Original Research Paper

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EFFECT OF SUBCLINICAL HYPOTHYROIDISM ON MATERNAL AND PERINATAL OUTCOME

Dr Shabnam Rizvi	Associate Professor Department of Obstetrics and Gynecology Career Institute of Medical Sciences and Hospital.
Dr Gunjan Katiyar*	Assistant Professor Department of Obstetrics and Gynecology Career Institute of Medical Sciences and Hospital. *Corresponding Author
Dr Suman Gupta	Professor and Head Department of Obstetrics and Gynecology Career Institute of Medical Sciences and Hospital.

ABSTRACT **Background:** Adverse maternal outcomes and perinatal complications are closely associated with overt maternal hypothyroidism, but whether these complications occur in women with subclinical hypothyroidism (SCH) during pregnancy remains controversial. The aim of this study was to evaluate the effects of SCH on maternal and perinatal outcomes during pregnancy. **Methods:** This retrospective cohort study was conducted by examining the pregnant women who applied to the Gynaecology Department of Career Institute of Medical Sciences and Hospital at their 6th to 14th gestational weeks and had antenatal follow-ups between February 1, 2020 and December 31, 2021. **Results:** The TSH concentration was significantly lower in the first trimester than in the third trimester (P,0.001). The fT4 concentration was higher in the first trimester than in the second and third trimesters (P,0.001). The incidences of GH and PROM were significantly higher in women with SCH than in euthyroid women (5% vs. 1.57%, P= 0.020; 10% vs. 5%, P= 0.002). IUGR was more frequent in women with SCH than in euthyroid women (7.5% vs. 1.3%, P,0.001). More LBW infants were delivered in the SCH group than in the euthyroid group (12.5% vs. 5%, P,0.001). **Conclusion:** The results of this study indicate that pregnant women with SCH had increased risks of GH and PROM, and their foetuses and infants had increased risks of IUGR and LBW. Thus, routine maternal thyroid function testing is necessary to improve maternal and perinatal outcomes.

KEYWORDS :

BACKGROUND:

Thyroid diseases are frequently seen during pregnancy. The frequency of thyroid disorders in pregnancy is 2-3%. Hypothyroidism can be overt or subclinical[1]; overt hypothyroidism is characterized by an elevated serum level of thyroid stimulating hormone (TSH.10 mIU/L) and a subnormal free thyroxine (fT4) level, whereas subclinical hypothyroidism (SCH) is characterized by an enhanced TSH level, usually beyond the upper reference limit, and a normal fT4 level. Untreated hypothyroidism is closely associated with several pregnancy-related disorders. Because foetal thyroid hormones originate almost exclusively from the maternal system before 12–14 weeks of gestation, maternal thyroid disorders in early pregnancy are closely related to foetal development.

Hypothyroidism is not readily recognized because it usually manifests as non-specific symptoms. SCH is often missed in pregnant women, although its prevalence is about 2–3%[2-3]. This condition has been associated with neurodevelopmental disorders in foetuses and infants and several adverse maternal outcomes, including gestational diabetes mellitus (GDM), preeclampsia, placental abruption, and preterm delivery[5-6]. Women who have been previously diagnosed with SCH are at increased risk of stillbirth and GDM in subsequent pregnancies[7].

However, no consensus has been reached about the need for universal thyroid function screening and the treatment of SCH during pregnancy. The American College of Obstetricians and Gynaecologists and the clinical practice guidelines of the Endocrine Society recommended the examination of thyroid function only in women with symptoms of thyroid disease or previous histories of thyroid disease and other associated conditions[8]. However, this screening protocol is not sufficient because pregnant women with SCH are often asymptomatic, with no history of immune disorder.

Aim And Objectives:

The present study was aimed to estimate the prevalence of SCH and associated maternal and perinatal outcomes, and to assess the risks of adverse outcomes associated with SCH.

MATERIAL AND METHODS:

This retrospective cohort study was conducted by examining the pregnant women who applied to the Gynaecology Department of Career Institute of Medical Sciences and Hospital at their 6th to 14th gestational weeks and had antenatal follow-ups between February 1, 2020 and December 31, 2021. Gestational age was calculated according to the last menstrual period or findings of ultrasound performed before the 20th gestational week.

Multiple pregnancy, smokers, alcohol users, pregnant women under 18 years old, those with diagnoses of chromosomal anomalies, maternal heart disease, history of autoimmune disorders, chronic drug users, overt thyroid disorder, or pregnant who were treated previously or presently with thyroxin or anti thyroid drugs, were not included in this study. All subjects were screened and gave birth at the hospital, and had resided in the local area for at least 5 years.

Fasting venous blood samples were collected in the morning from all participants. Serum was isolated after centrifugation and stored at –80uC until testing. Serum TSH and fT4 concentrations were measured by electrochemiluminescence immunoassay (DX2800; Beckman, Bremen, Germany) and associated diagnostic kits. Inter- and intra-assay coefficients of variation for each hormone ,10%. The assessment of thyroid function was based on the following local trimester-specific reference values (2.5th–97.5th percentiles) [20]: first trimester, TSH 0.09–3.47 mIU/L and fT4 6.00–12.25 ng/L; second trimester, TSH 0.20– 3.81 mIU/L and fT4 4.30–9.74 ng/L; and third trimester, TSH 0.67–4.99 mIU/L and fT4 4.56–8.50 ng/L. SCH was defined as a TSH concentration exceeding the trimester-specific reference value in combination with a normal fT4 concentration. Pregnant women with normal TSH and fT4 levels were considered to be euthyroid and served as control subjects.

RESULTS:

Maternal demographic characteristics are shown in Table 1. Of the 800 women, 760 (95%) had TSH and fT4 values within the normal reference ranges in the trimester of testing and were considered to be euthyroid, whereas 40 (5%) had high TSH levels coupled with normal fT4 levels and were considered to have SCH. Mean maternal age, education level, parity, gestational age at delivery, and delivery modes were similar in the two populations (Table 1).

Table 1. Maternal Demographic Characteristics

Maternal Demographic Characteristics	Euthyroid (n=760)	SCH (n=40)	P value
Maternal age in years	28.70±0.05	27.33±0.25	0.234
Educational level			0.890
Primary school	60(7.9%)	10(25%)	
Middle school	445(58.5%)	18(45%)	
College or university	255(33.5%)	12(30%)	
Parity			0.856

Nulliparity	650(85.5%)	32(80%)	
Multiparity	110(14.5%)	08(20%)	
Gestational age at delivery in weeks	37.12±0.009	38.56±0.002	0.077
Mode of delivery			0.021
Vaginal	200(26.3%)	10(25%)	
Assisted	80(10.5%)	07(17.5%)	
Cesarean section	480(63.15%)	23(57.5%)	

Table 2 presents the TSH and fT4 concentrations of patients with SCH in different trimesters. The TSH concentration was significantly lower in the first trimester than in the third trimester (P,0.001). The fT4 concentration was higher in the first trimester than in the second and third trimesters (P,0.001)

Table 2. TSH And fT4 Concentrations In Women With SCH By Trimester.

Trimester	TSH concentration (mIU/L)	fT4 concentration (ng/L)
First	4.35±0.13	8.33±0.18
Second	4.67±0.16	6.64±0.13
Third	6.54±0.14	6.68±0.55

Maternal outcomes in the two groups are compared in Table 3. No significant difference in the incidence of GDM, placenta previa, placental abruption, or preterm birth was observed between groups. The incidences of GH and PROM were significantly higher in women with SCH than in euthyroid women (5% vs. 1.57%, P= 0.020; 10% vs. 5%, P= 0.002).

Table 3. Maternal Outcomes Of Euthyroid Women And Those With SCH.

Maternal outcomes	Euthyroid(n=760)	SCH(n=40)	P value
Gestational hypertension	12(1.57%)	2(5%)	0.020
Gestational diabetes mellitus	30(3.9%)	1(2.5%)	0.118
Placenta previa	08(1.05%)	1(2.5%)	0.389
Placenta abruption	06(0.78%)	0(0.0%)	0.654
Premature rupture of membrane	38(5%)	4(10%)	0.002
Premature delivery	32(4.2%)	2(5%)	0.977

Comparisons of selected perinatal outcomes are shown in Table 4. No significant difference in the incidence of foetal distress or stillbirth was observed between the SCH and euthyroid groups. IUGR was more frequent in women with SCH than in euthyroid women (7.5% vs. 1.3%, P,0.001). More LBW infants were delivered in the SCH group than in the euthyroid group (12.5% vs. 5%, P,0.001). 4 foetuses and infants had obvious malformation, and this outcome was observed more often in the SCH group than in the euthyroid group (2.5% vs. 0.52%, P,0.038).

Table 4. Perinatal Outcomes Of Euthyroid Women And Those With SCH.

Perinatal outcomes	Euthyroid(n=760)	SCH(n=40)	P value
IUGR	10(1.3%)	3(7.5%)	<0.001
Low birth weight	38((5.0%)	5(12.5%)	<0.001
Fetal distress	15(1.9%)	4(10%)	0.425
Still birth	5(0.65%)	1(2.5%)	0.250
Malformation	4(0.52%)	1(2.5%)	0.038

DISCUSSION:
Subclinical hypothyroidism is a condition characterized with increased thyroid stimulating hormone (TSH) levels with normal free thyroxine (fT4) levels without any symptoms of hypothyroidism. Although a correlation was found between adverse maternal outcomes and overt maternal hypothyroidism, the relationship between subclinical hypothyroidism (SCH) in pregnancy and perinatal complications is not clear.

The current study was performed to gain insight into the impacts of SCH on maternal and perinatal outcomes. In our study sample, 4.63% of pregnant women were diagnosed with SCH. Pregnant women with SCH had increased risks of developing GH and PROM. Foetuses and infants of women with SCH had significantly higher risks of IUGR and LBW compared with those born to euthyroid mothers. Universal thyroid function screening before pregnancy is not currently recommended; thyroid hormone concentrations are typically measured only in women at high risk of thyroid disorders, and

screening for thyroid dysfunction in early pregnancy is controversial[9].

CONCLUSION:
Our results suggest that SCH is associated with several foetal and infant defects, as well as maternal dysfunction. Further investigation of the effects of thyroid function screening and prospective medical intervention on SCH in a randomized, placebo-controlled experiment could aid the verification of these associations with adverse obstetric outcomes.

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