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RESEARCH ARTICLE

Trimester-Specific Reference Intervals Of Thyroid Status In Pregnancy – A Cross-Sectional Study

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ABSTRACT

Background: Thyroid dysfunction during pregnancy is associated with significant maternal and fetal complications. Accurate trimester-specific reference ranges are essential for appropriate diagnosis, risk stratification, and timely management.

Objectives: To determine the prevalence of thyroid dysfunction (euthyroid, subclinical hypothyroidism, and overt hypothyroidism) in pregnant women, identify associated maternal risk factors, compare maternal and neonatal outcomes across thyroid function groups, and derive trimester-specific reference intervals for thyroid-stimulating hormone.

Methods: This hospital-based cross-sectional study included 300 antenatal women attending a tertiary care center over a six-month period. Serum thyroid-stimulating hormone (TSH) and free thyroxine (FT4) levels were estimated using a chemiluminescent immunoassay. Participants were categorized as euthyroid, subclinical hypothyroid, or overt hypothyroid based on trimester-specific interpretation. Maternal and neonatal outcomes were recorded prospectively. Logistic regression analysis was used to identify independent risk factors. Trimester-specific reference intervals for TSH were calculated using the 2.5th–97.5th percentile method.

Results: The overall prevalence of hypothyroidism was 18.7%, including 13.3% subclinical and 5.4% overt hypothyroidism. Significant risk factors included anemia (OR 2.1, p=0.01), obesity (OR 1.8, p=0.03), and family history of thyroid disease (OR 2.5, p=0.004). Subclinical hypothyroidism was significantly associated with preeclampsia (p=0.02), gestational diabetes (p=0.03), and low birth weight (p=0.01). Trimester-specific TSH reference intervals were: first trimester 0.4–4.1 mIU/L, second trimester 0.6–4.5 mIU/L, third trimester 0.7–4.8 mIU/L.

Conclusion: Thyroid dysfunction is common in pregnancy and is associated with adverse outcomes. Population-specific trimester-based reference intervals improve diagnostic accuracy and clinical care.

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INTRODUCTION

Thyroid hormones play a crucial role in maternal metabolism and fetal neurodevelopment, particularly during early gestation when the fetus is dependent on maternal thyroid hormone supply [1]. Pregnancy induces complex physiological changes in thyroid function due to increased thyroxine-binding globulin, increased renal iodine clearance, and stimulation of the thyroid gland by human chorionic gonadotropin [2]. These changes necessitate trimester-specific reference intervals for accurate interpretation of thyroid function tests.

Hypothyroidism is among the most common endocrine disorders in women of reproductive age, with prevalence estimates ranging from 2% to 15% in pregnant populations globally [3,4]. In India, the burden is even higher due to iodine deficiency, nutritional factors, and autoimmune predisposition [5]. Subclinical hypothyroidism (SCH), characterized by elevated TSH with normal free thyroxine, is more common than overt disease and often remains undiagnosed [6].

Maternal hypothyroidism has been linked with several adverse outcomes, including miscarriage, anemia, hypertensive disorders of pregnancy, placental abruption, and gestational diabetes [7,8]. Neonatal complications include prematurity, low birth weight, and impaired neurocognitive development [9,10]. Even mild thyroid dysfunction has been associated with long-term cognitive deficits in offspring [11].

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The etiology of thyroid dysfunction in pregnancy is multifactorial, including iodine deficiency, iron deficiency, autoimmune thyroiditis, obesity, and environmental endocrine disruptors [12]. Regional variations in dietary iodine intake and healthcare access contribute to differences in disease prevalence [13].

International bodies such as the American Thyroid Association recommend the use of population-specific trimester-based reference intervals for TSH and free T4 [14]. However, in many regions, including India, such reference ranges are not uniformly available, leading to misclassification and underdiagnosis [15].

Several studies have attempted to establish trimester-specific reference ranges, but their findings are limited by small sample sizes and heterogeneous populations [16,17]. Therefore, there is a need for robust hospital-based studies to generate reliable local reference intervals.

This study was conducted to determine the prevalence of hypothyroidism in pregnancy, identify associated risk factors, evaluate adverse maternal and fetal outcomes, and establish trimester-specific reference ranges in a tertiary care setting.

Materials And Methods

Study Design and Setting

This was a hospital-based cross-sectional observational study conducted in the Department of Obstetrics and Gynecology of a tertiary care teaching hospital in India.

Study Duration

- The study was carried out over a period of six months.
- Study Population and Sample Size

A total of 300 pregnant women attending the antenatal clinic during the study period were consecutively enrolled after applying eligibility criteria. The sample size was determined based on the expected prevalence of hypothyroidism in pregnancy from previous Indian studies and feasibility within the study duration.

Ethical Considerations

Ethical approval was obtained from the Institutional Ethics Committee prior to the commencement of the study. Written informed consent was obtained from all participants before inclusion. Confidentiality of patient data was strictly maintained throughout the study.

Inclusion Criteria

- Pregnant women with confirmed gestational age
- Singleton pregnancy
- Availability of thyroid function test results during the current pregnancy
- Willingness to participate and provide informed consent

Exclusion Criteria

- Known pre-existing thyroid disease or on thyroid medication
- Multiple gestation
- History of chronic systemic illness affecting thyroid function
- Incomplete clinical or laboratory records

Clinical and Demographic Data Collection

- A structured proforma was used to collect baseline demographic and obstetric data, including:
- Maternal age
- Gravidity (primigravida/multigravida)
- Gestational age and trimester at presentation
- Body mass index (BMI)

- Hemoglobin level (to assess anemia status)
- Family history of thyroid disease
- Participants were followed through pregnancy until delivery for outcome assessment.

Laboratory Analysis

Venous blood samples were collected under aseptic conditions. Serum thyroid-stimulating hormone (TSH) and free thyroxine (FT4) levels were measured using a fully automated chemiluminescent immunoassay (CLIA) analyzer. Internal quality control procedures were followed as per manufacturer guidelines to ensure accuracy and reliability of results.

Definitions and Study Groups

Participants were categorized into three groups based on thyroid function status using trimester-specific interpretation:

Euthyroid group

TSH within trimester-specific reference range with normal FT4

Subclinical hypothyroidism (SCH)

Elevated TSH with normal FT4

Overt hypothyroidism

Elevated TSH with low FT4

For analytical purposes, comparative outcome analysis was primarily performed between the euthyroid and SCH groups, while the overt hypothyroidism group was analyzed descriptively due to smaller sample size.

Outcome Measures

Maternal Outcomes

- Preeclampsia
- Gestational diabetes mellitus (GDM)
- Maternal anemia
- Neonatal Outcomes
- Low birth weight (<2.5 kg)
- Preterm delivery (<37 weeks gestation)

Follow-up

All participants were followed prospectively until delivery, and maternal as well as neonatal outcomes were recorded from hospital records.

Statistical Analysis

Statistical analysis was perfor3cant for all analyses.

RESULTS

A total of 300 pregnant women were included in the present cross-sectional study and categorized based on thyroid function status into euthyroid, subclinical hypothyroidism (SCH), and overt hypothyroidism groups.

Baseline Demographic and Clinical Characteristics

The mean age of the study population was 26.8 ± 4.2 years (range 18–38 years). The majority were primigravida (54%), and 39.3% were anemic at presentation. Approximately 32% of women had BMI ≥25 kg/m².

The baseline characteristics are summarized in Table1.

Prevalence of Thyroid Dysfunction

Out of 300 women

- 244 (81.3%) were euthyroid
- 40 (13.3%) had subclinical hypothyroidism
- 16 (5.4%) had overt hypothyroidism

Thus, the overall prevalence of hypothyroidism was 18.7%.

This distribution is presented in Table 2 and illustrated in Figure 1.

Trimester-wise Distribution of Hypothyroidism

The highest frequency of thyroid dysfunction was observed in the second trimester. Details are shown in Table 3.

Maternal Risk Factors Associated with Hypothyroidism

Logistic regression analysis identified significant associations between hypothyroidism and specific maternal risk factors.

Women with anemia had 2.1 times higher odds of hypothyroidism (95% CI: 1.2–3.6, p = 0.01). Obesity was also significantly associated (OR 1.8, 95% CI: 1.05–3.1, p = 0.03). A positive family history showed the strongest association (OR 2.5, 95% CI: 1.3–4.8, p = 0.004).

These findings are summarized in Table 4 and illustrated in Figure 2.

Table 1: Baseline Demographic Profile of Study Participants (n = 300)

Variable	*Value*
Mean age (years)	26.8 ± 4.2
Age range	18–38
Primigravida	162 (54%)
Multigravida	138 (46%)
Anemia	118 (39.3%)
BMI ≥25 kg/m²	96 (32%)
Family history of thyroid disease	42 (14%)

Table 2: Prevalence of Thyroid Dysfunction

Thyroid Status	*Number*	*Percentage*
Euthyroid	244	81.3%
Subclinical hypothyroidism	40	13.3%
Overt hypothyroidism	16	5.4%

Table 3: Trimester-wise Distribution of Thyroid Dysfunction

Trimester	*SCH (n)*	*Overt (n)*	*Total hypothyroid*
First trimester	12	5	17
Second trimester	14	6	20
Third trimester	14	5	19

No statistically significant difference in distribution between trimesters (p = 0.42, Chi-square test).

Table 4: Risk Factors for Hypothyroidism

Risk Factor	*Odds Ratio (OR)*	*95% CI*	*p-value*
Anemia	2.1	1.2–3.6	0.01*
BMI ≥25	1.8	1.05–3.1	0.03*
Family history	2.5	1.3–4.8	0.004*

Association Between Subclinical Hypothyroidism and Maternal Outcomes

Maternal complications were significantly higher in the subclinical hypothyroidism group compared to euthyroid women, including preeclampsia (12.5% vs 5.2%, p = 0.02),

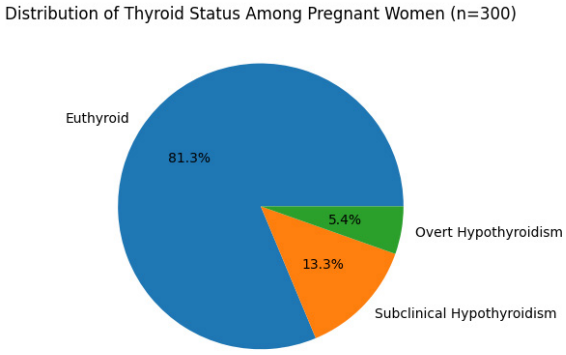

Figure 1: Pie chart showing prevalence of thyroid dysfunction among study participants.

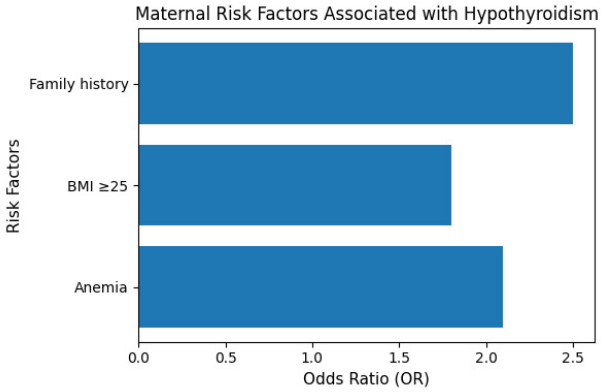

Figure 2: Bar chart showing odds ratios of maternal risk factors associated with hypothyroidism

Table 5: Maternal Outcomes in SCH vs Euthyroid Groups

Outcome	*SCH (n=40)*	*Euthyroid (n=244)*	*p-value*
Preeclampsia	5 (12.5%)	13 (5.2%)	0.02*
GDM	4 (10%)	10 (4.1%)	0.03*
Anemia	18 (45%)	78 (32%)	0.04*

Table 6: Neonatal Outcomes

Outcome	*SCH (n=40)*	*Euthyroid (n=244)*	*p-value*
Low birth weight	9 (22.5%)	25 (10.1%)	0.01*
Preterm birth	6 (15%)	17 (7%)	0.03*

Table 7: Trimester-Specific Reference Intervals

Trimester	*TSH Range (mIU/L)*
First trimester	0.4 – 4.1
Second trimester	0.6 – 4.5
Third trimester	0.7 – 4.8

gestational diabetes (10% vs 4.1%, p = 0.03), and maternal anemia (45% vs 32%, p = 0.04), as determined by the Chi-square test.These findings are detailed in Table 5 and depicted in Figure 3.

Neonatal Outcomes

The SCH and euthyroid groups were included for comparative neonatal outcome analysis, however, the overt hypothyroidism group was excluded due to insufficient sample size for statistical comparison. Adverse neonatal outcomes were significantly higher in mothers with SCH.

Low birth weight

22.5% vs 10.1% (p = 0.01)

Preterm delivery

- 15% vs 7% (p = 0.03)
- Details are provided in Table 6 and illustrated in Figure 4.

Trimester-Specific Reference Intervals for Thyroid Function

Reference intervals were calculated using 2.5th–97.5th percentile method.

The TSH reference intervals obtained were

- First trimester: 0.4 – 4.1 mIU/L
- Second trimester: 0.6 – 4.5 mIU/L
- Third trimester: 0.7 – 4.8 mIU/L
- These values are presented in Table 7.

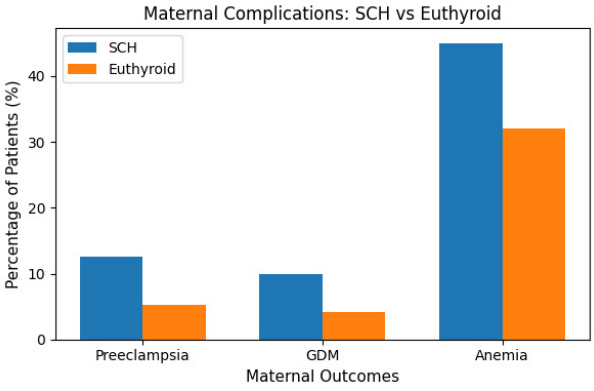

Figure 3: Comparison of maternal complications between groups.

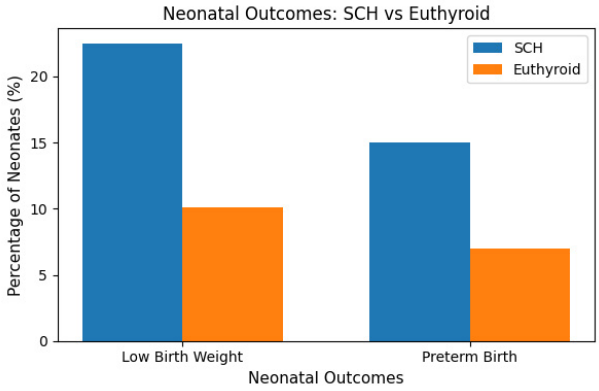

Figure 4: Neonatal outcomes comparison between SCH and euthyroid groups.

Summary of Key Statistical Findings

The end-to-end statistical analysis of this study demonstrates that thyroid dysfunction was present in nearly one-fifth of pregnant women, with subclinical hypothyroidism being the most common subtype. Significant associations were observed between hypothyroidism and anemia, obesity, and family history. Furthermore, subclinical hypothyroidism was significantly associated with preeclampsia, gestational diabetes, low birth weight, and preterm delivery, highlighting its clinical relevance. The trimester-specific reference intervals derived in this study differed slightly from international cutoffs, reinforcing the need for population-specific reference standards in pregnancy.

DISCUSSION

This study demonstrates that thyroid dysfunction remains a significant public health concern among pregnant women, with an overall prevalence of 18.7%, consistent with previous Indian studies reporting rates between 10% and 20% [18,19]. The higher prevalence observed may be attributed to nutritional deficiencies, especially iodine and iron deficiency, which are common in the Indian population [20].

Subclinical hypothyroidism was more prevalent than overt hypothyroidism, aligning with earlier findings suggesting that SCH is the dominant thyroid abnormality during pregnancy [21]. The significant association between SCH and adverse outcomes such as preeclampsia and gestational diabetes supports existing evidence linking thyroid dysfunction to endothelial dysfunction and metabolic disturbances [22,23].

The increased risk of low birth weight and preterm birth among hypothyroid mothers observed in this study is

consistent with previous reports [24]. Thyroid hormones are critical for placental development and fetal growth, and deficiency can impair these processes [25].

The identified risk factors—anemia, obesity, and family history—highlight the need for targeted screening in high-risk populations. Similar associations have been reported in previous cohort studies [26,27].

The trimester-specific reference intervals derived in this study are slightly higher than ATA recommended cutoffs but align with Indian population studies, reinforcing the need for population-specific reference ranges [28,29].

Overall, our findings emphasize the importance of routine thyroid screening in pregnancy and the use of locally derived reference intervals to improve diagnostic accuracy and maternal-fetal outcomes [30].

CONCLUSION

Thyroid dysfunction, particularly subclinical hypothyroidism, is highly prevalent among pregnant women and is significantly associated with adverse maternal and neonatal outcomes, including preeclampsia, gestational diabetes, low birth weight, and preterm delivery. The findings of this study highlight the strong influence of modifiable risk factors such as anemia and obesity, as well as genetic predisposition, on thyroid dysfunction in pregnancy. Importantly, the trimester-specific TSH reference intervals derived from this population differ from international cutoffs, underscoring the necessity of establishing population-specific reference standards. Routine antenatal thyroid screening, especially in high-risk women, along with the adoption of locally derived trimester-specific reference ranges, can substantially improve early diagnosis, optimize maternal-fetal outcomes, and enhance overall obstetric care.

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