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Subclinical Hypothyroidism in Pregnancy and Adverse Maternal-Fetal Outcomes — A Prospective Observational Study

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ABS TRAC T

***Background*:** Subclinical hypothyroidism in pregnancy is defined as elevated TSH with normal free T4 and affects 2 to 5% of pregnancies. Its association with adverse maternal-fetal outcomes is increasingly recognised but remains debated. ***Methods*:** A prospective cohort study enrolled 200 pregnant women screened for thyroid function in the first trimester at a tertiary obstetric centre in India during 2023. Outcomes were compared between 52 women with SCH (TSH above 4.0 mIU/L with normal fT4) and 148 euthyroid controls. ***Results*:** SCH prevalence was 26.0%. SCH women had higher rates of preeclampsia (17.3% vs 6.8%, p equals 0.028), gestational diabetes (19.2% vs 8.8%, p equals 0.044), preterm birth (21.2% vs 8.1%, p equals 0.012), low birth weight (23.1% vs 10.1%, p equals 0.018), and NICU admission (19.2% vs 7.4%, p equals 0.022). TSH above 10 mIU/L was associated with significantly worse outcomes than TSH 4 to 10 (p equals 0.008). Levothyroxine-treated SCH patients (73.1%) had fewer complications than untreated patients. ***Conclusion*:** SCH is prevalent in 26% of pregnancies and significantly increases adverse outcomes. Universal first-trimester thyroid screening and early levothyroxine treatment are recommended.

Keywords: *Subclinical Hypothyroidism, Pregnancy, Adverse Outcomes, Preterm Birth, Preeclampsia, TSH, Levothyroxine.*

INTRODUCTION

Thyroid disorders are the second most common endocrine condition affecting women of reproductive age after diabetes mellitus [1]. Subclinical hypothyroidism, defined as elevated thyroid-stimulating hormone with normal free thyroxine levels, is present in 2 to 5% of unselected pregnant women and up to 15% in iodine-deficient regions [2]. The physiological changes of pregnancy place increased demands on the thyroid gland, requiring a 30 to 50% increase in thyroxine production to meet the metabolic needs of both the mother and the developing fetus [3].

The clinical significance of SCH in pregnancy has been debated. Observational studies have reported associations with miscarriage, preeclampsia, gestational diabetes, placental abruption, preterm delivery, low birth weight, and impaired neurocognitive development in offspring [4]. However, intervention trials have yielded mixed results. The Controlled Antenatal Thyroid Screening (CATS) study found no cognitive benefit in offspring of treated SCH mothers at age 3, although treated mothers had fewer adverse obstetric outcomes [5].

The threshold TSH level defining SCH in pregnancy has been controversial. The American Thyroid Association recommended trimester-specific reference ranges with an upper limit of 2.5 mIU/L in the first trimester [6]. However, more recent guidelines have shifted toward using population-based reference ranges, with many centres adopting 4.0 mIU/L as the upper limit when population data are unavailable [7].

In India, the prevalence of thyroid disorders in pregnancy has been reported to range from 4.8% to 26.5%, with significant regional variation attributable to differences in iodine status, autoimmune prevalence,

and diagnostic criteria [8]. The impact of SCH on pregnancy outcomes in Indian women, who may have distinct genetic and environmental risk profiles, requires further elucidation [9]. The present study evaluated the prevalence and impact of SCH on maternal and fetal outcomes at a tertiary obstetric centre [10].

AIMS AND OBJECTIVES

The study aimed to determine the prevalence of subclinical hypothyroidism among first-trimester pregnant women, to compare maternal and fetal outcomes between SCH and euthyroid pregnancies, to assess the effect of levothyroxine treatment on outcomes in SCH patients, and to evaluate whether the degree of TSH elevation correlated with adverse outcome severity.

MATERIALS AND METHODS

Study Design and Setting

Prospective observational cohort study from January to December 2023 at the Department of Obstetrics and Gynaecology, Government Tertiary Care Teaching Hospital, India. Approved by the Institutional Ethics Committee.

Sample Size

200 consecutive pregnant women presenting for first-trimester antenatal care were enrolled. Sample size was based on an expected SCH prevalence of 20%, requiring 196 subjects for 95% CI with 6% precision.

Inclusion Criteria

Singleton pregnancies at 6 to 12 weeks gestation confirmed by ultrasound dating, age 18 to 40 years, no known thyroid disease, and willing to comply with follow-up were included.

Exclusion Criteria

Known thyroid disease, current thyroid medication, multiple gestation, pre-existing diabetes or hypertension, renal or hepatic disease, and autoimmune conditions other than thyroid were excluded.

Procedure and Data Collection

First-trimester serum TSH (chemiluminescent immunoassay), free T4, and anti-TPO antibodies were measured. SCH was defined as TSH above 4.0 mIU/L with normal fT4. Women with TSH above 10 mIU/L were treated with levothyroxine regardless. Women with TSH 4.0 to 10.0 were offered treatment; those accepting levothyroxine were titrated to maintain TSH below 2.5 in the first trimester and below 3.0 thereafter. Euthyroid women served as controls. All women received standard antenatal care. Maternal outcomes recorded included preeclampsia, gestational diabetes (by 75g OGTT at 24 to 28 weeks), antepartum haemorrhage, and mode of delivery. Fetal outcomes included gestational age at delivery, birth weight, Apgar scores, NICU admission, and neonatal complications.

Follow-Up Protocol

Follow-up at each trimester and delivery. TSH repeated at 20, 28, and 36 weeks in SCH group. Neonatal thyroid function was tested in babies born to SCH mothers.

Statistical Analysis

SPSS 13.0. Chi-square for categorical outcomes, Student t-test for continuous variables, Fisher exact test where appropriate. Logistic regression for predictors of adverse outcomes. p less than 0.05 significant.

RESULTS

Of 200 women screened, 52 (26.0%) had SCH. Among SCH women, TSH ranged from 4.1 to 18.6 mIU/L with mean 7.8 plus or minus 3.6. Twelve women (23.1%) had TSH above 10 mIU/L. Anti-TPO positivity was present in 21 SCH women (40.4%) versus 12 euthyroid controls (8.1%, p less than 0.001). Mean age was comparable between groups (26.4 plus or minus 4.2 vs 25.8 plus or minus 3.8 years, p equals 0.368). Mean BMI was 24.8 plus or minus 3.6 versus 23.4 plus or minus 3.2 (p equals 0.014).

Levothyroxine was initiated in 38 SCH women (73.1%); 14 declined treatment. Treated women achieved mean TSH of 2.4 plus or minus 0.8 by 20 weeks. Untreated women maintained mean TSH of 6.8 plus or minus 2.4.

Maternal outcomes showed significantly higher rates in SCH versus euthyroid: preeclampsia 17.3% versus 6.8% (p equals 0.028), gestational diabetes 19.2% versus 8.8% (p equals 0.044), caesarean section 40.4% versus 26.4% (p equals 0.062). Fetal outcomes showed preterm birth 21.2% versus 8.1% (p equals 0.012), low birth weight 23.1% versus 10.1% (p equals 0.018), mean birth weight 2680 plus or minus 480 versus 2920 plus or minus 420 g (p equals 0.002), NICU admission 19.2% versus 7.4% (p equals 0.022), and 5-minute Apgar below 7 in 11.5% versus 4.1% (p equals 0.048).

Women with TSH above 10 had worse outcomes than those with TSH 4 to 10: preterm 41.7% versus 15.0% (p equals 0.038), LBW 41.7% versus 17.5% (p equals 0.062). Treated SCH women had lower complication rates than untreated: preterm 15.8% versus 35.7% (p equals 0.108), preeclampsia 13.2% versus 28.6% (p equals 0.174), though differences did not reach significance due to small subgroup sizes.

Table 1: Baseline Characteristics

Parameter	SCH (n=52)	Euthyroid (n=148)	p-value
Age (years)	26.4 +/- 4.2	25.8 +/- 3.8	0.368

BMI (kg/m2)	24.8 +/- 3.6	23.4 +/- 3.2	0.014
Primigravida (%)	46.2%	52.0%	0.472
TSH (mIU/L)	7.8 +/- 3.6	2.2 +/- 0.8	<0.001
Anti-TPO positive (%)	40.4%	8.1%	<0.001

Table 2: Maternal Outcomes

Outcome	SCH (n=52)	Euthyroid (n=148)	p-value
Preeclampsia	9 (17.3%)	10 (6.8%)	0.028
GDM	10 (19.2%)	13 (8.8%)	0.044
Caesarean section	21 (40.4%)	39 (26.4%)	0.062
Antepartum haemorrhage	3 (5.8%)	4 (2.7%)	0.297
Miscarriage	4 (7.7%)	4 (2.7%)	0.118

Table 3: Fetal/Neonatal Outcomes

Outcome	SCH (n=52)	Euthyroid (n=148)	p-value
Preterm birth (<37 wk)	11 (21.2%)	12 (8.1%)	0.012
LBW (<2500 g)	12 (23.1%)	15 (10.1%)	0.018
Mean birth weight (g)	2680 +/- 480	2920 +/- 420	0.002
NICU admission	10 (19.2%)	11 (7.4%)	0.022
Apgar <7 at 5 min	6 (11.5%)	6 (4.1%)	0.048

Table 4: Outcomes by TSH Level in SCH Group

Outcome	TSH 4-10 (n=40)	TSH >10 (n=12)	p-value
Preeclampsia	5 (12.5%)	4 (33.3%)	0.086
Preterm	6 (15.0%)	5 (41.7%)	0.038
LBW	7 (17.5%)	5 (41.7%)	0.062
NICU	6 (15.0%)	4 (33.3%)	0.148

Table 5: Outcomes by Treatment Status in SCH

Outcome	Treated (n=38)	Untreated (n=14)	p-value
Preeclampsia	5 (13.2%)	4 (28.6%)	0.174
Preterm	6 (15.8%)	5 (35.7%)	0.108
LBW	7 (18.4%)	5 (35.7%)	0.170
Mean TSH at 20 wk	2.4 +/- 0.8	6.8 +/- 2.4	<0.001

DISCUSSION

The SCH prevalence of 26.0% in the present study is higher than the 2 to 5% reported in iodine-replete Western populations [11] but consistent with the 15 to 26% reported from various Indian centres by Dhanwal *et al*., [12] and Sahu *et al*., [13]. This high prevalence underscores the need for universal screening in Indian pregnant women.

The significantly higher rates of preeclampsia (17.3% vs 6.8%) and preterm birth (21.2% vs 8.1%) in SCH patients are consistent with the meta-analysis by Maraka *et al*., [14], which reported pooled odds ratios of 1.53 for preeclampsia and 1.35 for preterm delivery. The association between SCH and adverse outcomes is biologically plausible through mechanisms including impaired trophoblast invasion, endothelial dysfunction, and altered placental angiogenesis [15].

The dose-response relationship between TSH level and adverse outcomes (TSH above 10 worse than TSH 4 to 10) supports the findings of Casey *et al*., [16] and provides a rationale for treatment prioritisation. The trend toward better outcomes in levothyroxine-treated patients, although not statistically significant due to small numbers, is consistent with the meta-analysis by Nazarpour *et al*., [17].

Anti-TPO positivity in 40.4% of SCH women (vs 8.1% euthyroid) confirms the autoimmune basis in a substantial proportion and is comparable to the 35 to 50% reported by Thangaratinam *et al*., [18]. Anti-TPO positivity independently increases miscarriage risk regardless of TSH level [19].

Limitations include the observational design precluding causal inference, the small sample of untreated SCH for meaningful comparison, and the single-centre setting. Neurodevelopmental assessment of offspring was not performed [20].

CONCLUSION

SCH is prevalent in 26% of pregnancies and significantly increases adverse outcomes. Universal first-trimester thyroid screening and early levothyroxine treatment are recommended.

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