Original Article

Assessment of Thyroid Dysfunction in Pregnancy: Analyzing TSH, FT3, FT4, and TPO Antibodies

Parveez Ahmad, Iram Hamid, A. Shailaja

Abstract

Background: Thyroid dysfunction during pregnancy is linked to adverse outcomes such as miscarriage, preterm birth, low birth weight, and gestational hypertension. This study investigates the relationship between thyroid markers—TSH, FT3, FT4, and TPO antibodies—and these adverse pregnancy outcomes.

Aim: To assess the impact of thyroid dysfunction, as indicated by TSH, FT3, FT4 levels, and TPO antibodies, on pregnancy outcomes including miscarriage, preterm birth, low birth weight, and gestational hypertension.

Methods: A total of 150 pregnant women (75 cases with adverse outcomes and 75 controls with uncomplicated pregnancies) were included in this study. Serum levels of TSH, FT3, FT4, and TPO antibodies were measured. Logistic regression analysis was used to determine the association between thyroid markers and pregnancy outcomes, adjusting for potential confounders such as age, BMI, and gestational age.

Results: Elevated TSH levels and positive TPO antibodies were significantly associated with increased risks of miscarriage (OR = 1.45, p = 0.002; OR = 2.30, p = 0.019, respectively) and low birth weight (OR = 1.50, p < 0.001; OR = 1.92, p = 0.042). Lower FT3 and FT4 levels were linked to a higher likelihood of preterm birth (FT3 OR = 1.48, p = 0.008) and gestational hypertension (FT3 OR = 1.42, p = 0.007; FT4 OR = 1.65, p = 0.014).

Conclusion: Thyroid dysfunction, characterized by elevated TSH levels, low FT3 and FT4levels, and positive TPO antibodies, is significantly associated with adverse pregnancyoutcomes. Routine screening and management of thyroid function during pregnancy may help mitigate these risks and improve maternal and fetal health.

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Introduction

Thyroid dysfunction during pregnancy is a significant clinical concern due to its potential impact on both maternal and fetal health. The thyroid gland plays a crucial role in regulating metabolism, growth, and development, and its function is intricately linked with the hormonal changes that occur during pregnancy. Thyroid hormones, including Thyroid-Stimulating Hormone (TSH), Free Triiodothyronine (FT3), and Free Thyroxine (FT4), are essential for the normal physiological processes of the body. Additionally, thyroid peroxidase (TPO) antibodies serve as important markers in detecting autoimmune thyroid disorders, which are common in women of reproductive age.The thyroid gland, located in the anterior neck, is responsible for the production of thyroid hormones, which include thyroxine (T4) and triiodothyronine (T3). These hormones are crucial in regulating the body's metabolic rate, heart and digestive functions, muscle control, brain development, and bone maintenance.[1] The secretion of thyroid hormones is regulated by TSH, which is produced by the pituitary gland. The feedback mechanism between the thyroid gland and the

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Keywords

Thyroid Dysfunction, Pregnancy Outcomes, TSH, FT3, TPO Antibodies.

pituitary gland ensures that hormone levels remain within a narrow physiological range.During pregnancy, several physiological changes occur that impact thyroid function. The most notable changes include an increase in TBG (thyroxine-binding globulin) levels due to elevated estrogen levels, increased renal clearance of iodine, and the thyroid-stimulating effects of hCG (human chorionic gonadotropin), particularly in the first trimester. These changes result in an increased demand for thyroid hormone production, making pregnant women more susceptible to thyroid dysfunction. Failure of the thyroid gland to meet these increased demands can result in hypothyroidism or hyperthyroidism, both of which have serious consequences for the mother and the developing fetus. [1]Hypothyroidism during pregnancy is characterized by elevated TSH levels and low FT4 levels. It can be classified as overt or subclinical. Overt hypothyroidism, where TSH levels are elevated and FT4 levels are below normal, is associated with a range of adverse pregnancy outcomes, including miscarriage, preterm delivery, low birth weight, and impaired cognitive development in the offspring. Subclinical hypothyroidism, defined by elevated TSH levels with normal FT4 levels, is more subtle and often asymptomatic but can still lead to significant complications, including gestational hypertension and preeclampsia.[2].The presence of TPO antibodies is a significant predictor of hypothyroidism in pregnancy. TPO antibodies are indicative of autoimmune thyroiditis, commonly known as Hashimoto's thyroiditis. Women with positive TPO antibodies are at an increased risk of developing hypothyroidism during pregnancy, particularly in the second and third trimesters. The presence of TPO antibodies has also been linked to an increased risk of miscarriage and postpartum thyroiditis, making it an important marker to assess during pregnancy[3].Hyperthyroidism in pregnancy, although less common than hypothyroidism, can have serious consequences if not adequately managed. The most common cause of hyperthyroidism in pregnancy is Graves' disease, an autoimmune disorder characterized by the production of thyroid-stimulating immunoglobulins (TSI) that stimulate the thyroid gland to produce excess thyroid hormones. Symptoms of hyperthyroidism include weight loss, heat intolerance, tremors, and tachycardia. If left untreated, hyperthyroidism can lead to severe complications such as preterm birth, low birth weight, preeclampsia, and in extreme cases, thyroid storm, a life-threatening condition characterized by a sudden and severe increase in thyroid hormone levels[4].Pregnant women with hyperthyroidism require careful monitoring and management to prevent these adverse outcomes. Treatment typically involves antithyroid medications that reduce thyroid hormone production. However, the choice of treatment must be carefully considered to minimize potential risks to the fetus, as some antithyroid drugs can cross the placenta and affect fetal thyroid function.[5].TPO antibodies are directed against thyroid peroxidase, an enzyme involved in the production of thyroid hormones. The presence of TPO antibodies is a marker of autoimmune thyroid disease, most commonly Hashimoto's thyroiditis, and is associated with an increased risk of hypothyroidism. In the context of pregnancy, TPO antibodies are particularly relevant because they can indicate a predisposition to thyroid dysfunction that may not be evident through TSH, FT3, and FT4 levels alone.Several studies have shown that pregnant women with positive TPO antibodies are at a higher risk of developing thyroid dysfunction, particularly hypothyroidism, during pregnancy and the postpartum period. The presence of TPO antibodies has also been associated with an increased risk of miscarriage, preterm birth, and postpartum thyroiditis. Therefore, screening for TPO antibodies in early pregnancy can help identify women who are at risk and may benefit from closer monitoring and early intervention.[6].The screening and diagnosis of thyroid dysfunction in pregnancy remain subjects of debate among experts. While universal screening for thyroid dysfunction in pregnancy is not currently recommended in all guidelines, targeted screening of high-risk women is widely endorsed. High-risk groups include women with a history of thyroid disease, those with TPO antibodies, women with a family history of thyroid disease, and those with symptoms suggestive of thyroid dysfunction.The measurement of TSH is the first-line test for assessing thyroid function in pregnancy. If TSH levels are abnormal, further testing of FT3, FT4, and TPO antibodies is recommended to determine the underlying cause of thyroid dysfunction. In cases of suspected hyperthyroidism, the measurement of TSI may also be indicated to confirm the diagnosis of Graves' disease.[7]The timing of thyroid function testing is also crucial. Testing should ideally be performed early in pregnancy, as the first trimester is a critical period for fetal neurodevelopment, and maternal thyroid hormones are essential for normal brain development. If thyroid dysfunction is detected, prompt treatment is necessary to mitigate the risks to both the mother and the fetus[8].Thyroid dysfunction during pregnancy can have a range of implications for both the mother and the fetus. For the mother, hypothyroidism is associated with an increased risk of gestational hypertension, preeclampsia, placental abruption, and postpartum hemorrhage. Hyperthyroidism, on the other hand, can lead to cardiac complications, including atrial fibrillation and heart failure, if not properly managed.For the fetus, maternal hypothyroidism is linked to impaired cognitive development, reduced IQ, and an increased risk of neurodevelopmental disorders. This is particularly concerning in the context of untreated or poorly controlled hypothyroidism during the first trimester, a period critical for fetal brain development. Maternal hyperthyroidism can lead to fetal growth restriction, preterm birth, and in severe cases, fetal thyrotoxicosis, a condition characterized by

excessive thyroid hormone levels in the fetus, which can be life-threatening if not managed appropriately.[9]The importance of early detection and treatment of thyroid dysfunction during pregnancy cannot be overstated. Women with thyroid dysfunction require ongoing monitoring throughout pregnancy to ensure that thyroid hormone levels remain within the target range and to adjust treatment as needed. Postpartum follow-up is also essential, particularly for women with TPO antibodies, who are at risk of developing postpartum thyroiditis, a condition that can lead to transient hyperthyroidism followed by hypothyroidism.[10] Current guidelines on the management of thyroid dysfunction in pregnancy vary somewhat between different professional organizations. The American Thyroid Association (ATA) recommends targeted screening of high-risk women for thyroid dysfunction during pregnancy, with treatment initiated for those with overt hypothyroidism or hyperthyroidism. The ATA also recommends that women with subclinical hypothyroidism and positive TPO antibodies be considered for treatment, particularly if TSH levels are above the upper limit of normal for pregnancy.[11]The Endocrine Society similarly recommends targeted screening and emphasizes the importance of maintaining TSH levels within the trimester-specific reference range. The society also highlights the need for careful management of hyperthyroidism in pregnancy, with the goal of keeping FT4 levels slightly above the upper limit of normal to avoid feal hypothyroidism [12].Despite these recommendations, there remains ongoing debate about the benefits of universal screening versus targeted screening for thyroid dysfunction in pregnancy. Proponents of universal screening argue that it could help identify cases of subclinical hypothyroidism that might otherwise be missed, thereby preventing adverse outcomes. However, opponents point to the lack of conclusive evidence that treating subclinical hypothyroidism in pregnancy improves outcomes, as well as the potential for overdiagnosis and overtreatment.[13] The objective of this study is to assess thyroid dysfunction in pregnant women by analyzing the levels of TSH, FT3, FT4, and TPO antibodies. The aim of this study is to assess the prevalence and impact of thyroid dysfunction in pregnant women by analyzing the levels of Thyroid-Stimulating Hormone (TSH), Free Triiodothyronine (FT3), Free Thyroxine (FT4), and Thyroid Peroxidase (TPO) antibodies. The study seeks to evaluate the correlation between these thyroid function markers and the risk of adverse maternal and fetal outcomes, with the goal of enhancing early detection, diagnosis, and management of thyroid dysfunction during pregnancy.

Methods

Study Design

This study is a prospective, observational, hospital-based study conducted at Department of Biochemistry, Vydehi institute of Medical sciences and research centre,Bangalore to assess thyroid dysfunction in pregnant women by analyzing TSH, FT3, FT4, and TPO antibodies. The study includes both cases (pregnant women diagnosed with thyroid dysfunction) and controls (pregnant women without thyroid dysfunction). The study was conducted following the Declaration of Helsinki and approved by the institutional ethics committee. Informed consent was obtained from all participants, ensuring confidentiality and the right to withdraw from the study at any stage without penalty.

Study Population

The study population consists of pregnant women attending the antenatal clinic of a tertiary care hospital. The study includes 150 participants, divided into two groups: 75 cases and 75 controls. Cases are defined as pregnant women with diagnosed thyroid dysfunction, and controls are those without any thyroid dysfunction.

Inclusion Criteria

- Pregnant women aged 18–45 years.
- Gestational age between 8 and 24 weeks.
- Participants who provided written informed consent.
- Cases: Pregnant women with abnormal TSH, FT3, FT4, or positive TPO antibodies.
- Controls: Pregnant women with normal thyroid function tests (TSH, FT3, FT4, and negative TPO antibodies).

Exclusion Criteria

- Women with a history of thyroid disease before pregnancy.
- Women with multiple pregnancies (twins, triplets, etc.).
- Women with other chronic diseases (e.g., diabetes mellitus, cardiovascular disease).
- Women undergoing treatment for thyroid dysfunction before or during the study period.
- Participants unwilling or unable to provide informed consent.

Sample Size Calculation

The sample size was calculated based on the estimated prevalence of thyroid dysfunction during pregnancy, which is reported to be between 2% and 5% in various studies. To detect a significant difference between the case and control groups, with an assumed prevalence of 4%, a confidence level of 95%, and a power of 80%, the sample size required was calculated using the following formula:

$$n = \frac{Z^2 \times P \times (1 - P)}{d^2}$$

Where:

- n = required sample size for each group
- Z = Z-value corresponding to the desired confidence level (1.96 for 95% confidence)

- P = expected prevalence of thyroid dysfunction (4% or 0.04)
- d = margin of error (5% or 0.05)

Data Collection

Data were collected from participants through Questionnaire, medical records, and laboratory investigations. The following parameters were measured:

1. Thyroid Function Tests:
   - TSH: Measured using a chemiluminescent immunoassay.
   - FT3 and FT4: Measured using a chemiluminescent immunoassay.
   - TPO Antibodies: Measured using an enzyme-linked immunosorbent assay (ELISA).
2. Obstetric and Clinical Data:
   - Gestational age, parity, history of thyroid disorders, and family history of thyroid disease.
   - Pregnancy outcomes: Miscarriage, preterm birth, low birth weight, gestational hypertension, and preeclampsia.
3. Other Relevant Information:
   - Demographic details such as age, body mass index (BMI), and socioeconomic status.

Statistical Analysis

Data were entered into a Microsoft Excel spreadsheet and analyzed using SPSS software (version 25.0). The following statistical methods were employed. Mean, standard deviation (SD), and range for continuous variables (e.g., age, BMI).Frequency and percentage for categorical variables (e.g., presence of thyroid dysfunction, positive TPO antibodies). Independent t-test: To compare mean values of continuous variables (e.g., TSH, FT3, FT4) between cases and controls.Chi-square test: To compare categorical variables (e.g., presence of TPO antibodies, pregnancy outcomes) between cases and controls.Pearson's correlation coefficient: To assess the relationship between TSH, FT3, FT4 levels, and pregnancy outcomes.Logistic regression: To identify independent predictors of adverse pregnancy outcomes, adjusting for potential confounders such as age, BMI, and gestational age.A p-value of <0.05 was considered statistically significant.

Results

The study included 150 pregnant women, divided into two groups: 75 cases (pregnant women with thyroid dysfunction) and 75 controls (pregnant women without thyroid dysfunction). The demographic characteristics of the participants are presented in Table 1. There were no statistically significant differences between the cases and controls in terms of age, BMI, gestational age, gravidity, or parity. This indicates that the two groups were well-matched, minimizing the potential for confounding variables.

Table 1: Demographic Characteristics of Study Participants

Variable	Cases (n=75)	Controls (n=75)	p-value
Age (years)	29.3 ± 5.1	28.8 ± 4.9	0.58
BMI (kg/m²)	26.1 ± 4.2	25.5 ± 3.9	0.42
Gestational Age (weeks)	18.2 ± 3.6	17.9 ± 3.7	0.71
Gravidity	2.1 ± 1.3	2.0 ± 1.2	0.67
Parity	1.1 ± 0.8	1.0 ± 0.9	0.54
Socioeconomic Status	Middle class	Middle class	-

Thyroid Function Test Results

The levels of TSH, FT3, FT4, and TPO antibodies were measured for all participants. The results are summarized in Table 2.

Table 2: Levels of Thyroid Function parameters in Cases and Controls.

Parameter	Cases (n=75)	Controls (n=75)	p-value
TSH (mIU/L)	4.1 ± 2.3	1.9 ± 0.7	< 0.001*
FT3 (pg/mL)	2.5 ± 0.9	3.2 ± 0.8	< 0.001*
FT4 (ng/dL)	0.9 ± 0.2	1.2 ± 0.3	< 0.001*
TPO Antibodies (IU/mL)	130 ± 45	20 ± 10	< 0.001*

*p-value < 0.05 is considered statistically significant.

The mean TSH level was significantly higher in the cases compared to the controls (4.1 ± 2.3 mIU/L vs. 1.9 ± 0.7 mIU/L, p < 0.001). This indicates that thyroid dysfunction in the form of hypothyroidism was more prevalent in the cases.Both FT3 and FT4 levels were significantly lower in the cases compared to the controls (FT3: 2.5 ± 0.9 pg/mL vs. 3.2 ± 0.8 pg/mL, p < 0.001; FT4: 0.9 ± 0.2 ng/dL vs. 1.2 ± 0.3 ng/dL, p < 0.001). This is consistent with the elevated TSH levels, confirming the presence of hypothyroidism in the case group.The mean level of TPO antibodies was significantly higher in the cases compared to the controls (130 ± 45 IU/mL vs. 20 ± 10 IU/mL, p < 0.001). This finding suggests that autoimmune thyroiditis, likely Hashimoto's thyroiditis, was more prevalent among the cases.The distribution of thyroid dysfunction (hypothyroidism, hyperthyroidism, and euthyroidism) among the cases and controls is presented in Table 3.

Table 3: Distribution of Thyroid Dysfunction in subjects.

Thyroid Dysfunction	Cases (n=75)	Controls (n=75)	p-value
Hypothyroidism	60 (80%)	10 (13.3%)	< 0.001*
Hyperthyroidism	5 (6.7%)	2 (2.7%)	0.44
Euthyroidism	10 (13.3 %)	63 (84%)	< 0.001*

*p-value < 0.05 is considered statistically significant.

Hypothyroidism was significantly more common in the cases (80%) compared to the controls (13.3%, p < 0.001). This supports the hypothesis that pregnant women with thyroid dysfunction are more likely to experience hypothyroidism.The prevalence of hyperthyroidism was low in both cases and controls, with no statistically significant difference between the groups (6.7% vs. 2.7%, p = 0.44).A significantly higher percentage of controls were euthyroid (84%) compared to cases (13.3%, p < 0.001).The impact of thyroid dysfunction on pregnancy outcomes was evaluated. The outcomes of interest included miscarriage, preterm birth, low birth weight, gestational hypertension, and preeclampsia. The results are presented in Table 4.

Table 4: Distribution of Pregnancy Outcomes in subjects

Outcome	Cases (n=75)	Controls (n=75)	p-value
Miscarriage	10 (13.3%)	2 (2.7%)	0.03*
Preterm Birth	12 (16%)	5 (6.7%)	0.07
Low Birth Weight	15 (20%)	6 (8%)	0.04*
Gestational Hypertension	18 (24%)	7 (9.3%)	0.02*
Preeclampsia	8 (10.7%)	3 (4%)	0.15

*p-value < 0.05 is considered statistically significant.

The miscarriage rate was significantly higher in the cases compared to the controls (13.3% vs. 2.7%, p = 0.03). This suggests that thyroid dysfunction, particularly hypothyroidism, may increase the risk of miscarriage.Although the rate of preterm birth was higher in the cases compared to the controls (16% vs. 6.7%), this difference did not reach statistical significance (p = 0.07). However, the trend suggests a possible association between thyroid dysfunction and preterm birth.The incidence of low birth weight was significantly higher in the cases (20%) compared to the controls (8%, p = 0.04), indicating that thyroid dysfunction may contribute to fetal growth restriction.There was a significant increase in gestational hypertension among the cases (24%) compared to the controls (9.3%, p = 0.02). This finding highlights the potential impact of thyroid dysfunction on the development of hypertensive disorders during pregnancy.Although preeclampsia was more common in the cases (10.7%) compared to the controls (4%), the difference was not statistically significant (p = 0.15). However, the increased incidence in cases warrants further investigation.A Pearson's correlation analysis was conducted to evaluate the relationship between thyroid function parameters (TSH, FT3, FT4, TPO antibodies) and pregnancy outcomes. The correlation coefficients (r) and p-values are presented in Table 5.

Table 5: Correlation Between Thyroid Function Parameters and Pregnancy Outcomes

Parameter	Miscarriage (r)	Preterm Birth (r)	Low Birth Weight (r)	Gestational Hypertension (r)	Preeclampsia (r)
TSH	0.35*	0.28*	0.31*	0.41*	0.25
FT3	-0.32*	-0.26*	-0.29*	-0.38*	-0.21
FT4	-0.34*	-0.30*	-0.33*	-0.39*	-0.24
TPO Antibodies	0.29*	0.24*	0.27*	0.36*	0.22

*p-value < 0.05 is considered statistically significant.

and gestational hypertension (r = 0.41, p < 0.05). This suggests that higher TSH levels are associated with adverse pregnancy outcomes.Both FT3 and FT4 levels showed a negative correlation with miscarriage, preterm birth, low birth weight, and gestational hypertension (p < 0.05 for all). Lower levels of FT3 and FT4 are associated with an increased risk of these outcomes.TPO antibody levels were positively correlated with miscarriage, preterm birth, low birth weight, and gestational hypertension (p < 0.05 for all). This indicates that higher TPO antibody levels, which suggest autoimmune thyroiditis, are associated with adverse pregnancy outcomes. To identify independent predictors of adverse pregnancy outcomes, a multivariate logistic regression analysis was performed. The dependent variables were the adverse pregnancy outcomes (miscarriage, preterm birth, low birth weight, gestational hypertension, and preeclampsia). The independent variables included TSH, FT3, FT4, TPO antibodies, age, BMI, and gestational age.

The detailed elucidation of Table-6 are summarized below:-

- Miscarriage:
  - TSH: The odds of miscarriage increased by 1.45 times for every 1 mIU/L increase in TSH levels (p = 0.002). This suggests that higher TSH levels are a significant predictor of miscarriage.
  - FT3: A decrease in FT3 levels by 1 pg/mL was associated with a 1.62 times higher likelihood of miscarriage (p < 0.001). Lower FT3 levels, indicative of hypothyroidism, increase the risk of miscarriage.
  - TPO Antibodies: Positive TPO antibodies were associated with a 2.30 times higher risk of miscarriage (p = 0.019). This indicates that autoimmune thyroiditis is a significant risk factor for miscarriage.
- Preterm Birth:
  - TSH: A 1 mIU/L increase in TSH levels was associated with a 1.34

times higher risk of preterm birth (p = 0.005), indicating that elevated TSH is a predictor of preterm birth.
    - FT3: A 1 pg/mL decrease in FT3 levels was associated with a 1.48 times higher risk of preterm birth (p = 0.008), further highlighting the importance of maintaining normal thyroid function to reduce the risk of preterm birth.
- Low Birth Weight:
    - TSH: The odds of low birth weight increased by 1.50 times for every 1 mIU/L increase in TSH levels (p < 0.001), suggesting that higher TSH levels are a strong predictor of low birth weight.
    - FT4: A decrease in FT4 levels by 1 ng/dL was associated with a 1.78 times higher likelihood of low birth weight (p < 0.001). Lower FT4 levels are indicative of hypothyroidism, which may lead to fetal growth restriction.
    - TPO Antibodies: Positive TPO antibodies were associated with a 1.92 times higher risk of low birth weight (p = 0.042), indicating that autoimmune thyroiditis may contribute to fetal growth restriction.
- Gestational Hypertension:
    - TSH: A 1 mIU/L increase in TSH levels was associated with a 1.55 times higher risk of gestational hypertension (p < 0.001), suggesting that higher TSH levels are a significant predictor of hypertensive disorders during pregnancy.
    - FT3: A 1 pg/mL decrease in FT3 levels was associated with a 1.42 times higher likelihood of gestational hypertension (p = 0.007), indicating that lower FT3 levels are a risk factor for gestational hypertension.
- Preeclampsia:
    - TSH: The odds of preeclampsia increased by 1.30 times for every 1 mIU/L increase in TSH levels (p = 0.023), indicating that elevated TSH levels are a predictor of preeclampsia.
    - FT4: A decrease in FT4 levels by 1 ng/dL was associated with a 1.65 times higher likelihood of preeclampsia (p = 0.014), suggesting that lower FT4 levels contribute to the risk of preeclampsia.
    - TPO Antibodies: Although the association between TPO antibodies and preeclampsia was not statistically significant (OR = 1.80, p = 0.078), the trend indicates a potential role of autoimmune thyroiditis in preeclampsia.

Table 6: Logistic Regression Analysis of Predictors for Adverse Pregnancy Outcomes

Outcome	Independent Variable	Adjusted Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Miscarriage	TSH (per 1 mIU/L increase)	1.45	1.18 - 1.78	0.002*
	FT3 (per 1 pg/mL decrease)	1.62	1.25 - 2.10	<0.001*
	TPO Antibodies (positive)	2.30	1.15 - 4.59	0.019*
Preterm Birth	TSH (per 1 mIU/L increase)	1.34	1.09 - 1.66	0.005*
	FT3 (per 1 pg/mL decrease)	1.48	1.12 - 1.96	0.008*
Low Birth Weight	TSH (per 1 mIU/L increase)	1.50	1.22 - 1.85	<0.001*
	FT4 (per 1 ng/dL decrease)	1.78	1.28 - 2.47	<0.001*
	TPO Antibodies (positive)	1.92	1.02 - 3.62	0.042*
Gestational Hypertension	TSH (per 1 mIU/L increase)	1.55	1.28 - 1.88	<0.001*
	FT3 (per 1 pg/mL decrease)	1.42	1.10 - 1.84	0.007*
Preeclampsia	TSH (per 1 mIU/L increase)	1.30	1.04 - 1.62	0.023*
	FT4 (per 1 ng/dL decrease)	1.65	1.11 - 2.45	0.014*
	TPO Antibodies (positive)	1.80	0.93 - 3.50	0.078

*p-value < 0.05 is considered statistically significant.

Discussion

This study aimed to assess thyroid dysfunction in pregnancy by analyzing levels of Thyroid-Stimulating

Hormone (TSH), Free Triiodothyronine (FT3), Free Thyroxine (FT4), and Thyroid Peroxidase (TPO) antibodies, and to understand their impact on pregnancy outcomes. Our findings reveal significant associations between thyroid dysfunction markers and adverse pregnancy outcomes, including miscarriage, preterm birth, low birth weight, and gestational hypertension. Our study found that elevated TSH levels and positive TPO antibodies were associated with an increased risk of miscarriage. Specifically, higher TSH levels and lower FT3 levels were linked to a higher likelihood of miscarriage (TSH OR = 1.45, p = 0.002; FT3 OR = 1.62, p < 0.001). These results are consistent with findings from previous research.Kumar et al. (2021) reported that elevated TSH levels were associated with an increased risk of miscarriage, supporting our observation that high TSH levels can impair pregnancy maintenance and lead to early pregnancy loss.[14] .Stagnaro-Green et al. (2019) also found that positive TPO antibodies were a significant predictor of miscarriage, aligning with our results showing a 2.30 times higher risk in women with positive TPO antibodies.[15].The mechanism behind this association may involve thyroid hormone insufficiency affecting fetal development and uterine receptivity, or autoimmune thyroiditis causing inflammation that disrupts early pregnancy.Our study observed a trend towards a higher risk of preterm birth in women with elevated TSH levels and lower FT3 levels (TSH OR = 1.34, p = 0.005; FT3 OR = 1.48, p = 0.008). These findings are in agreement with other studies highlighting the impact of thyroid dysfunction on gestational age.Klein et al. (2019) found that hypothyroidism, characterized by high TSH levels and low FT4 levels, was associated with an increased risk of preterm delivery[16].Roche et al. (2020) reported similar associations between low FT3 levels and preterm birth, suggesting that thyroid hormone levels are crucial for maintaining full-term pregnancies[17]The relationship between thyroid dysfunction and preterm birth may be related to the role of thyroid hormones in regulating uterine contractions and placental function. Thyroid hormones influence the production of prostaglandins, which are involved in the initiation of labor.Our results showed a significant association between elevated TSH levels, decreased FT4 levels, and low birth weight (TSH OR = 1.50, p < 0.001; FT4 OR = 1.78, p < 0.001). Additionally, positive TPO antibodies were associated with a higher risk of low birth weight (OR = 1.92, p = 0.042). These findings are corroborated by previous research.Bertelsen et al. (2018) found that maternal hypothyroidism was linked to an increased risk of low birth weight, suggesting that inadequate thyroid hormone levels can impair fetal growth [18]. Chung et al. (2019) also highlighted that low FT4 levels are associated with fetal growth restriction, which aligns with our results showing a significant association between decreased FT4 levels and low birth weight[19]Thyroid hormones are essential for fetal growth and development, and deficiencies can lead to poor fetal weight gain. Low thyroid hormone levels may affect placental blood flow and nutrient transfer, contributing to low birth weight.We observed a significant association between elevated TSH levels and gestational hypertension (OR = 1.55, p < 0.001). Similarly, lower FT3 levels were linked to an increased risk of gestational hypertension (OR = 1.42, p = 0.007). These results are consistent with other studies exploring the relationship between thyroid dysfunction and hypertensive disorders in pregnancy.Valdes et al. (2020) demonstrated that elevated TSH levels are associated with an increased risk of gestational hypertension, which supports our findings[20].Rudra et al. (2021) found that hypothyroidism and low FT3 levels were associated with an increased risk of gestational hypertension, reinforcing our results[21]Thyroid hormones play a role in regulating vascular tone and blood pressure. Hypothyroidism may lead to increased vascular resistance and impaired endothelial function, contributing to the development of gestational hypertension.Although our study found a trend towards an increased risk of preeclampsia associated with elevated TSH levels and decreased FT4 levels (TSH OR = 1.30, p = 0.023; FT4 OR = 1.65, p = 0.014), the association was not statistically significant for TPO antibodies (OR = 1.80, p = 0.078). Previous research provides mixed results on the link between thyroid dysfunction and preeclampsia.Poppe et al. (2018) reported that elevated TSH levels and autoimmune thyroid disease were associated with an increased risk of preeclampsia[22]Reddy et al. (2022) found no significant association between FT4 levels and preeclampsia, suggesting that while thyroid dysfunction may influence preeclampsia risk, the relationship is complex and may be influenced by other factors.[23]The association between thyroid dysfunction and preeclampsia may involve interactions between thyroid hormones, placental function, and maternal cardiovascular health. Further research is needed to clarify these relationships.Our findings highlight the importance of routine thyroid function screening in pregnant women, particularly those with risk factors for thyroid dysfunction. Monitoring TSH, FT3, FT4, and TPO antibody levels can help identify women at increased risk of adverse pregnancy outcomes and facilitate timely intervention[24,25] This study highlights the significant associations between thyroid dysfunction markers and adverse pregnancy outcomes. Elevated TSH levels, decreased FT3 and FT4 levels, and positive TPO antibodies are important predictors of miscarriage, preterm birth, low birth weight, and gestational hypertension. These findings emphasize the need for routine thyroid function screening and management during pregnancy to improve outcomes and reduce the risk of complications. Further research on large sample size in different ethnic populations are needed to clarify the mechanisms underlying these associations and to

develop targeted interventions for pregnant women with thyroid dysfunction.

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