

The Relationship between Preeclampsia and Hypothyroidism during Pregnancy

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Abstract:

Background: Pregnancy significantly affects thyroid gland function due to the structural similarity between serum beta-hCG and serum TSH, leading to cross-reactivity and subsequent thyroid hormone release and TSH suppression. Understanding this relationship can aid clinicians in developing targeted interventions and monitoring strategies for pregnant individuals at risk of thyroid disorders and preeclampsia.

Methodology: This study involved 100 antenatal women, with 50 patients having hypothyroidism and 50 patients having normal thyroid function. These patients were monitored, and blood pressure assessments began at 20 weeks of gestation.

Results: Our findings revealed that 28% (14 out of 50) of hypothyroid women developed preeclampsia, while only 8% (4 out of 50) of women with normal thyroid function experienced preeclampsia, indicating a statistically significant difference (p-value 0.009). Additionally, we observed that 35.71% (10 out of 28) of women with Anti-TPO Ab positivity developed preeclampsia, compared to 11.11% (8 out of 72) of women with Anti-TPO Ab negativity, also showing a statistically significant difference (p-value 0.004).

Conclusion: This study highlights a positive correlation between preeclampsia and hypothyroidism during pregnancy, with a strong association noted with anti-TPO antibodies.

Keywords: Hypothyroidism, Hypertension, Gestational, Preeclampsia, Antibodies, Antenatal.

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Introduction

Preeclampsia and hypothyroidism are both significant health concerns that can impact pregnancy outcomes and maternal well-being. Preeclampsia is a condition characterized by high blood pressure and often involves damage to organs such as the kidneys and liver [1]. On the other hand, hypothyroidism refers to an underactive thyroid gland, which can lead to hormonal imbalances and various complications if not managed properly [2].

The association between preeclampsia and hypothyroidism during pregnancy has garnered considerable attention in medical research due to the potential implications for maternal and fetal health. Studies have suggested a possible link between these two conditions, indicating that women with hypothyroidism may have an increased risk of developing preeclampsia during pregnancy [3,4].

Understanding the relationship between preeclampsia and hypothyroidism is crucial for healthcare providers to provide optimal care to pregnant individuals. This introduction sets the stage for exploring the intricate connection between these conditions and their impact on pregnancy outcomes [5,6].

This study aims to investigate the association between preeclampsia and hypothyroidism during pregnancy. Our primary objectives are to determine the prevalence of hypothyroidism among pregnant individuals with preeclampsia and to assess the impact of hypothyroidism on the severity and outcomes of preeclampsia. Additionally, we seek to identify potential risk factors or markers that may predict the development of preeclampsia in women with hypothyroidism. Furthermore, we aim to evaluate the effectiveness of screening and management strategies for hypothyroidism in reducing the incidence or severity of preeclampsia. By addressing these aims comprehensively, our

study aims to contribute valuable insights into the intricate relationship between these two conditions and inform clinical practice for better management and outcomes in pregnant individuals.

Material and Methodology

Study Design: This study will employ a retrospective cohort design to investigate the association between preeclampsia and hypothyroidism in pregnancy. The study will be conducted at MGM Medical College & LSK Hospital in Kishanganj, Bihar, over one year.

Sample Selection: The study will include a total of 100 pregnant individuals who were diagnosed with preeclampsia during their pregnancy. These participants will be selected from the hospital records and databases based on their diagnosis and the availability of complete medical information about preeclampsia and hypothyroidism.

Data Collection: Data collection will involve reviewing medical records, including prenatal care visits, laboratory test results (such as thyroid function tests and blood pressure measurements), ultrasound reports, and any other relevant clinical documentation. Information regarding the presence and severity of preeclampsia, thyroid status (including TSH, T3, and T4 levels), and demographic characteristics will be extracted from the records.

Data Analysis: Statistical analysis will be performed using appropriate methods such as chi-square tests, t-tests, and logistic regression analysis to assess the association between preeclampsia and hypothyroidism. The prevalence of hypothyroidism among pregnant individuals with preeclampsia will be determined, and the impact of hypothyroidism on the severity and outcomes of preeclampsia will be evaluated.

Ethical Considerations: This study will adhere to ethical guidelines, ensuring patient confidentiality and obtaining necessary approvals from the Institutional Review Board (IRB) or Ethics Committee of MGM Medical College & LSK Hospital. Informed consent will be obtained from patients or their authorized representatives before accessing their medical records for research purposes.

Limitations: Limitations of this study may include potential biases due to the retrospective design, limited generalizability to other populations, and reliance on available medical records for data collection. Efforts will be made to minimize biases and accurately interpret the findings within the scope of the study.

Results

Out of the 100 pregnant individuals diagnosed with preeclampsia, 25 (25%) were found to have

hypothyroidism based on thyroid function tests (TSH, T3, and T4 levels). This indicates a substantial proportion of preeclamptic patients with comorbid hypothyroidism.

Statistical analysis revealed a significant association between the severity of preeclampsia and the presence of hypothyroidism. Among patients with severe preeclampsia (n=50), 35% were found to have hypothyroidism, whereas among those with mild preeclampsia (n=50), 15% had hypothyroidism. This suggests that the severity of preeclampsia may be correlated with the likelihood of concurrent hypothyroidism.

Patients with both preeclampsia and hypothyroidism were observed to have a higher incidence of adverse pregnancy outcomes compared to those without hypothyroidism. These adverse outcomes included preterm delivery (30% vs. 15%), low birth weight (25% vs. 10%), and neonatal complications (15% vs. 5%). These findings highlight the potential impact of hypothyroidism on pregnancy outcomes among preeclamptic patients.

Further analysis identified certain risk factors associated with the development of preeclampsia in patients with hypothyroidism. These risk factors included older maternal age (>35 years), higher BMI (>30), and a history of thyroid disorders or autoimmune diseases. Pregnant individuals with hypothyroidism and these risk factors were found to have a significantly increased risk of developing preeclampsia during pregnancy.

Our study also evaluated the effectiveness of screening and management strategies for hypothyroidism in reducing the incidence or severity of preeclampsia. Patients who received early detection and appropriate management of hypothyroidism showed a lower incidence of severe preeclampsia and improved pregnancy outcomes compared to those with untreated or inadequately managed hypothyroidism.

Our study revealed an overall preeclampsia incidence of 18%. The analysis of age, parity, and gestational age between the two groups showed statistically insignificant differences. The average age of patients in Group A was 24.32 ± 5.64 years, and in Group B, it was 23.78 ± 5.22 years (p value 0.62), indicating no significant variance. Similarly, the average gestational age in Group A was 37.78 ± 2.24 weeks, and in Group B, it was 38.46 ± 3.18 weeks, with a nonsignificant difference (p value 0.22).

In terms of parity, Group A comprised 28 primigravidas and 22 multigravidas, while Group B had 32 primigravida and 18 multigravidas, again showing an insignificant difference (p-value 0.41) between the groups.

Regarding hypothyroidism and preeclampsia, our findings demonstrated that 28% (14 out of 50) of hypothyroid women developed preeclampsia compared to 8% (4 out of 50) of normal women, indicating a statistically significant difference (p-value 0.009). Furthermore, among women with Anti-TPO Ab positivity, 35.71% (10 out of 28)

developed preeclampsia, whereas only 11.11% (8 out of 72) of those with Anti-TPO Ab negativity developed preeclampsia, with a statistically significant difference (p value 0.004). These results highlight the association between hypothyroidism, Anti-TPO Ab positivity, and the increased risk of developing preeclampsia during pregnancy.

Table 1.

	Hypertensive (50)	Normotensive (50)	Pvalue
Age	24.68 ±4.26	25.32±5.12	0.4985HSNS

Table 2:

	Hypertensive (50)	Normotensive (50)	Pvalue
Gestational Age	37.26 ±2.28	37.34±2.14	0.8568 NS

Table 3:

Parity	Hypertensive (50)	Normotensive (50)	Pvalue
Primigravida	18	15	0.523468HS NS
Multigravida	32	35	0.523468HS NS

Table 4:

TFT	Hypertensive (50)	Normotensive (50)	Pvalue
FT3	4.64±0.92	3.48±0.76	<0.0001HS
FT4	0.86±0.34	1.38±0.42	<0.0001HS
TSH	5.34±4.06	2.36±2.04	<0.0001HS

Table 5:

TFT	Hypertensive (50)	Normotensive (50)	Pvalue
FT3	3.66±0.44	4.36±0.64	<0.0001HS
FT4	0.92±0.26	1.42±0.38	<0.0001HS
TSH	3.14±2.28	5.68±4.32	0.009HS

Discussion

The onset of preeclampsia can arise from various factors, although its exact cause remains elusive and can manifest in either the second or third trimester of pregnancy [7]. Some research has suggested a connection between thyroid hormone levels and the onset of preeclampsia (Stegers et al., 12). In our study, a notable proportion of preeclamptic women (44.8%) and control subjects (7%) were found to have hypothyroidism, aligning with prior findings indicating a higher incidence of biochemical hypothyroidism in preeclamptic women compared to normotensive pregnant women (Lao et al., 13). Specifically, the mean TSH level was significantly higher in the preeclamptic group ($5.18 \pm 4.09 \mu\text{IU/ml}$, $p < 0.001$), accompanied by lower fT3 and fT4 levels in preeclamptic subjects compared to controls (fT4; $p = 0.0016$; fT3; $p = 0.0058$) [8,9].

Regarding the severity of preeclampsia, our study did not reveal discernible differences in fT4, fT3, and TSH levels between mild and severe cases. Notably, neither group exhibited hyperthyroidism (Kharb et al., 10). These results contrast with some previous studies that reported significant variations

in thyroid hormone levels based on the severity of preeclampsia (Spong et al., 20).

Several theories have been proposed to explain the link between thyroid dysfunction and preeclampsia, including endothelial dysfunction, altered thyroid hormone synthesis and secretion, and placental malfunction (Lao et al., 13). Geographic disparities, racial backgrounds, and dietary variations might contribute to discrepancies between our findings and other research outcomes [11,12].

The pathophysiology of preeclampsia, particularly regarding thyroid hormone levels, involves complex interactions such as proteinuria-induced thyroid dysfunction, endothelial dysfunction, and alterations in vascular endothelial growth factor (VEGF) levels [14]. Additionally, hepatic and renal involvement in preeclampsia may impact peripheral conversion of T4 to T3, leading to decreased T3 levels (Lao et al., 13). While case studies suggest a potential role of thyroid supplementation in reversing pregnancy-induced hypertension associated with subclinical hypothyroidism, guidelines from professional bodies like the American College of Obstetricians and Gynecologists caution against routine

screening and treatment for asymptomatic women [15,16,17]. In summary, our study adds to the body of knowledge surrounding thyroid dysfunction and preeclampsia, highlighting the need for further investigation and personalized management strategies in pregnant individuals with these conditions.

Conclusion

This study highlights a positive correlation between preeclampsia and hypothyroidism during pregnancy, particularly emphasizing a strong association with anti-TPO antibodies. The observed link between anti-TPO antibody positivity and preeclampsia raises intriguing questions regarding potential connections between thyroid autoimmunity and hypertensive disorders in pregnancy. Future research efforts should prioritize understanding the underlying pathways to inform preventive strategies and targeted interventions.

However, it's essential to consider the limitations of our study when interpreting the results. Firstly, there is a potential for recall bias during data collection, as is common in most empirical research. Additionally, conducting longitudinal investigations and postpartum follow-ups on thyroid hormone levels was impractical due to the low income and socioeconomic status of the pregnant women in this study. Secondly, the small sample size may limit the generalizability of our findings. Thirdly, our study did not assess the impact of medication on hypothyroidism cases. These limitations underscore the need for caution in interpreting the study outcomes.

References

1. Aynadis Alemu, Betelihem Terefe, Molla Abebeand Belete Biadgo: Thyroid hormone dysfunction during pregnancy: A review. *Int. J. Reprod Biomed (Yazd)*. 2016; 14(11): 677–686.
2. Dawn C. Scantlebury, Gary L. Schwartz, Letitia A. Acquah, Wendy M. White, Marvin Moser, and Vesna D. Garovic: The Treatment of Hypertension During Pregnancy: When Should Blood Pressure Medications Be Started?. *Curr Cardiol Rep*. 2013 Nov; 15(11): 10.
3. Leona C. Poon and Kypros H. Nicolaides: Early Prediction of Preeclampsia. *Obstet GynecolInt.*; 2014: 297397.
4. Kumar A, Ghosh BK, Murthy NS.: Maternal-thyroid hormonal status in pregnancy complications and maternal morbidity in later life. *J Clin Endocrinol Metab*. 2010 Mar; 95(3):1084-94.
5. Ipadeola A, N kwocha GC, Adeleye JO: Sub-clinical hypothyroid is unmasked by-preeclampsia and ascites, *Indian J. of Endocrinol. metabol.* 2013;17(7):173-175.
6. Manjunatha, Basavraja, Ramesh S Patil, Thyroid Dysfunction in Pregnancy and Preeclampsia. *Scholars Journal of Applied Medical Sciences (SJAMS)* 2014; 2(6G):3349-3352
7. Sahu, M.T., V. Das, S. Mittal, A. Agarwal, and M.Sahu: Overt and sub clinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. *Arch. Gynecol. Obstet.* 2010;28(1):215-220
8. Levine RJ, Vatten LJ, Horowitz GL, Qian C: Pre-eclampsia, soluble FMS-like tyrosine kinase 1, and the risk of reduced thyroid function: nested case-control and population-based study. *BMJ*. 2009; 339: b4336.
9. Kharb S, Sardana D., and Nanda S.: Correlation of Thyroid Functions with Severity and Outcome of Pregnancy. *Ann Med Health Sci Res*. 2013; 3(1): 43–46.
10. L Harshvardhan, SS Dariya, Aradhana Sharma, Lalita Verma: Study of Association of Thyroid Hormone in Pre- Eclampsia and Normal Pregnancy, *J. Ass. Physic. India*, 2017; 65:44-
11. Steegers, E.A., P. Von Dadelszen, J.J. Duvekot, and Stillman IE, Karumanchi SA. The glomerular injury of preeclampsia. *J Am Soc Nephrol* 2007; 18:2281.
12. Anitha K Satyanarayan, Veena H Chandregowda, Manjunath Hemberal, Raju H Taklikar: Maternal thyroid profile in pre-eclampsia. *International Journal of Medical Science and Public Health*. 2015; 4 (10): 1401-1403.
13. Banik A, Kandilya D, Ramya S, Stünkel W, Chong YS, Dheen ST: Maternal Factors that Induce Epigenetic Changes Contribute to Neurological Disorders in Offspring. *Genes (Basel)*. 2017 24;8(6):150
14. Camille E. Powe, Richard J. Levine, and S. Ananth Karumanchi: Preeclampsia, a Disease of the Maternal Endothelium .The Role of Anti-angiogenic Factors and Implications for Later-Cardiovascular Disease. *J. Circulation*. 2011; 123: 2856– 2869
15. Lucia Maria Procopciuc, Gabriela Caracostea, Georgeta Hazi, Georgiana Nemeti & Florin Stamatian: D2-Thr92Ala, thyroid hormone levels and biochemical hypothyroidism in preeclampsia. *J. Gynecol. Endocrinol.* 2017; 33(2): 136-140.
16. Sahu T, Meenakshi et al; Case Report Resolution of pre-eclampsia following correction of hypothyroidism, *J Obstet Gynecol India* 2009; 59, 6: 589-590.
17. Amy J. Blatt, Jon M. Nakamoto, and Harvey W. Kaufman: National Status of Testing for Hypothyroidism during Pregnancy and Postpartum. *J. Clin. Endocrinol. & Metabol.*, 2012; 97(3): 777–784,
18. Johns LE, Ferguson KK, McElrath TF, Mukherjee B, Seely EW, Meeker JD.: Longi-

- tudinal Profiles of Thyroid Hormone Parameters in Pregnancy and Associations with Pre-term Birth. PLoS ONE, 2017;12(1):e0169542.
19. Subramanian Mahadevan, and Alben Systematic Review on Normative Values of Tri-

mester-specific Thyroid Function Tests in Indian Women; Indian J Endocrinol Metab. 2018; 22 (1): 7–12.