et al., and Ohashi et al.[25,26] This finding can be attributed to the robust and well-implemented management protocols in place in the study institution, which places special care in the prevention of conditions such as IUFD. Similar to what has been reported by Sannaboraiah et al., the incidence of premature birth was also found to be significantly higher in the SCH group as compared to euthyroid group ($P=0.035$).[27] Consequentially, it was seen that the incidence of LBW babies was also significantly higher in the SCH group mothers ($P=0.004$), a finding that also conforms to that reported by Sannaboraiah et al., and Goel et al.[27,28]

Limitations of the study

Two thyroid function tests were performed in our study to screen pregnant subjects. Measuring antithyroid antibodies would have provided more precise data.The study population was not followed up after delivery. Randomization was not done and selection bias may have played a role in our results as the physicians were not blinded to the method of induction and cervical ripenig. The study was a cross-sectional investigation conducted at a hospital with a small sample size.This needs to be done in a community with a sizable sample size to validate and establish the generalizability of data on pregnant mothers living in other parts of India.

CONCLUSION

The findings of the present study indicate that not only the burden of SCH is high in pregnant women among the study population but also the condition was significantly associated with a number of different maternal as well as fetal complications and adverse events. Therefore, SCH should be taken into cognizance when evaluating pregnant women, and care must be taken to manage the condition, lest it lead to severe adverse squeals.

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TD and ND- Concept, design of study and literature search, experimental studies; **TD, ND, SB-** Data acquisition, data analysis, statistical analysis; **AB and SB-** Manuscript preparation; **TD, SB, AB, NB-** Manuscript editing and manuscript review.

Work attributed to:
Department of Obstetrics and Gynecology, North Bengal Medical College and Hospital, Darjeeling, West Bengal, India.

Orcid ID:
Arunava Biswas - https://orcid.org/0000-0002-9676-3410

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