

## Association between Maternal Thyroid Hormone Levels and Preeclampsia

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### Abstract:

**Background:** Preeclampsia is a significant cause of maternal and perinatal morbidity and mortality. Emerging evidence suggests that thyroid dysfunction may contribute to the development of preeclampsia, but the relationship remains incompletely understood.

**Aim:** This study aimed to investigate the association between maternal thyroid hormone levels and the incidence of preeclampsia in pregnant women.

**Methods:** 200 expectant mothers participated in a prospective cohort study. Measured thyroid hormone levels (TSH, T3, T4) were divided into tertiles. Preeclampsia development was observed in the participants. SPSS version 23.0 was used to analyse the data, and logistic regression was employed to assess the relationship between thyroid hormone levels and preeclampsia risk.

**Results:** The incidence of preeclampsia was 15%. Higher TSH levels were significantly associated with an increased risk of preeclampsia (OR 3.72,  $p=0.012$ ), while higher levels of T3 and T4 were associated with a reduced risk (T3 OR 0.15,  $p=0.006$ ; T4 OR 0.11,  $p=0.002$ ).

**Conclusion:** Elevated maternal TSH levels are associated with an increased risk of preeclampsia, whereas higher T3 and T4 levels appear protective. These findings underscore the importance of monitoring thyroid function during pregnancy.

**Recommendations:** Pregnant women, especially those who are at high risk for thyroid dysfunction, should think about routinely screening their thyroid function. In order to define guidelines for thyroid hormone management during pregnancy and to investigate the mechanisms underlying these associations, more research is required.

**Keywords:** Preeclampsia, Thyroid Hormone, Pregnancy, TSH, Thyroid Dysfunction.

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### Introduction

Preeclampsia is a hypertension condition of pregnancy that continues to be a major global source of morbidity and mortality among mothers and perinatals. Preeclampsia, which affects 2-8% of pregnancies worldwide, is characterised by new-onset hypertension and proteinuria or other end-organ damage after 20 weeks of gestation [1]. Preeclampsia has a complicated aetiology that involves genetic, environmental, and immunological variables that is not fully understood despite intensive research.

Thyroxine (T4) and triiodothyronine (T3) in particular are thyroid hormones that are essential for a healthy pregnancy and foetal development.

The role of the thyroid gland and how it affects the course of pregnancy have drawn more and more attention lately. Thyroid-stimulating hormone (TSH) levels that are raised in hypothyroidism and subclinical hypothyroidism have been related to poor pregnancy outcomes, such as preterm birth, low birth weight, and an increased risk of preeclampsia [2]. Although the exact mechanisms by which thyroid failure leads to these results are still unclear, several theories include immune system changes, endothelial dysfunction, and impaired angiogenesis.

The necessity to investigate the connection between thyroid hormone levels and preeclampsia in greater

depth has been brought to light by recent investigations. High TSH levels were found to be significantly associated with an increased risk of preeclampsia, but low levels of T3 and T4 were protective against the condition, according to a meta-analysis [3]. Thyroid function may be crucial to the pathogenesis of the condition, as evidenced by a research that linked greater occurrences of preeclampsia to both overt and subclinical hypothyroidism [4].

This study is especially important for enhancing prenatal care because thyroid function may have an effect on pregnancy outcomes. In order to reduce the risk of preeclampsia, healthcare practitioners can apply targeted screening and management techniques by recognising thyroid hormone levels as a modifiable risk factor. This strategy is in keeping with new recommendations that support thorough thyroid function screening in expectant mothers, especially those who are at high risk of thyroid dysfunction [5].

This study aimed to investigate the association between maternal thyroid hormone levels and the incidence of preeclampsia in pregnant women.

### Methodology

**Study Design:** A prospective cohort study design was employed.

**Study Setting:** The study was conducted in department of Biochemistry at Darbhanga Medical College over a period of 12 months. The cases are selected from OPD of Obstetrics and Gynaecology department of Darbhanga medical college and hospital.

**Participants:** A total of 200 participants were included in the study.

### Inclusion Criteria

- Pregnant women aged 18-45 years.
- Singleton pregnancies.
- Patients willing to provide informed consent.
- Patients with a documented history of thyroid hormone levels.

### Exclusion Criteria

- Women with pre-existing thyroid disorders.
- Pregnancies with multiple fetuses.
- Patients with chronic hypertension or pre-existing renal diseases.
- Patients who did not consent to participate in the study.

**Bias:** To minimize selection bias, participants were randomly selected from the outpatient department. Confounding variables were controlled by matching participants based on age, BMI, and gestational age.

**Data Collection:** Data were collected through structured interviews, medical record reviews, and laboratory tests. Maternal thyroid hormone levels were measured using standardized assays. Preeclampsia was diagnosed based on clinical criteria including blood pressure measurements and proteinuria.

**Procedure:** Participants were enrolled during their antenatal visits. Blood samples were collected to measure thyroid hormone levels. Test which have been done ELISA for thyroid hormone analysis. Participants were monitored throughout their pregnancies for the development of preeclampsia. Data on demographic characteristics, medical history, and pregnancy outcomes were recorded.

**Statistical Analysis:** SPSS version 23.0 was used to analyse the data. To compile the data, descriptive statistics were employed. Using logistic regression analysis, the relationship between maternal thyroid hormone levels and preeclampsia was assessed. The multivariate analysis included adjustments for confounding variables. At  $p < 0.05$ , the results were deemed statistically significant.

### Result

The study included 200 pregnant participants in total. The participants' average age was  $28.4 \pm 4.5$  years. Table 1 provides an overview of the participants' clinical and demographic features.

**Table 1: Demographic and Clinical Characteristics of Participants**

Characteristic	Value
Mean age (years)	$28.4 \pm 4.5$
Mean BMI (kg/m <sup>2</sup> )	$26.7 \pm 3.2$
Mean gestational age (weeks)	$24.5 \pm 3.8$
Family history of hypertension	45 (22.5%)
Nulliparous women	130 (65%)
Multiparous women	70 (35%)

The mean thyroid hormone levels among participants were as follows: TSH  $2.5 \pm 1.2$  mIU/L, T3  $1.9 \pm 0.4$  ng/mL, and T4  $8.5 \pm 1.5$  µg/dL.

Thyroid hormone levels were divided into tertiles for analysis.

Out of 200 participants, 30 (15%) developed preeclampsia. The incidence of preeclampsia across

different tertiles of thyroid hormone levels is shown in Table 2.

**Table 2: Incidence of Preeclampsia by Thyroid Hormone Levels**

Thyroid Hormone Tertile	Number of Participants	Number with Preeclampsia	Incidence (%)
<b>TSH (mIU/L)</b>			
1 ( $\leq 1.8$ )	66	5	7.6
2 (1.9 - 3.1)	68	9	13.2
3 ( $\geq 3.2$ )	66	16	24.2
<b>T3 (ng/mL)</b>			
1 ( $\leq 1.6$ )	65	18	27.7
2 (1.7 - 2.1)	70	8	11.4
3 ( $\geq 2.2$ )	65	4	6.2
<b>T4 (<math>\mu\text{g/dL}</math>)</b>			
1 ( $\leq 7.2$ )	67	20	29.9
2 (7.3 - 9.1)	68	7	10.3
3 ( $\geq 9.2$ )	65	3	4.6

Logistic regression analysis was performed to evaluate the association between thyroid hormone levels and the risk of preeclampsia. The results are presented in Table 3.

**Table 3: Logistic Regression Analysis of Thyroid Hormone Levels and Preeclampsia**

Variable	Odds Ratio (95% CI)	p-value
<b>TSH (mIU/L)</b>		
1 ( $\leq 1.8$ )	Reference	
2 (1.9 - 3.1)	1.84 (0.62 - 5.42)	0.272
3 ( $\geq 3.2$ )	3.72 (1.34 - 10.36)	0.012
<b>T3 (ng/mL)</b>		
1 ( $\leq 1.6$ )	Reference	
2 (1.7 - 2.1)	0.34 (0.11 - 1.03)	0.056
3 ( $\geq 2.2$ )	0.15 (0.04 - 0.58)	0.006
<b>T4 (<math>\mu\text{g/dL}</math>)</b>		
1 ( $\leq 7.2$ )	Reference	
2 (7.3 - 9.1)	0.27 (0.09 - 0.82)	0.021
3 ( $\geq 9.2$ )	0.11 (0.03 - 0.43)	0.002

## Discussion

In this study, 200 pregnant women at Darbhanga Medical College were examined to see whether maternal thyroid hormone levels were associated with an increased risk of preeclampsia. The participants' average age was 28.4 years, and their average body mass index was 26.7 kg/m<sup>2</sup>. TSH, T3, and T4 thyroid hormone levels were tested and classified into tertiles. Preeclampsia was experienced by 15% of the 200 individuals during their pregnancies.

The incidence of preeclampsia varied significantly across the tertiles of thyroid hormone levels. For TSH, the incidence of preeclampsia increased from 7.6% in the lowest tertile to 24.2% in the highest tertile. Conversely, for T3 and T4, the incidence of preeclampsia decreased with increasing hormone levels, with the highest tertiles showing the lowest incidence rates (6.2% for T3 and 4.6% for T4).

An odds ratio of 3.72 for the highest tertile relative to the lowest indicated a significant correlation between elevated TSH levels and an increased risk of preeclampsia, according to a logistic regression

study. On the other hand, with odds ratios of 0.15 and 0.11 for the highest tertiles, respectively, higher levels of T3 and T4 were linked to a lower risk of preeclampsia.

The results of this study indicate a strong association between maternal thyroid hormone levels and the risk of preeclampsia. Elevated TSH levels were found to significantly increase the risk of developing preeclampsia. This finding aligns with the understanding that hypothyroidism or subclinical hypothyroidism, indicated by high TSH levels, may contribute to adverse pregnancy outcomes, including preeclampsia. The mechanisms behind this association could involve endothelial dysfunction, altered immune responses, and imbalances in angiogenic factors, all of which are implicated in the pathophysiology of preeclampsia.

On the other hand, higher levels of T3 and T4 were associated with a protective effect against preeclampsia. These thyroid hormones play crucial roles in metabolism, vascular function, and immune modulation, which may help mitigate the risk factors associated with preeclampsia. The

protective effect observed in this study suggests that maintaining adequate thyroid function during pregnancy could be beneficial in reducing the risk of preeclampsia.

These findings highlight the importance of monitoring thyroid hormone levels during pregnancy as part of routine prenatal care. Early identification and management of thyroid dysfunction may help prevent the development of preeclampsia and improve pregnancy outcomes.

An analysis of a retrospective cohort study assessed the relationship between perinatal and obstetric outcomes and the mother's thyroid condition as determined by TSH. Maternal TSH levels higher than 4 mIU/L were linked to a 2.17-fold increased risk of preterm and a 2.83-fold increased risk of neonatal respiratory distress syndrome (RDS). This study comprised 8,413 pregnant women with singleton births. Elevated TSH levels were also associated with a higher risk ratio for preeclampsia/eclampsia, but this link was not statistically significant [6].

200 participants participated in a case-control study at Babylon Teaching Hospital, which revealed that preeclamptic patients' TSH levels were noticeably higher than those of healthy pregnant women. In preeclampsia, T3 levels were markedly reduced, with a discernible drop from severe to mild instances. Though not much, preeclamptic women also had reduced T4 levels [7].

The relationship between maternal thyroid dysfunction and the risk of prenatal hypertension and preeclampsia was examined in a cohort study with 41,647 participants. It was discovered that overt hypothyroidism was linked to a 2.59-fold greater risk of severe preeclampsia, whereas isolated hypothyroxinemia was connected with a 1.32-fold increased risk of preeclampsia. Pregnancy-related diabetes mellitus (GDM) was linked to a lower likelihood of TSH receptor antibody positivity [8].

In 107 pregnant women, the effects of maternal TSH, FT3, and FT4 were examined in relation to the incidence of preeclampsia and gestational hypertension. It was discovered that, in comparison to women with gestational hypertension, preeclamptic women had significantly greater TSH levels and lower FT3 levels. According to the study, preeclampsia is more common when thyroid function is compromised [9].

A study that included 100 preeclamptic women and 95 normotensive pregnant women looked at the connection between thyroid function, iodine status, and preeclampsia risk. It was discovered that, in comparison to women with normotension, those with severe preeclampsia had considerably higher TSH levels and lower urinary iodine

concentrations, suggesting a possible connection between thyroid function and preeclampsia [10].

### Conclusion

Higher TSH levels were found to be substantially linked to a higher risk of preeclampsia, according to the analysis. On the other hand, there was a correlation between a lower risk of preeclampsia and higher levels of T3 and T4. To be more precise, compared to individuals in the lowest tertile of TSH, those in the highest tertile had an odds ratio of 3.72 for developing preeclampsia. With odds ratios of 0.15 and 0.11 for T3 and T4, respectively, the greatest tertiles were linked to a protective effect against preeclampsia.

According to these results, there may be a significant correlation between the risk of preeclampsia and maternal thyroid hormone levels, specifically elevated TSH and decreased T3 and T4. To investigate the underlying mechanisms and any therapeutic implications of these correlations, more research is necessary.

### References

1. Mol BW, Roberts CT, Thangaratnam S, Magee LA, De Groot CJ, Hofmeyr GJ. Preeclampsia. *Lancet*. 2016;387(10022):999-1011.
2. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, et al. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid*. 2017;27(3):315-389.
3. Korevaar TI, Derakhshan A, Taylor PN, Meima ME, Chen L, Bliddal S, et al. Association of thyroid function test abnormalities and thyroid autoimmunity with preterm birth: a systematic review and meta-analysis. *JAMA*. 2019;322(7):632-641.
4. Liu X, He S, Zhang Y, Wang Y, Ma J, Chen L, et al. High-normal thyroid function and risk of pre-eclampsia in pregnant women without thyroid disease: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2018;18(1):1-11.
5. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid*. 2011;21(10):1081-1125.
6. Lee S, Cabral H, Aschengrau A, Pearce E. Associations Between Maternal Thyroid Function in Pregnancy and Obstetric and Perinatal Outcomes. *Obstetrical & Gynecological Survey*. 2020.
7. Mousa B. Detection of Relationship between Maternal Thyroid Hormones and Severity of Preeclampsia. *International Journal of Medical*

- Research and Health Sciences. 2018; 7:127-131.
8. Wang J, Gong X, Peng T, Wu J. Association of thyroid function during pregnancy with the risk of preeclampsia and gestational diabetes mellitus. *Endocrine practice*. 2021.
  9. Medjedovic E, Stanojevic M, Kurjak A, Begić E, Iglica A, Jonuzović-Prošić S. Association between maternal thyroid function and risk of gestational hypertension and preeclampsia. *Journal of Perinatal Medicine*. 2022; 50:904-909.
  10. Businge C, Longo-Mbenza B, Kengne A. Mildly elevated thyroid-stimulating hormone is associated with endothelial dysfunction and severe preeclampsia among pregnant women with insufficient iodine intake in Eastern Cape province, South Africa. *Annals of Medicine*. 2021; 53:1082-1088.