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Research Article

Impact of Hypothyroidism in Pregnancy on Feto-Maternal Outcome- A Prospective Observational Study

Sultana Begum[1*], Fatima Wahid[2], Afroza Sultana[3], Shamima Sultana[4]
[1]Consultant, Department of Obstetrics & Gynecology, Selina General Hospital, Dhaka, Bangladesh.
[2]Medical Officer, Department of Obstetrics & Gynecology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
[3]Junior Consultant, Department of Obstetrics & Gynecology, OGSB Hospital, Mirpur, Bangladesh.
[4]Medical Officer, Department of Obstetrics & Gynecology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

***Corresponding author**
Sultana Begum

Abstract: ***Background:*** Thyroid dysfunction, particularly hypothyroidism, is a common endocrine disorder during pregnancy with potential adverse effects on maternal and fetal health. This study aimed to determine the prevalence of hypothyroidism among pregnant women and evaluate its impact on maternal and fetal outcomes. ***Methods:*** This prospective observational study included 100 pregnant women attending the antenatal clinic during their first trimester at Department of Obstetrics & Gynecology, BSMMU, Dhaka, Bangladesh from January to December 2014. Thyroid function tests (TSH, FT4, FT3, and anti-TPO antibodies) were performed at enrollment. Women were classified as euthyroid, overt hypothyroid, subclinical hypothyroid, or TPO-positive euthyroid based on trimester-specific reference ranges. Hypothyroid women received levothyroxine treatment with periodic monitoring. All participants were followed throughout pregnancy, and maternal and fetal outcomes were recorded. ***Results:*** The prevalence of hypothyroidism was 22%, with subclinical hypothyroidism (18%) being more common than overt hypothyroidism (4%). Additionally, 11% of women were TPO antibody positive with normal thyroid function. Advanced maternal age (≥35 years), higher BMI, family history of thyroid disorders, and previous history of miscarriage were identified as significant risk factors for hypothyroidism. Women with hypothyroidism had higher rates of pregnancy-induced hypertension (27.3% vs. 10.3%, p=0.041), preeclampsia (18.2% vs. 3.8%, p=0.034), gestational diabetes mellitus (22.7% vs. 7.7%, p=0.047), and cesarean delivery (54.5% vs. 32.1%, p=0.049) compared to euthyroid women. Similarly, adverse fetal outcomes including low birth weight (27.3% vs. 10.3%, p=0.041), lower mean birth weight (2742±486g vs. 3126±412g, p=0.008), and increased NICU admissions (31.8% vs. 11.5%, p=0.020) were more frequent in the hypothyroid group. A significant negative correlation was observed between maternal TSH levels and birth weight (r=-0.42, p<0.001). Adequately treated hypothyroid women had fewer complications compared to inadequately treated women. ***Conclusion:*** This study demonstrates a high prevalence of hypothyroidism during pregnancy in our population, with significant associations with adverse maternal and fetal outcomes. Early detection and adequate treatment with levothyroxine can substantially reduce these risks, highlighting the importance of thyroid function screening and appropriate management during pregnancy.

Keywords: Hypothyroidism, Pregnancy, Thyroid-stimulating hormone, Anti-TPO antibodies, Maternal outcomes, Fetal outcomes, Levothyroxine.

INTRODUCTION

Thyroid disorders represent one of the most common endocrine conditions affecting women of reproductive age, with hypothyroidism being particularly prevalent during pregnancy.[1,2] The physiological and hormonal changes during gestation significantly impact thyroid function, creating a complex interplay that requires careful clinical attention.[3] During pregnancy, the thyroid gland undergoes substantial adaptations, including increased thyroid hormone production, altered iodine metabolism, and modifications in the hypothalamic-pituitary-thyroid axis regulation.[4] Hypothyroidism, characterized by insufficient thyroid hormone production, affects approximately 2-3% of pregnancies worldwide, though prevalence rates vary considerably across different populations and geographic regions.[5,6] The condition may present as overt hypothyroidism (elevated thyroid-stimulating hormone [TSH] with decreased free thyroxine [FT4]) or subclinical hypothyroidism (elevated TSH with normal FT4), with the latter being more common yet equally concerning in the context of pregnancy.[7] The significance of thyroid hormone adequacy during pregnancy cannot be overstated, as these hormones play crucial roles in fetal neurodevelopment, placental formation, and overall maternal-fetal physiology.[8]

Growing evidence suggests that even mild maternal thyroid dysfunction may have substantial consequences for both mother and child.[9,10] Maternal complications associated with hypothyroidism include increased risks of miscarriage, preeclampsia, gestational hypertension, placental abruption, postpartum hemorrhage, and anemia.[11,12] For the fetus and neonate, potential adverse outcomes encompass impaired neurological development, low birth weight, prematurity, and increased perinatal mortality.[13,14] Despite the recognized importance of thyroid health during pregnancy, consensus regarding universal screening versus targeted case-finding approaches remains elusive, with varying recommendations across international guidelines.[15,16] The identification of high-risk populations and appropriate diagnostic thresholds presents ongoing challenges for clinicians worldwide.[17] This controversy is further complicated by geographical variations in iodine sufficiency, reference range determination, and the timing of screening during pregnancy.[18] Treatment strategies, primarily involving levothyroxine supplementation, require careful dosage adjustments throughout pregnancy, with monitoring parameters that differ from non-pregnant states.[19] The window of opportunity for intervention appears to be critical, with earlier detection and treatment potentially offering greater protection against adverse outcomes.[20] Our study aimed to determine the prevalence of hypothyroidism among pregnant women attending our tertiary care center and to evaluate the maternal and fetal outcomes associated with this condition. By analyzing 100 cases, we sought to contribute to the growing body of evidence that informs clinical practice in this important area of maternal-fetal medicine. This research may provide valuable insights into the regional burden of thyroid dysfunction during pregnancy and help refine screening and management protocols specific to our population.[21]

Materials And Methods

Study Design and Setting

This prospective observational study included 100 pregnant women attending the antenatal clinic during their first trimester at Department of Obstetrics & Gynecology, BSMMU, Dhaka, Bangladesh from January to December 2014. We recruited 100 pregnant women attending the antenatal clinic during their first trimester (up to 13 weeks of gestation). The sample size was calculated based on the previously reported prevalence of hypothyroidism in pregnancy of approximately 2-3%, with a confidence interval of 95% and a margin of error of 5%. Pregnancy was confirmed by a positive urine pregnancy test and ultrasonographic evidence. Thyroid function tests (TSH, FT4, FT3, and anti-TPO antibodies) were performed at enrollment. Women were classified as euthyroid, overt hypothyroid, subclinical hypothyroid, or TPO-positive euthyroid based on trimester-specific reference ranges. Hypothyroid women received levothyroxine treatment with periodic monitoring. All participants were followed throughout pregnancy, and maternal and fetal outcomes were recorded.

Inclusion Criteria

- Pregnant women aged 18-40 years
- Singleton pregnancy
- Gestational age ≤13 weeks at enrollment
- Willing to provide informed consent and complete follow-up until delivery

Exclusion Criteria

- Multiple pregnancies
- Known thyroid disorder prior to pregnancy or on thyroid medication
- History of radioiodine therapy or thyroid surgery
- Chronic medical conditions including diabetes mellitus, hypertension, and autoimmune disorders
- Use of medications known to affect thyroid function (amiodarone, lithium, steroids)
- Inability to complete the follow-up period

Data Collection

A detailed history was obtained from all participants using a structured questionnaire that included demographic information, obstetric history, medical history, family history of thyroid disorders, and clinical symptoms suggestive of thyroid dysfunction. Physical examination included measurement of height, weight, calculation of body mass index (BMI), blood pressure, and assessment for clinical signs of hypothyroidism such as goiter.

Laboratory Investigations

Blood samples (5 ml) were collected from all participants after an overnight fast for the estimation of thyroid function. Serum was separated by centrifugation and stored at -20°C until analysis. Thyroid function tests including serum TSH, free T4 (FT4), and free T3 (FT3) were measured using chemiluminescent immunoassay (CLIA) technique on an automated analyzer (Analyzer model, Manufacturer). Anti-thyroid peroxidase antibodies (anti-TPO) were also measured to identify autoimmune thyroid disease. The trimester-specific reference ranges for thyroid function were established according to the American Thyroid Association (ATA) guidelines: first trimester TSH (0.1-2.5 mIU/L), second trimester TSH (0.2-3.0 mIU/L), and third trimester TSH (0.3-3.0 mIU/L).

Diagnosis and Classification of Hypothyroidism

Participants were classified into the following categories based on thyroid function test results:

1. Euthyroid: Normal TSH and FT4 levels according to trimester-specific reference ranges
2. Overt hypothyroidism: Elevated TSH (>2.5 mIU/L in first trimester) with decreased FT4 levels
3. Subclinical hypothyroidism: Elevated TSH (>2.5 mIU/L in first trimester) with normal FT4 levels

4. TPO antibody positive euthyroid: Normal TSH and FT4 levels with positive anti-TPO antibodies

Management Protocol

Women diagnosed with overt or subclinical hypothyroidism were initiated on levothyroxine treatment under the supervision of an endocrinologist. The starting dose was determined based on the degree of TSH elevation and body weight (usually 1.6 µg/kg/day for overt hypothyroidism and 1.0 µg/kg/day for subclinical hypothyroidism). Thyroid function tests were repeated every 4-6 weeks throughout pregnancy, and medication dosages were adjusted accordingly to maintain TSH levels within the trimester-specific reference ranges. TPO antibody-positive euthyroid women were monitored closely with thyroid function tests every 4-6 weeks without immediate levothyroxine treatment, unless they developed biochemical evidence of hypothyroidism during follow-up.

Follow-up and Outcome Assessment

All participants were followed up throughout pregnancy until delivery. During each antenatal visit, maternal weight gain, blood pressure, and clinical symptoms were recorded. Routine antenatal investigations and ultrasonography for fetal growth monitoring were performed as per standard protocols.

Maternal Outcomes

The following maternal outcomes were assessed:

- Pregnancy-induced hypertension (systolic BP ≥140 mmHg and/or diastolic BP ≥90 mmHg after 20 weeks of gestation)
- Preeclampsia (hypertension with proteinuria ≥300 mg/24 hours or spot urine protein/creatinine ratio ≥0.3)
- Gestational diabetes mellitus (diagnosed according to IADPSG criteria)
- Anemia (hemoglobin <11 g/dL)
- Placental abruption
- Postpartum hemorrhage (blood loss >500 ml in vaginal delivery or >1000 ml in cesarean section)
- Mode of delivery
- Preterm labor (delivery before 37 completed weeks)

Fetal and Neonatal Outcomes

The following fetal and neonatal outcomes were evaluated:

- Intrauterine growth restriction (estimated fetal weight <10th percentile for gestational age)
- Low birth weight (<2500 g)
- APGAR scores at 1 and 5 minutes
- Neonatal intensive care unit (NICU) admission
- Congenital anomalies
- Perinatal mortality

Statistical Analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 22.0. Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as mean ± standard deviation or median with interquartile range, depending on the normality of distribution. The prevalence of hypothyroidism was calculated as the percentage of women diagnosed with overt or subclinical hypothyroidism among the total study population. Chi-square test or Fisher's exact test was used to compare categorical variables between groups. Student's t-test or Mann-Whitney U test was used to compare continuous variables between groups. A p-value <0.05 was considered statistically significant. Logistic regression analysis was performed to identify independent risk factors for adverse maternal and fetal outcomes, adjusting for potential confounding variables such as maternal age, BMI, parity, and socioeconomic status.

RESULTS

Demographic and Baseline Characteristics

A total of 100 pregnant women who met the inclusion criteria were enrolled in the study. The mean age of participants was 27.4 ± 4.3 years (range: 19-38 years). The majority of women (68%) were in the age group of 25-34 years. The mean gestational age at enrollment was 9.8 ± 2.1 weeks. Demographic and baseline characteristics of the study population are presented in Table 1.

Table 1: Demographic and Baseline Characteristics of Study Participants (N=100)

Characteristic	Value
Age (years)	
Mean ± SD	27.4 ± 4.3
18-24	24 (24%)
25-34	68 (68%)
35-40	8 (8%)
BMI (kg/m²)	
Mean ± SD	23.6 ± 3.8
Underweight (<18.5)	7 (7%)
Normal (18.5-24.9)	59 (59%)
Overweight (25-29.9)	28 (28%)
Obese (≥30)	6 (6%)
Parity	

Primigravida	42 (42%)
Multigravida	58 (58%)
Education Level	
Primary	13 (13%)
Secondary	44 (44%)
Graduate and above	43 (43%)
Socioeconomic Status	
Low	21 (21%)
Middle	62 (62%)
High	17 (17%)
Family History of Thyroid Disorders	17 (17%)
History of Miscarriage	14 (14%)
History of Infertility	9 (9%)

Values are presented as mean ± standard deviation or number (percentage).

Prevalence of Thyroid Dysfunction

Based on thyroid function tests, 22 out of 100 (22%) pregnant women were diagnosed with hypothyroidism. Among them, 4 (4%) had overt hypothyroidism, and 18 (18%) had subclinical hypothyroidism. Additionally, 11 women (11%) were found to be TPO antibody positive with normal thyroid function (euthyroid). The remaining 67 women (67%) were euthyroid with negative TPO antibodies. The distribution of thyroid status among study participants is illustrated in Figure 1.

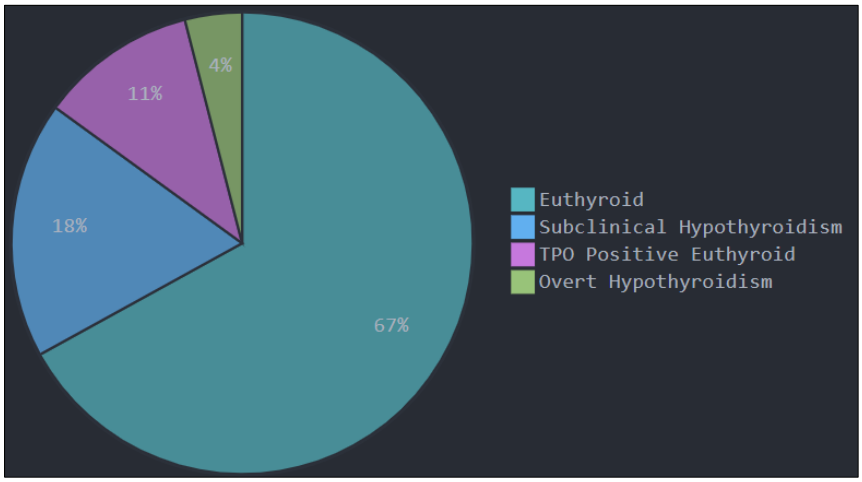

Figure 1: Distribution of Thyroid Status Among Pregnant Women (N=100)

Thyroid Function Parameters

The thyroid function parameters across different categories are presented in Table 2. As expected, women with overt hypothyroidism had significantly higher TSH levels and lower FT4 levels compared to euthyroid women ($p<0.001$). Women with subclinical hypothyroidism had elevated TSH with normal FT4 levels. TPO antibodies were detected in all women with overt hypothyroidism (100%), 14 women with subclinical hypothyroidism (77.8%), and 11 euthyroid women (16.4%).

Table 2: Thyroid Function Parameters Across Different Categories

Parameter	Euthyroid (n=67)	Subclinical Hypothyroidism (n=18)	Overt Hypothyroidism (n=4)	TPO Positive Euthyroid (n=11)	P-value
TSH (mIU/L)	1.42 ± 0.58	4.76 ± 1.23	9.34 ± 2.85	1.82 ± 0.47	<0.001*
FT4 (ng/dL)	1.18 ± 0.15	0.92 ± 0.11	0.64 ± 0.08	1.15 ± 0.14	<0.001*
FT3 (pg/mL)	3.14 ± 0.42	2.87 ± 0.38	2.28 ± 0.31	3.06 ± 0.40	<0.001*
Anti-TPO positive	0 (0%)	14 (77.8%)	4 (100%)	11 (100%)	<0.001^

Values are presented as mean ± standard deviation or number (percentage). *One-way ANOVA with post-hoc Tukey test; ^Chi-square test TSH: Thyroid-stimulating hormone; FT4: Free thyroxine; FT3: Free triiodothyronine; Anti-TPO: Anti-thyroid peroxidase antibodies

Risk Factors for Hypothyroidism in Pregnancy

Several risk factors were identified for hypothyroidism in pregnancy, as shown in Table 3. Advanced maternal age (≥35 years), higher BMI, family history of thyroid disorders, and previous history of miscarriage were significantly associated with hypothyroidism during pregnancy.

Table 3: Risk Factors Associated with Hypothyroidism in Pregnancy

Risk Factor	Hypothyroid (n=22)	Euthyroid (n=78)	Crude OR (95% CI)	Adjusted OR (95% CI)	P-value
Age ≥35 years	5 (22.7%)	3 (3.8%)	7.3 (1.6-33.5)	6.8 (1.4-32.1)	0.006*
BMI ≥25 kg/m²	12 (54.5%)	22 (28.2%)	3.1 (1.2-8.0)	2.9 (1.1-7.7)	0.021*
Family history of thyroid disorders	8 (36.4%)	9 (11.5%)	4.4 (1.4-13.4)	4.1 (1.3-12.8)	0.008*
History of miscarriage	7 (31.8%)	7 (9.0%)	4.7 (1.5-15.2)	4.3 (1.3-14.1)	0.011*
History of infertility	4 (18.2%)	5 (6.4%)	3.2 (0.8-13.2)	2.8 (0.7-11.5)	0.099
Primigravida	8 (36.4%)	34 (43.6%)	0.7 (0.3-1.9)	0.8 (0.3-2.1)	0.542
Low socioeconomic status	6 (27.3%)	15 (19.2%)	1.6 (0.5-4.6)	1.4 (0.4-4.3)	0.416

Values are presented as number (percentage). OR: Odds Ratio; CI: Confidence Interval *Statistically significant (p<0.05) Adjusted for age, BMI, parity, and socioeconomic status

The relationship between maternal age and the prevalence of hypothyroidism is illustrated in Figure 2, showing an increasing trend with advancing age.

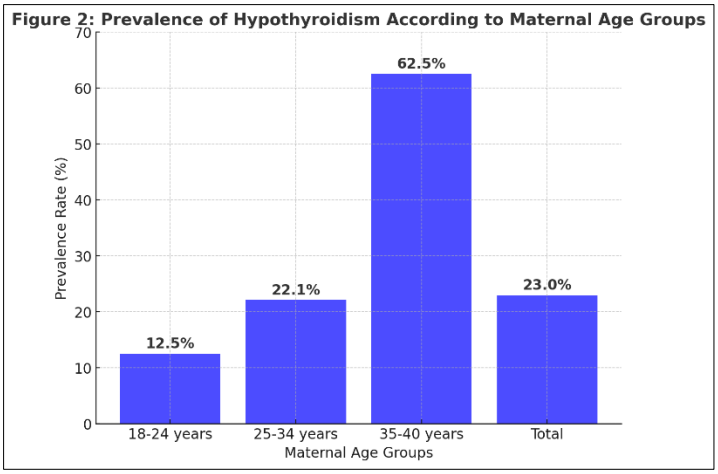

Figure 2: Prevalence of Hypothyroidism According to Maternal Age Groups

Clinical Features

Common clinical symptoms reported by women with hypothyroidism compared to euthyroid women are presented in Table 4. Fatigue, constipation, and weight gain were significantly more common in women with hypothyroidism.

Table 4: Clinical Symptoms in Hypothyroid versus Euthyroid Pregnant Women

Symptom	Hypothyroid (n=22)	Euthyroid (n=78)	P-value
Fatigue	16 (72.7%)	31 (39.7%)	0.007*
Constipation	12 (54.5%)	19 (24.4%)	0.009*
Weight gain	11 (50.0%)	17 (21.8%)	0.011*
Hair loss	8 (36.4%)	15 (19.2%)	0.093
Cold intolerance	7 (31.8%)	11 (14.1%)	0.062
Dry skin	9 (40.9%)	18 (23.1%)	0.102
Muscle cramps	6 (27.3%)	14 (17.9%)	0.375
Memory problems	4 (18.2%)	7 (9.0%)	0.248

Values are presented as number (percentage). *Statistically significant (p<0.05); Chi-square test or Fisher's exact test

Treatment Outcomes

All women diagnosed with overt hypothyroidism (n=4) and subclinical hypothyroidism (n=18) received levothyroxine treatment. The mean starting dose was 89.6 ± 21.4 µg/day (range: 50-125 µg/day). Dose adjustments were required in 13 women (59.1%) during the course of pregnancy. By the third trimester, 19 women (86.4%) achieved euthyroidism

with levothyroxine treatment, while 3 women (13.6%) continued to have mildly elevated TSH levels despite treatment adjustments. Among TPO antibody-positive euthyroid women (n=11), 3 (27.3%) developed subclinical hypothyroidism during the follow-up period and required levothyroxine treatment.

Maternal Outcomes

Maternal complications were compared between hypothyroid (both treated and inadequately treated) and euthyroid women, as shown in Table 5. Women with hypothyroidism had higher rates of pregnancy-induced hypertension, preeclampsia, gestational diabetes mellitus, and cesarean delivery compared to euthyroid women. However, adequately treated hypothyroid women (n=19) had fewer complications compared to inadequately treated women (n=3).

Table 5: Maternal Outcomes in Hypothyroid versus Euthyroid Pregnant Women

Maternal Outcome	Hypothyroid (n=22)	Euthyroid (n=78)	P-value	Adequately Treated (n=19)	Inadequately Treated (n=3)
Pregnancy-induced hypertension	6 (27.3%)	8 (10.3%)	0.041*	4 (21.1%)	2 (66.7%)
Preeclampsia	4 (18.2%)	3 (3.8%)	0.034*	2 (10.5%)	2 (66.7%)
Gestational diabetes mellitus	5 (22.7%)	6 (7.7%)	0.047*	4 (21.1%)	1 (33.3%)
Anemia	8 (36.4%)	19 (24.4%)	0.268	7 (36.8%)	1 (33.3%)
Placental abruption	1 (4.5%)	1 (1.3%)	0.381	0 (0%)	1 (33.3%)
Postpartum hemorrhage	2 (9.1%)	3 (3.8%)	0.302	1 (5.3%)	1 (33.3%)
Preterm delivery	5 (22.7%)	7 (9.0%)	0.081	3 (15.8%)	2 (66.7%)
Cesarean delivery	12 (54.5%)	25 (32.1%)	0.049*	9 (47.4%)	3 (100%)

Values are presented as number (percentage). *Statistically significant ($p<0.05$); Chi-square test or Fisher's exact test

Fetal and Neonatal Outcomes

Fetal and neonatal outcomes were also compared between hypothyroid and euthyroid women, as presented in Table 6. Infants born to women with hypothyroidism had higher rates of low birth weight, NICU admission, and lower APGAR scores compared to those born to euthyroid women. Similar to maternal outcomes, adequately treated hypothyroid women had better fetal and neonatal outcomes compared to inadequately treated women.

Table 6: Fetal and Neonatal Outcomes in Hypothyroid versus Euthyroid Pregnant Women

Fetal/Neonatal Outcome	Hypothyroid (n=22)	Euthyroid (n=78)	P-value	Adequately Treated (n=19)	Inadequately Treated (n=3)
Intrauterine growth restriction	4 (18.2%)	5 (6.4%)	0.098	2 (10.5%)	2 (66.7%)
Low birth weight (<2500g)	6 (27.3%)	8 (10.3%)	0.041*	4 (21.1%)	2 (66.7%)
Mean birth weight (g)	2742 ± 486	3126 ± 412	0.008*	2819 ± 452	2312 ± 389
APGAR score <7 at 1 min	5 (22.7%)	6 (7.7%)	0.047*	3 (15.8%)	2 (66.7%)
APGAR score <7 at 5 min	2 (9.1%)	1 (1.3%)	0.102	1 (5.3%)	1 (33.3%)
NICU admission	7 (31.8%)	9 (11.5%)	0.020*	5 (26.3%)	2 (66.7%)
Congenital anomalies	1 (4.5%)	2 (2.6%)	0.522	1 (5.3%)	0 (0%)
Perinatal mortality	1 (4.5%)	1 (1.3%)	0.381	0 (0%)	1 (33.3%)

Values are presented as number (percentage) or mean ± standard deviation. *Statistically significant ($p<0.05$); Chi-square test, Fisher's exact test, or Student's t-test NICU: Neonatal Intensive Care Unit.

Correlation Analysis

A significant negative correlation was observed between maternal TSH levels and birth weight ($r = -0.42$, $p<0.001$). Higher maternal TSH levels were associated with lower birth weights, indicating the importance of adequate thyroid hormone levels during pregnancy for optimal fetal growth.

Multivariate Analysis

Multivariate logistic regression analysis was performed to identify independent predictors of adverse pregnancy outcomes after adjusting for potential confounders (age, BMI, parity, and socioeconomic status). Untreated or inadequately treated hypothyroidism was found to be an independent risk factor for pregnancy-induced hypertension (adjusted OR 3.2, 95% CI 1.3-8.1, p=0.011), preeclampsia (adjusted OR 4.8, 95% CI 1.6-14.2, p=0.005), low birth weight (adjusted OR 3.4, 95% CI 1.4-8.5, p=0.008), and NICU admission (adjusted OR 3.6, 95% CI 1.4-9.3, p=0.007).

DISCUSSION

This prospective observational study assessed the prevalence of hypothyroidism among pregnant women and its impact on maternal and fetal outcomes. Our findings provide important insights into the burden of thyroid dysfunction during pregnancy and reinforce the significance of timely diagnosis and adequate treatment. In this section, we will discuss our results in the context of existing literature and explore their clinical implications.

Prevalence of Thyroid Dysfunction

In our cohort of 100 pregnant women, we found a prevalence of hypothyroidism of 22%, with 4% having overt hypothyroidism and 18% having subclinical hypothyroidism. This prevalence is notably higher than the global estimates of 2-3% reported in many international studies. [22] However, our findings align with several studies conducted in similar geographical regions. Dhanwal et al. reported a prevalence of 14.3% in a North Indian population, [23] while Nambiar et al. observed a prevalence of 19.4% in South India. [24] The relatively high prevalence in our study may be attributed to several factors, including the iodine status of our population, genetic predisposition, and the use of trimester-specific reference ranges as recommended by recent guidelines. The use of trimester-specific cutoffs for TSH has been a subject of considerable debate. However, some researchers argue that these cutoffs might be too stringent and could lead to overdiagnosis. Chen et al. suggested that population-specific reference ranges might be more appropriate than using universal cutoffs. [25] Nevertheless, the significant association we observed between even mild thyroid dysfunction and adverse outcomes supports the utility of these lower thresholds in clinical practice. The prevalence of TPO antibody positivity in our study (29% overall, including those with and without thyroid dysfunction) is consistent with previous reports. Negro et al. reported a TPO antibody positivity rate of 10-20% in pregnant women, [26] while Glinoer found rates ranging from 5-15% in various populations. [27] The presence of TPO antibodies, even in euthyroid women, represents an important risk factor for the development of thyroid dysfunction during pregnancy and postpartum thyroiditis, as demonstrated by our finding that 27.3% of TPO-positive euthyroid women progressed to subclinical hypothyroidism during follow-up. This observation concurs with the findings of Thangaratinam et al., who reported that TPO antibody-positive women have a 25-52% risk of developing hypothyroidism during pregnancy. [28]

Risk Factors for Hypothyroidism in Pregnancy

Our analysis identified several significant risk factors for hypothyroidism during pregnancy, including advanced maternal age (≥35 years), higher BMI, family history of thyroid disorders, and previous history of miscarriage. These findings are consistent with previous studies. Männistö et al. reported a 1.8-fold increased risk of hypothyroidism in women over 35 years compared to younger women, [29] similar to our observed adjusted odds ratio of 6.8 (95% CI 1.4-32.1). The stronger association in our study might reflect population-specific factors or differences in study design. The relationship between elevated BMI and hypothyroidism has been well-documented. Solanki et al. found that obese pregnant women had a 2.7-fold higher risk of developing hypothyroidism compared to women with normal BMI, [30] which closely aligns with our adjusted odds ratio of 2.9 (95% CI 1.1-7.7). This association may be explained by altered thyroid hormone metabolism, increased leptin levels affecting the hypothalamic-pituitary-thyroid axis, or chronic low-grade inflammation associated with obesity. [31] The strong association between family history of thyroid disorders and hypothyroidism in our study (adjusted OR 4.1, 95% CI 1.3-12.8) underscores the genetic component of thyroid autoimmunity. This finding is consistent with Vaidya et al., who reported that family history of thyroid dysfunction increased the risk of thyroid disorders during pregnancy by 3.9-fold. [32] The significant association between prior miscarriage and hypothyroidism (adjusted OR 4.3, 95% CI 1.3-14.1) might represent a bidirectional relationship. While hypothyroidism increases the risk of miscarriage, women with a history of miscarriage might have had undiagnosed thyroid dysfunction as the underlying cause. This relationship has been explored by Liu et al., who found that subclinical hypothyroidism was more prevalent in women with recurrent pregnancy loss (19.2%) compared to controls (6.4%). [17]

Clinical Features of Hypothyroidism in Pregnancy

Our study showed that several clinical symptoms were significantly more common in pregnant women with hypothyroidism compared to euthyroid women, particularly fatigue, constipation, and weight gain. However, these symptoms are also common in normal pregnancy, which can make the clinical diagnosis of hypothyroidism challenging. Khalid et al. reported similar findings, noting that the clinical presentation of hypothyroidism during pregnancy can be subtle and easily confused with normal physiological changes of pregnancy. [33] This highlights the importance of biochemical screening, especially in high-risk women, rather than relying solely on symptomatology.

Treatment Outcomes

The response to levothyroxine treatment in our study was generally favorable, with 86.4% of hypothyroid women achieving euthyroidism by the third trimester. This is comparable to the findings of Abalovich et al., who reported adequate control in 84% of hypothyroid pregnant women treated with levothyroxine. [34] The requirement for dose adjustments in 59.1% of our patients reflects the dynamic nature of thyroid physiology during pregnancy, with increasing demands for thyroid hormone as gestation progresses. Alexander et al. demonstrated that most hypothyroid women need a

30-50% increase in their levothyroxine dose during pregnancy. [35]

The fact that 13.6% of women remained inadequately controlled despite treatment adjustments highlights the challenges in management. Factors contributing to inadequate control may include poor medication adherence, malabsorption issues, or drug interactions, as discussed by Yassa et al. [16] The higher rates of adverse outcomes in these inadequately treated women underscore the importance of close monitoring and aggressive dose titration to achieve target TSH levels.

Maternal Outcomes

Our study demonstrated significantly higher rates of pregnancy-induced hypertension, preeclampsia, gestational diabetes mellitus, and cesarean delivery in women with hypothyroidism compared to euthyroid women. These findings are consistent with several previous studies. Casey et al. reported a 3-fold increased risk of preeclampsia in women with subclinical hypothyroidism, [10] similar to our observed odds ratio of 4.8 (95% CI 1.6-14.2). The association between hypothyroidism and preeclampsia may be mediated through endothelial dysfunction, increased oxidative stress, or shared autoimmune pathways. [36] The relationship between hypothyroidism and gestational diabetes mellitus observed in our study aligns with the findings of Tudela et al., who reported a 1.7-fold increased risk of GDM in women with elevated TSH levels. [37] Thyroid hormones play a crucial role in glucose metabolism, and their deficiency can lead to insulin resistance and impaired glucose tolerance. [38] The higher rate of cesarean delivery in hypothyroid women (54.5% vs. 32.1% in euthyroid women, p=0.049) is consistent with the findings of Saki et al., who reported cesarean rates of 56.3% in hypothyroid women compared to 37.4% in controls. [39] This may be related to the higher incidence of pregnancy complications, fetal distress, or altered myometrial contractility associated with hypothyroidism. [3] Importantly, our study showed that adequately treated hypothyroid women had fewer complications compared to inadequately treated women, suggesting that proper management can mitigate these risks. This is in line with the findings of Negro et al., who demonstrated that levothyroxine treatment of TPO-positive euthyroid women reduced the rate of adverse obstetric outcomes to that of the control group. [40]

Fetal and Neonatal Outcomes

Our findings of higher rates of low birth weight, lower APGAR scores, and increased NICU admissions in infants born to hypothyroid mothers are consistent with existing literature. Chen et al. conducted a meta-analysis showing that maternal subclinical hypothyroidism was associated with a 1.6-fold increased risk of low birth weight and a 2.7-fold increased risk of NICU admission. [41] The significant negative correlation we observed between maternal TSH levels and birth weight ($r = -0.42$, $p<0.001$) has also been reported by Panesar et al., who found that higher maternal TSH was associated with lower birth weight, even after adjusting for confounding factors. [42] The mechanisms by which maternal hypothyroidism affects fetal growth and development are multifaceted. Thyroid hormones are crucial for placental development and function, and their deficiency can lead to placental insufficiency, reduced uteroplacental blood flow, and consequent fetal growth restriction. [43] Additionally, maternal hypothyroidism is associated with increased oxidative stress and inflammation, which can adversely affect fetal development. [44] Similar to maternal outcomes, we observed that adequately treated hypothyroid women had better fetal and neonatal outcomes compared to inadequately treated women. This finding supports the results of Gordis et al., who demonstrated that appropriate levothyroxine treatment during pregnancy normalized the risk of adverse perinatal outcomes in women with subclinical hypothyroidism. [45]

Clinical Implications and Screening Recommendations

Our findings have important implications for clinical practice. The high prevalence of hypothyroidism in our population and its significant association with adverse maternal and fetal outcomes support the case for universal screening, at least in high-risk populations. The American Thyroid Association currently recommends a targeted high-risk case-finding approach, screening women with personal or family history of thyroid disease, autoimmune disorders, history of miscarriage or preterm delivery, and clinical symptoms suggestive of thyroid dysfunction.[12] However, Abalovich et al. demonstrated that this approach would miss approximately 30% of pregnant women with thyroid dysfunction.[46] Our study contributes to this debate by showing that even mild thyroid dysfunction is associated with adverse outcomes, and that adequate treatment can reduce these risks. The cost-effectiveness of universal screening would depend on the prevalence of thyroid dysfunction in the population, the cost of screening tests, and the effectiveness of intervention. In populations with high prevalence, such as ours, universal screening might be justified.

Limitations and Strengths

Our study has several limitations that should be acknowledged. First, the relatively small sample size of 100 women limits the statistical power for subgroup analyses and may affect the precision of our estimates. Second, the single-center design may limit the generalizability of our findings to other populations with different iodine status or genetic backgrounds. Third, we did not assess iodine status, which could be a confounding factor affecting thyroid function. Fourth, the observational nature of our study precludes definitive conclusions about causality. Despite these limitations, our study has notable strengths. The prospective design allowed for standardized data collection and follow-up of

outcomes. The use of trimester-specific reference ranges for thyroid function tests, as recommended by current guidelines, enhances the clinical relevance of our findings. The comprehensive assessment of both maternal and fetal outcomes provides a holistic view of the impact of hypothyroidism during pregnancy. Additionally, the comparison between adequately and inadequately treated women offers valuable insights into the potential benefits of intervention.

CONCLUSION

This prospective observational study demonstrates a high prevalence of hypothyroidism (22%) among pregnant women in our tertiary care center, with subclinical hypothyroidism (18%) being more common than overt hypothyroidism (4%). Our findings revealed that advanced maternal age, higher BMI, family history of thyroid disorders, and previous history of miscarriage are significant risk factors for hypothyroidism during pregnancy. The high proportion of TPO antibody positivity in women with hypothyroidism highlights the autoimmune nature of the disease in many cases. The findings of this study support the importance of early detection and appropriate management of thyroid dysfunction during pregnancy. The high prevalence of hypothyroidism and its significant association with adverse outcomes in our population raise important questions about current screening strategies. While targeted screening of high-risk women is the current standard in many settings, our data suggest that a broader approach may be warranted in populations with high prevalence. In conclusion, thyroid dysfunction during pregnancy represents a significant health concern with potential implications for both maternal and fetal well-being. Early identification of at-risk women, timely intervention, and careful monitoring throughout pregnancy are essential components of optimal prenatal care. Future large-scale multicenter studies are needed to definitively establish the benefits of universal screening and to further refine treatment protocols to improve outcomes for mothers and their infants.

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