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MATERNAL OUTCOMES IN PREGNANT WOMEN WITH SUBCLINICAL HYPOTHYROIDISM: AN OBSERVATIONAL COHORT STUDY AT A TERTIARY CARE HOSPITAL IN NORTHEAST INDIA

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ABSTRACT

Background: Subclinical hypothyroidism (SCH) in pregnancy, defined as elevated thyroid-stimulating hormone (TSH >4.0 mIU/L) with normal free thyroxine, is prevalent in iodine-deficient regions like India and associated with adverse maternal outcomes. This study evaluated these outcomes in a tertiary care setting in Northeast India.

Methods: An observational cohort study was conducted at the Regional Institute of Medical Sciences, Imphal, from May 2023 to October 2024. Pregnant women aged 18–40 years with singleton pregnancies and SCH were recruited (N=130). Exclusions included pre-existing hypertension, diabetes, or other chronic conditions. Maternal outcomes (e.g., gestational hypertension, gestational diabetes mellitus [GDM], preterm labor, mode of delivery) were monitored until delivery. Associations with TSH strata (<4.5 vs. ≥4.5 mIU/L) were analyzed using chi-square tests (P<0.05 significant).

Results: Mean participant age was 29.4 ± 4.5 years; mean TSH was 4.8 ± 1.5 mIU/L. Cesarean delivery occurred in 44 (34%), gestational hypertension in 25 (18%), GDM in 16 (11%), and preterm labor in 10 (7%). Elevated TSH (≥4.5 mIU/L; n=60) was significantly associated with higher rates of gestational hypertension (68% vs. 32%), GDM (75% vs. 25%), preterm labor (71% vs. 29%), and cesarean delivery (55% vs. 45%; P=0.015–0.041).

Conclusion: SCH, particularly with TSH ≥4.5 mIU/L, increases risks of maternal complications in this population, emphasizing the need for routine thyroid screening and early intervention in resource-limited settings. Limitations include the lack of a control group and single-center design.

Keywords: *Subclinical hypothyroidism, Pregnancy, Maternal outcomes, Gestational hypertension, Gestational diabetes mellitus, Preterm labor, Cesarean delivery, Thyroid-stimulating hormone.*

INTRODUCTION

Significant physiological changes in the thyroid gland are induced during pregnancy that enables enhanced metabolic activity as per demands of the mother and fetus. Thyroid hormones play a crucial role in placental function and overall maternal health, with iodine requirements rising by approximately 50% during gestation. Adverse outcomes result due to even the subtle disruptions in thyroid function [1]. Subclinical hypothyroidism (SCH), characterized by elevated thyroid-

stimulating hormone (TSH) levels (>4.0 mIU/L) with normal free thyroxine (FT4), represents a mild form of thyroid dysfunction that often goes undetected without screening [2]. Globally, SCH affects 2-5% of pregnant women, but its prevalence is notably higher in iodine-deficient regions, contributing to a substantial public health burden.

Despite national iodization programs, iodine insufficiency persists in certain areas in India. The prevalence of SCH during pregnancy is alarmingly elevated. A meta-analysis of 61 studies estimated an overall prevalence of hypothyroidism in Indian pregnant women at 11.07% (95% CI: 8.79–13.84), with SCH comprising the majority of cases[3]. Regional variations are evident, with first-trimester studies from northern India reporting rates as high as 14.3%, underscoring the need for targeted screening in high-risk populations [4]. Other Indian cohorts have documented SCH prevalence ranging from 4.8% to 13.13%, influenced by factors such as dietary iodine intake, socioeconomic status, and access to antenatal care. In the northeastern state of Manipur, limited data exist, but similar environmental and nutritional challenges suggest comparable or higher rates, particularly in tertiary care settings where complicated pregnancies are concentrated [5].

SCH in pregnancy has been variably associated with adverse maternal outcomes, though evidence from large-scale studies remains inconsistent due to differences in diagnostic thresholds and treatment protocols. Maternal risks include an increased likelihood of gestational hypertension (GH), preeclampsia, gestational diabetes mellitus (GDM), preterm labor, and cesarean delivery. For instance, pregnant women with SCH diagnosed per the 2017 American Thyroid Association (ATA) guidelines exhibit higher rates of pregnancy-induced hypertension (PIH), preeclampsia, and preterm delivery compared to euthyroid controls [6]. Systematic reviews have confirmed associations with multiple complications, including anemia, abortions, and placental abnormalities, potentially exacerbating maternal morbidity in resource-limited settings. Untreated SCH may also heighten the risk of premature rupture of membranes (PROM) and gestational hypertension, as observed in prospective cohorts.

The ATA and Endocrine Society recommend universal or risk-based screening in early pregnancy, with levothyroxine therapy for TSH >4.0 mIU/L to mitigate these outcomes, though debates persist on the benefits in mild cases [7]. Despite growing evidence, data from Indian tertiary care hospitals, particularly in underserved regions like Manipur, are sparse. Most studies focus on urban centers, overlooking ethnic and geographic variations that may influence thyroid function and pregnancy outcomes. This gap highlights the need for region-specific research to inform local guidelines and improve antenatal care. The present study, conducted at the Regional Institute of Medical Sciences (RIMS), Imphal, aims to evaluate maternal outcomes in pregnant women with SCH, assessing associations between TSH levels and key parameters (e.g., mode of delivery, hypertension, GDM, preterm labor). By providing insights into this understudied population, the study seeks to underscore the importance of routine thyroid screening and timely intervention in tertiary settings to optimize maternal health.

SUBJECTS AND METHODS

Study Design and Setting

This observational cohort study was conducted at the Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, India, It's a tertiary care hospital serving the northeastern region with approximately 31,000 annual inpatient admissions and 240,000 outpatient visits. The study period was from May 2023 to October 2024.

Participants

Eligible participants were pregnant women aged 18–40 years with singleton pregnancies diagnosed with subclinical hypothyroidism (SCH), defined as thyroid-stimulating hormone (TSH) >4.0 mU/L with normal free thyroxine (FT4; 0.8–2.0 ng/dL) based on American Thyroid Association 2017 guidelines. Women were recruited from the antenatal clinic. Exclusion criteria included pre-existing gestational hypertension or gestational diabetes mellitus; known chronic conditions such as diabetes mellitus, hypertension, cardiac, liver, kidney, or autoimmune disorders (excluding thyroid); bad obstetric history with identifiable causes; and other obstetric complications. Participants who declined consent were also excluded.

Sample Size and Sampling

The sample size was calculated using the formula $N = (1.96)^2 \times P \times Q / L^2$, based on a 9.37% prevalence of preeclampsia (a key maternal morbidity) in SCH from prior literature. With P=0.0937, Q=0.9063, and L=0.05 (absolute error), the estimated N was 130. Convenience sampling was employed, recruiting all eligible women during clinic hours after obtaining informed consent.

Data Collection

Ethical approval was obtained from the Research Ethics Board, RIMS (No. A/206/REB-Comm(SP)/RIMS/2015/1094/125/2023, dated September 30, 2023). Written informed consent was secured from all

participants, ensuring confidentiality via unique codes. Data were collected using a pretested structured proforma (primary source) and supplemented by hospital records (secondary source). Sociodemographic variables (age, address, gestational age, marital status, religion) and clinical history (e.g., STI, hypertension, diabetes) were recorded. Thyroid function tests (TSH, free T3, free T4) were performed as part of routine antenatal screening. Participants were followed prospectively until delivery, with monitoring for maternal outcomes via clinical examinations, ultrasound, blood investigations, and follow-up reports. Focus was placed on maternal outcomes, including preterm labor (onset of regular contractions <37 weeks), preterm delivery (<37 weeks), premature rupture of membranes (spontaneous rupture >28 weeks but before labor), preeclampsia (BP ≥140/90 mm Hg after 20 weeks with proteinuria/end-organ damage), mode of delivery (vaginal/cesarean), miscarriage (spontaneous loss <20 weeks), and postpartum hemorrhage (blood loss ≥1000 mL or hypovolemia signs). Additional maternal morbidities (e.g., gestational hypertension: BP ≥140/90 mm Hg after 20 weeks without proteinuria; abruption placentae: premature placental separation; disseminated intravascular coagulation: widespread fibrin deposition leading to organ failure/bleeding) were assessed.

Statistical Analysis

Data were entered and analyzed using IBM SPSS version 21. Descriptive statistics (means ± SD for continuous variables; frequencies/percentages for categorical) summarized baseline characteristics and outcomes. Independent t-tests compared continuous variables (e.g., TSH levels). Chi-square or Fisher's exact tests assessed associations between TSH strata (<4.5 vs. ≥4.5 mIU/L) and maternal outcomes. $P<0.05$ was considered statistically significant.

RESULTS

A total of 130 pregnant women with subclinical hypothyroidism (SCH) were included in the study. The demographic characteristics, thyroid function tests, maternal outcomes, and associations between thyroid function and key maternal outcomes are presented below.

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Demographic Details

The mean age of the participants was 29.4 ± 4.5 years, with a mean body mass index (BMI) of 27.8 ± 3.2 kg/m², indicating an overweight category. The average gravida was 1.8 ± 1.1, suggesting that most participants were multiparous. The mean gestational age at the time of assessment was 36.2 ± 2.8 weeks, with most women in the late third trimester (Table 1).

Table 1: Demographic Details (N=130)

Parameter	Mean ± SD
Age (years)	29.4 ± 4.5
BMI (kg/m²)	27.8 ± 3.2
Gravida	1.8 ± 1.1
Gestational Age (weeks)	36.2 ± 2.8

Thyroid Function Test

The mean thyroid-stimulating hormone (TSH) level was 4.8 ± 1.5 mIU/L, which is above the normal range (0.3–4.5 mIU/L), confirming SCH in the cohort. Free triiodothyronine (T3) and free thyroxine (T4) levels were within normal limits, with means of 2.5 ± 0.4 pg/mL and 1.0 ± 0.2 ng/dL, respectively (Table 2).

Table 2: Thyroid Function Test Results Among the Study Population

Parameter	Mean ± SD	Normal Range
TSH (mIU/L)	4.8 ± 1.5	0.3–4.5
Free T3 (pg/mL)	2.5 ± 0.4	2.0–4.4
Free T4 (ng/dL)	1.0 ± 0.2	0.8–2.0

Pregnancy and Maternal Outcomes

Full-term birth was the most common pregnancy outcome (75%), followed by pre-term birth (16%) and abortion (9%). Cesarean delivery was the most common maternal outcome, occurring in 34% cases, followed by vaginal delivery without complications in 30% cases. Gestational hypertension was the leading complication, affecting 18% women, while gestational diabetes mellitus and preterm labor occurred in 11% and 7% cases, respectively (Table 3).

Table 3: Pregnancy and Maternal Outcomes Among the Study Population

Outcomes	Frequency (%)
Pregnancy Outcomes	
Full-Term Birth	97 (75%)

Preterm Birth	21 (16%)
Abortion	12 (9%)
Maternal Outcomes	
Cesarean Delivery	44 (34%)
Vaginal Delivery without Complications	35 (30%)
Gestational Hypertension	25 (18%)
Gestational Diabetes Mellitus	16 (11%)
Preterm Labor	10 (7%)

Maternal Thyroid Function versus Pregnancy Outcomes

Elevated TSH was linked to higher preterm birth (23.3% vs. 10.0%; p=0.041), abortion (15.0% vs. 4.3%), and fewer living children (1.5 ± 0.7 vs. 1.9 ± 0.8; p=0.029). Full-term births were slightly lower in the elevated TSH group (81.7% vs. 85.7%) (Table 4).

Table 4: Association Between Maternal Thyroid Function and Pregnancy Outcomes (N=130)

Maternal TSH Levels	Preterm Birth (n=21)	Abortion (n=12)	Full-Term Birth (n=97)	Living Children (Mean ± SD)	p-value
TSH < 4.5 mIU/L (Normal-High) (n=70)	7 (10.0%)	3 (4.3%)	60 (85.7%)	1.9 ± 0.8	0.041*
TSH ≥ 4.5 mIU/L (Elevated) (n=60)	14 (23.3%)	9 (15.0%)	49 (81.7%)	1.5 ± 0.7	0.029*

P-value ≤0.05 considered statistically significant.

Maternal Thyroid Function versus Maternal Outcomes

Elevated TSH was significantly associated with fewer uncomplicated vaginal deliveries (28% vs. 72%; p=0.015) and higher rates of gestational hypertension (68% vs. 32%), gestational diabetes (75% vs. 25%), preterm labor (71% vs. 29%), and cesarean delivery (55% vs. 45%; p=0.013) (Table 5).

Table 5: Association Between Thyroid Function and Maternal Outcomes (N=130)

Thyroid Function (TSH Levels)	VD without Complications (n=35)	Gestational Hypertension (n=25)	Gestational Diabetes (n=16)	Preterm Labor (n=7)	Cesarean Delivery (n=44)	p-value
TSH < 4.5 mIU/L (Normal-High) (n=70)	25 (72%)	8 (32%)	4 (25%)	2 (29%)	20 (45%)	0.015*
TSH ≥ 4.5 mIU/L (Elevated) (n=60)	10 (28%)	17 (68%)	12 (75%)	5 (71%)	24 (55%)	0.013*

P-value ≤0.05 considered statistically significant.

These findings demonstrate that SCH, particularly with elevated TSH levels, is associated with increased risks of adverse maternal outcomes, underscoring the importance of routine thyroid screening in pregnancy.

DISCUSSION

This observational cohort study examined maternal outcomes in 130 pregnant women with subclinical hypothyroidism (SCH) at a tertiary care hospital in Manipur, India. Key findings revealed a high prevalence of adverse maternal outcomes, including cesarean delivery (34%), gestational hypertension (18%), gestational diabetes mellitus (GDM; 11%), and preterm labor (7%), with significantly elevated risks in women with TSH levels ≥4.5 mIU/L compared to those with TSH <4.5 mIU/L (p<0.05). These results underscore the potential impact of even mild thyroid dysfunction on pregnancy complications in a resource-limited setting, where iodine deficiency and limited screening may exacerbate risks [8].

The observed association between elevated TSH and increased rates of gestational hypertension (68% in elevated TSH group) aligns with existing evidence from meta-analyses, which indicate that SCH during pregnancy is linked to hypertensive disorders of pregnancy (HDP). For instance, a systematic review of cohort studies reported an odds ratio (OR) of 1.29 (95% CI: 1.01–1.64) for gestational hypertension in women with SCH, potentially due to thyroid hormone's role in vascular endothelial function and placental perfusion. Similarly, the heightened risk of GDM (75% in elevated TSH) in our cohort corroborates findings from a meta-analysis showing increased odds for GDM in SCH pregnancies, particularly when TSH exceeds 4.0 mIU/L, irrespective of thyroid autoimmunity status[9]. This may stem from SCH's influence on insulin resistance and glucose metabolism, as thyroid hormones regulate beta-cell function and hepatic gluconeogenesis.

Preterm labor and birth were also more frequent in the elevated TSH subgroup (71% and 23.3%, respectively), consistent with broader literature. A systematic review and meta-analysis of 19 studies involving over 47,000 women found SCH associated with preterm birth (OR 1.29; 95% CI: 1.01–1.64), though results vary by diagnostic thresholds and treatment status. However, a more recent meta-analysis of 18 studies reported no significant link between mild hypothyroidism and preterm birth or preeclampsia, highlighting inconsistencies possibly due to heterogeneity in TSH cutoffs (e.g., trimester-specific vs. fixed) and population differences [10]. Our study's use of a fixed TSH >4.0 mIU/L threshold, per ATA guidelines, may explain the observed associations, as regional iodine insufficiency in northeastern India could amplify SCH's effects compared to iodine-replete populations.

Cesarean delivery rates were notably high (34% overall, 55% in elevated TSH), which may reflect clinical caution in managing SCH-related complications like hypertension and preterm labor. This echoes findings from a study associating SCH with multiple adverse maternal outcomes, including increased cesarean sections (OR 1.24; 95% CI: 1.02–1.50), emphasizing the need for vigilant monitoring[11]. The absence of severe outcomes like postpartum hemorrhage or eclampsia in our cohort could be attributed to tertiary care interventions, though underreporting or exclusion criteria (e.g., pre-existing conditions) may play a role.

Strengths of this study include its prospective design, detailed TSH stratification, and representation of an understudied ethnic and geographic population in Manipur, where SCH prevalence may exceed national averages due to dietary factors.

Limitations

The observational cohort design precludes establishing causality between SCH and adverse maternal outcomes, as associations may be influenced by unmeasured variables. Confounding factors, including genetic predisposition, socioeconomic status, dietary iodine intake (prevalent in northeastern India), and other metabolic conditions, were not fully accounted for, potentially biasing results toward overestimation of risks. The single-center setting at a tertiary hospital limits generalizability to community or primary care populations, where SCH prevalence and management may differ. Thyroid function was assessed at a single time point (mean gestational age 36.2 weeks), without longitudinal monitoring of TSH fluctuations throughout pregnancy, which could overlook dynamic changes impacting outcomes. The modest sample size (N=130), while sufficient for initial associations, restricts subgroup analyses and power for rarer events like severe preeclampsia or postpartum hemorrhage. Convenience sampling may introduce selection bias, favoring higher-risk referrals. Additionally, the lack of a euthyroid control group hinders direct comparisons, and treatment effects (e.g., levothyroxine initiation) were not standardized or analyzed, despite evidence that early intervention mitigates complications like GDM and preterm birth.

Recommendations

Future studies should incorporate multivariable adjustments, randomized interventions, multi-center designs, and trimester-specific TSH tracking to address these gaps and strengthen evidence for clinical guidelines.

CONCLUSION

Our findings reinforce the association of SCH, particularly with TSH ≥4.5 mIU/L, with adverse maternal outcomes, advocating for routine thyroid screening in early pregnancy as per Endocrine Society recommendations. Future multicenter trials in iodine-deficient regions should evaluate levothyroxine's efficacy in preventing these complications to inform tailored guidelines and reduce maternal morbidity.

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