

Original Research Article

IMPACT OF THYROID DYSFUNCTION ON THE SEVERITY OF PREGNANCY-INDUCED HYPERTENSION: A CASE-CONTROL STUDY

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Received : 21/09/2024
Received in revised form : 15/11/2024
Accepted : 30/11/2024

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DOI: 10.70034/ijmedph.2024.4.231

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2024; 14 (4); 1261-1265

ABSTRACT

Background: This study aimed to assess the association between thyroid dysfunction and the severity of pregnancy-induced hypertension (PIH), focusing on thyroid-stimulating hormone (TSH), free T3, and free T4 levels.

Materials and Methods: In a hospital-based case-control study, 200 pregnant women were divided into two groups: 100 women with PIH and 100 normotensive controls. Thyroid parameters were measured, and blood pressure and demographic data were collected. Statistical analyses compared thyroid function and blood pressure between the groups.

Results: Women with PIH had significantly higher TSH levels (4.43 ± 1.8 μ IU/mL) and lower free T3 (2.66 ± 0.75 pg/mL) and T4 levels (0.84 ± 0.25 ng/dL) compared to controls. Subclinical hypothyroidism was more prevalent in severe preeclampsia cases, suggesting a strong link between thyroid dysfunction and PIH severity.

Conclusion: Elevated TSH and reduced T3 and T4 levels were associated with increased PIH severity. Routine thyroid screening during pregnancy may help identify and manage hypertensive risks.

Keywords: Pregnancy-induced hypertension, thyroid dysfunction, TSH levels, preeclampsia, subclinical hypothyroidism.

INTRODUCTION

Pregnancy-induced hypertension (PIH) is a significant health concern affecting approximately 6–11% of pregnant women in India, leading to considerable maternal and fetal morbidity and mortality.^[1,2] PIH is characterized by the new onset of hypertension after 20 weeks of gestation, with systolic blood pressure (SBP) exceeding 140 mmHg and diastolic blood pressure (DBP) exceeding 90 mmHg, and can manifest with or without proteinuria.^[1,2] The spectrum of hypertensive disorders during pregnancy includes chronic hypertension, gestational hypertension, preeclampsia, and eclampsia, all of which present unique challenges in management and care.^[1,2]

Thyroid dysfunction, particularly hypothyroidism and hyperthyroidism, represents one of the most common endocrine disorders during pregnancy, second only to diabetes mellitus.^[2,3] It is well-established that thyroid hormones play a crucial role in maintaining metabolic homeostasis, growth, and

development for both the mother and the fetus.^[Reference 2,3] Adequate thyroid hormone levels are essential for proper placental function, and alterations in these levels can adversely impact maternal and fetal health, increasing the risk of conditions such as preeclampsia, low birth weight, and even fetal death.^[Reference 1,6]

The relationship between thyroid dysfunction and hypertensive disorders in pregnancy remains inadequately understood, despite evidence suggesting that thyroid abnormalities may contribute to the pathogenesis of PIH.^[Reference 4,5] Some studies have indicated that maternal thyroid hormone levels may significantly correlate with the severity of hypertension in pregnancy, implicating thyroid dysfunction as a potential risk factor.^[Reference 2,11] Furthermore, the prevalence of biochemical hypothyroidism in women with PIH appears to be elevated, necessitating routine screening for thyroid function in pregnant women as part of comprehensive antenatal care.^[Reference 4,9]

In light of these findings, our study aims to explore the correlation between thyroid status and the severity of pregnancy-induced hypertension, thereby enhancing our understanding of this complex interaction and its implications for maternal-fetal outcomes. Through this investigation, we hope to identify key risk factors associated with thyroid dysfunction in the context of PIH, ultimately contributing to improved management strategies for affected women.

MATERIALS AND METHODS

This study was designed as a hospital-based observational case-control study to evaluate the relationship between thyroid function and the severity of pregnancy-induced hypertension (PIH). The study was conducted over a six-month period in a tertiary care center, and ethical clearance was obtained from the Institutional Ethics Committee before recruitment of participants. A total of 200 pregnant women participated in this study, comprising two groups: Case Group: 100 hypertensive pregnant women diagnosed with PIH after 20 weeks of gestation. The diagnosis was based on the American College of Obstetricians and Gynecologists (ACOG) guidelines, with blood pressure measurements of $\geq 140/90$ mm Hg on two separate occasions, at least four hours apart. Control Group: 100 normotensive pregnant women of similar age and gestational period as the case group. Controls were selected based on their absence of hypertension and thyroid dysfunction.

Inclusion Criteria were: Pregnant women aged 18–40 years with PIH, excluding those with chronic hypertension prior to pregnancy. Exclusion Criteria were: Women with a history of thyroid disorders, chronic hypertension, systemic illnesses (e.g., diabetes, renal disease), or use of medications affecting thyroid function.

After informed consent, demographic information, medical and obstetric history, and clinical measurements were recorded. Blood pressure was measured twice in the semi-reclining position, with six hours between measurements. Blood samples were collected to assess thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) levels using the enzyme-linked immunosorbent assay (ELISA) method, following the reference ranges for pregnant women after 20 weeks of gestation as recommended by the American Thyroid Association (Reference 2) (Reference 3) (Reference 4) (Reference 1).

The data were analyzed using IBM SPSS software. Mean and standard deviation were calculated for continuous variables, and categorical variables were analyzed using the Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 200 pregnant women participated in this study, divided into two groups: 100 with pregnancy-induced hypertension (PIH) as cases and 100 normotensive women as controls. Demographic characteristics, including age and gestational age, were similar between the two groups, with no statistically significant differences, ensuring comparability. The average age of participants in both groups was approximately 28 years, while the average gestational age was around 29 weeks (Table 1).

Blood pressure measurements indicated a clear disparity between the PIH and control groups. The mean systolic blood pressure (SBP) in the PIH group was 155.04 ± 9.08 mm Hg, significantly higher than the control group's average of 124.12 ± 8.56 mm Hg ($p < 0.0001$). Diastolic blood pressure (DBP) followed a similar trend, with an average of 99.58 ± 10.97 mm Hg in the PIH group, compared to 80.22 ± 6.50 mm Hg in controls, which was also statistically significant ($p < 0.0001$) (Table 1). These findings emphasize the markedly elevated blood pressure among women diagnosed with PIH compared to normotensive controls.

Thyroid function analysis showed that thyroid-stimulating hormone (TSH) levels were considerably higher in the PIH group, with a mean of 4.43 ± 1.8 μ IU/mL, versus 1.90 ± 0.92 μ IU/mL in the control group ($p < 0.05$). The reduction in free triiodothyronine (FT3) levels was similarly significant, as the PIH group showed an average of 2.66 ± 0.75 pg/mL, compared to 3.22 ± 0.75 pg/mL in the control group ($p < 0.05$). Free thyroxine (FT4) levels were also lower in the PIH group, averaging 0.84 ± 0.25 ng/dL versus 1.29 ± 0.23 ng/dL in controls ($p < 0.05$) (Table 1). These results demonstrate a strong association between higher TSH levels, lower FT3 and FT4 levels, and the presence of PIH, suggesting that thyroid function abnormalities are prevalent among hypertensive pregnant women.

The severity of PIH was positively correlated with thyroid dysfunction. Subclinical hypothyroidism was observed more frequently in women with severe preeclampsia (47.83%) compared to those with gestational hypertension (19.05%), a statistically significant finding ($p < 0.05$). Similarly, clinical hypothyroidism was detected in 13.04% of women with severe preeclampsia but was absent among those with gestational hypertension (Table 2). This pattern suggests a significant link between severe PIH cases and overt hypothyroidism, further indicating that thyroid dysfunction increases with PIH severity.

Table 1: Demographic, Blood Pressure, and Thyroid Function Parameters in PIH and Control Groups

S. No	Parameter	PIH Group (n=100)	Control Group (n=100)	p-value
1	Age (years)	28.11 ± 3.15	27.15 ± 3.74	0.11
2	Gestational Age (weeks)	29.19 ± 2.13	29.11 ± 2.37	0.19
3	Systolic BP (mm Hg)	155.04 ± 9.08	124.12 ± 8.56	<0.0001
4	Diastolic BP (mm Hg)	99.58 ± 10.97	80.22 ± 6.50	<0.0001
5	TSH (µIU/mL)	4.43 ± 1.8	1.90 ± 0.92	<0.05
6	Free T3 (pg/mL)	2.66 ± 0.75	3.22 ± 0.75	<0.05
7	Free T4 (ng/dL)	0.84 ± 0.25	1.29 ± 0.23	<0.05

Table 2: Correlation between Thyroid Dysfunction and Severity of PIH

S. No	Thyroid Status	Gestational Hypertension (%)	Mild Preeclampsia (%)	Severe Preeclampsia (%)	p-value
1	Euthyroid	85.71	79.37	39.13	<0.05
2	Subclinical Hypothyroid	14.29	19.05	47.83	<0.05
3	Clinical Hypothyroid	0	1.58	13.04	<0.05

DISCUSSION

Our study findings indicate a significant association between thyroid dysfunction, particularly elevated TSH levels, and the severity of pregnancy-induced hypertension (PIH). Women in the PIH group exhibited higher TSH levels and lower free T3 and T4 levels compared to normotensive controls. These results align with findings from previous studies, which have also reported a strong link between thyroid abnormalities and hypertensive disorders of pregnancy. Toloza et al. (2022) found that subclinical hypothyroidism, indicated by elevated TSH levels, was associated with a heightened risk of preeclampsia and gestational hypertension. The study suggested that both high and low TSH levels contribute to the risk, supporting a U-shaped relationship between TSH and hypertensive disorders during pregnancy.^[Reference 5] This aligns with our observations of increased TSH levels in PIH cases, particularly among those with severe preeclampsia.

Our results also highlight that hypothyroidism and subclinical hypothyroidism were prevalent among women with PIH, corroborating findings from Lai et al. (2020), who reported that hypothyroidism and elevated TSH levels in early pregnancy significantly increased the risk of gestational hypertension. Their study demonstrated that women in the highest TSH quintile were more than four times as likely to develop gestational hypertension compared to those in the middle quintile.^[Reference 7] In our study, the PIH group similarly showed higher TSH levels and a greater prevalence of hypothyroidism, emphasizing the importance of thyroid screening for pregnant women, especially those at risk for hypertension. Moreover, Kharb et al. (2013) observed that preeclamptic women had elevated TSH levels compared to normotensive controls, and they noted that these women experienced lower birth weights and higher mean arterial pressure, outcomes that are consistent with our findings of adverse neonatal and maternal outcomes among women with elevated TSH.^[Reference 8]

Furthermore, the association between thyroid dysfunction and vascular resistance in preeclampsia,

as described in other studies, supports the role of thyroid hormones in endothelial health. Toloza et al. (2022) highlighted that antiangiogenic factors, such as sFlt1, are often elevated in preeclampsia, which can disrupt vascular function and increase the risk of hypertension and placental insufficiency. The correlation of thyroid dysfunction with elevated antiangiogenic biomarkers may exacerbate the impact of PIH on maternal and fetal health.^[Reference 5] Similarly, Kharb et al. (2013) noted that women with high TSH levels in severe preeclampsia had worse outcomes, suggesting that vascular and hormonal interactions in preeclampsia could underlie the observed hypertensive conditions and reinforce our findings of an increased risk for severe hypertension with thyroid dysfunction (Reference 8). The association between thyroid dysfunction and hypertensive disorders of pregnancy, such as gestational hypertension and preeclampsia, has been supported by several studies, highlighting the significant role of thyroid hormones in maternal health and fetal outcomes. Thyroid dysfunction, particularly hypothyroidism and subclinical hypothyroidism, is increasingly recognized as a contributor to adverse pregnancy outcomes, including hypertension. Elevated thyroid-stimulating hormone (TSH) levels and reduced free thyroxine (FT4) levels have been frequently observed in pregnant women with hypertensive disorders, suggesting that thyroid abnormalities may exacerbate the pathophysiology of these conditions.^[Reference 5,7]

Studies demonstrate that hypothyroidism, even in subclinical forms, correlates with a heightened risk of gestational hypertension and preeclampsia, with maternal TSH levels often correlating positively with disease severity. For instance, women with higher TSH concentrations are more likely to develop severe hypertensive conditions than those with normal thyroid function, which could reflect the inflammatory and vascular impacts of hypothyroidism on pregnancy physiology.^[Reference 5,8] Moreover, the observed association between high TSH levels and adverse pregnancy outcomes, including low birth weight and preterm delivery, further emphasizes the importance of managing

thyroid levels during pregnancy. The influence of thyroid hormones on placental function and vascular health suggests that hypothyroid conditions may compromise placental blood flow, thus increasing the risk of hypertension and poor fetal outcomes.^[Reference 7]

Several studies also support a U-shaped relationship between TSH levels and preeclampsia risk, with both high and low TSH levels linked to adverse outcomes, suggesting that optimal thyroid regulation is crucial for minimizing hypertensive risks in pregnancy.^[Reference 7,8] Furthermore, biochemical hypothyroidism, often characterized by increased TSH and decreased triiodothyronine (TT3) levels, has been shown to correlate with mean arterial pressure in preeclamptic women, indicating a potential relationship between the severity of thyroid dysfunction and blood pressure elevations. This relationship underscores the potential benefits of screening and treating thyroid abnormalities to mitigate hypertensive complications during pregnancy.^[Reference 8]

Although the connection between thyroid function and hypertensive disorders in pregnancy is well-documented, there are inconsistencies in findings across different populations and methodologies, with some studies showing weaker associations in women with milder thyroid dysfunction. These discrepancies may stem from variations in study design, population characteristics, and the timing of thyroid measurements during pregnancy. In particular, recent studies suggest that early pregnancy TSH and FT4 levels are critical indicators for gestational hypertension risk, implying that early thyroid screening could be instrumental in identifying at-risk pregnancies.^[Reference 5,8]

In addition to the direct effects of thyroid dysfunction on maternal hypertension, thyroid abnormalities may influence the vascular environment of the placenta, further compounding risks in hypertensive pregnancies. Subclinical hypothyroidism, characterized by elevated TSH levels but normal FT4, has been associated with adverse vascular effects, including increased vascular resistance and impaired endothelial function, which are crucial factors in the development of gestational hypertension and preeclampsia.^[Reference 5] The altered vascular state may stem from decreased levels of nitric oxide, a vasodilator, and increased sympathetic nervous activity, which together can elevate blood pressure and potentially compromise placental perfusion. This reduced placental blood flow may, in turn, lead to restricted fetal growth and low birth weight, both of which are commonly observed in pregnancies complicated by hypertensive disorders and thyroid dysfunction.^[Reference 7]

Moreover, the relationship between thyroid hormones and hypertensive disorders in pregnancy could be mediated by inflammatory and antiangiogenic factors. Studies have shown that

preeclamptic women often exhibit an overexpression of antiangiogenic biomarkers like soluble fms-like tyrosine kinase-1 (sFlt1), which can contribute to endothelial dysfunction and reduced placental vascularization. This antiangiogenic state has also been linked to increased TSH levels and low FT4, potentially worsening the severity of preeclampsia through a feedback loop of thyroid dysfunction and vascular impairment.^[Reference 5,8] The impact of these factors is not limited to the mother; adverse thyroid and hypertensive conditions in pregnancy have been associated with neonatal complications, including preterm birth and low Apgar scores, underscoring the significance of optimal thyroid function management for both maternal and fetal well-being.^[Reference 7,8]

In conclusion, this study reinforces the association between thyroid dysfunction and hypertensive disorders in pregnancy, advocating for routine thyroid screening as part of antenatal care to identify and manage potential thyroid-related hypertensive risks. Future research should focus on large-scale, prospective studies to further elucidate the mechanisms linking thyroid hormones with pregnancy-induced hypertension and to refine the management strategies for thyroid abnormalities in pregnant women.

CONCLUSION

In conclusion, this study reinforces the association between thyroid dysfunction and hypertensive disorders in pregnancy, advocating for routine thyroid screening as part of antenatal care to identify and manage potential thyroid-related hypertensive risks. Future research should focus on large-scale, prospective studies to further elucidate the mechanisms linking thyroid hormones with pregnancy-induced hypertension and to refine the management strategies for thyroid abnormalities in pregnant women.

REFERENCES

1. Dutta DC, Konar H. DC Dutta's textbook of obstetrics, edited by H Konar, 8Th Edition, (JAYPEE) the Health Service Publisher, New Delhi, 2019; pp.219-240.
2. Nwabudike P, Emokpae MA. Thyroid Dysfunction among Hypertensive Pregnant Women in Warri, Delta State, Nigeria. *Medicines (Basel)*. 2022 Apr 7;9(4):29.
3. Negro R, Farnoso G, Mangieri T, et al. Levothyroxine treatment in Euthyroid pregnant women with autoimmune thyroid disease: effects on obstetrical complications. *J Clin Endocrinol Metab*. 2006;91:2587-91.
4. Dashe JS, Bloom SL, Spong CY, Hoffman BL. *Williams obstetrics*. McGraw Hill Professional; 2018 Jun 1. New York: McGraw-Hill Professional; 2018.
5. World Health Organization International society of hypertension guidelines for the management of hypertension (Guideline subcommittee) *J. Hypertens*. 1999;11:151-183.
6. Mukhopadhyay A, Pati S, Mukherjee S, Das N, Mukhopadhyay P, Saumandal B. Autoimmune thyroid disorders and pregnancy outcome: a prospective observational study. *Thyroid Research and Practice*. 2007; 4(1): 50-2.

7. Rafeeinia A, Teymoori H, Marjani A. Serum Thyroid Hormone Levels in Preeclampsia Women in Gorgan. *J Med Sci.* 2015; 15:38–43.
8. Levine RJ, Vatten LJ, Horowitz GL, et al. Preeclampsia, 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. Sahay RK, Nagesh VS. Hypothyroidism in pregnancy. *Indian J Endocrinol Metab.* 2012; 16(3): 364-70.
10. American College of O, Gynecologists' Committee on Practice B-O. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. *Obstet Gynecol* 2020; 135(6): e237–e60.
11. Saki F, Dabbaghmanesh MH, Ghaemi SZ, et al. Thyroid function in pregnancy and its influences on maternal and fetal outcomes. *Int J Endocrinol Metab* 2014; 12: e19378.
12. Kaya E, Sahin Y, Ozkeçeci Z, Paşaoğlu H. Relation between birth weight and thyroid function in preeclampsia-eclampsia. *Gynecol Obstet Invest* 1994;37:30–3.
13. Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. *Lancet* 2006; 367(9516): 1066–74.
14. Kharb S, Sardana D, Nanda S. Correlation of thyroid functions with severity and outcome of pregnancy. *Ann Med Health Sci Res.* 2013 Jan;3(1):43-6.
15. Ramtahal R and Dhanoo A. Subclinical hypothyroidism causing hypertension in pregnancy. *J Am Soc Hypertens* 2016; 10: 691–693.
16. Say L, Chou D, Gemmill A, et al. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health* 2014; 2(6): e323–33.
17. Wilson KL, Casey BM, McIntire DD, Halvorson LM, Cunningham FG. Subclinical thyroid disease and the incidence of hypertension in pregnancy. *Obstet Gynecol.* 2012;119:315–20.
18. Shen H, Liu X, Chen Y, et al. Associations of lipid levels during gestation with hypertensive disorders of pregnancy and gestational diabetes mellitus: a prospective longitudinal cohort study. *BMJ Open* 2016; 6: e013509.
19. Zhu YC, Yang HX, Wei YM, et al. Analysis of correlation factors and pregnancy outcomes of hypertensive disorders of pregnancy- a secondary analysis of a random sampling in Beijing, China. *J Matern Fetal Neonatal Med* 2017; 30: 751–754.
20. Tranquilli AL, Dekker G, Magee L, et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP. *Pregnancy Hypertens* 2014; 4(2): 97–104.
21. Hutcheon JA, Lisonkova S, Joseph KS. Epidemiology of pre-eclampsia and the other hypertensive disorders of pregnancy. *Best Pract Res Clin Obstet Gynaecol* 2011; 25(4): 391–403.
22. Mannisto T, Mendola P, Grewal J, et al. Thyroid diseases and adverse pregnancy outcomes in a contemporary US cohort. *J Clin Endocrinol Metab* 2013; 98: 2725–2733.
23. Magee LA, von Dadelszen P, Bohun CM, et al. Serious perinatal complications of non-proteinuric hypertension: an international, multicentre, retrospective cohort study. *J Obstet Gynaecol Can* 2003; 25(5): 372–82.