

## CORRELATION OF THYROID STATUS WITH SEVERITY OF HYPERTENSION IN PREGNANCY

Prasanna Lakshmi<sup>1</sup>, P. Bakiavathy<sup>2</sup>

<sup>1</sup>Associate Professor, Department of Obstetrics and Gynaecology, Govt. Sivagangai Medical College, Sivaganga, Tamil Nadu, India.

<sup>2</sup>Associate Professor, Department of Obstetrics and Gynaecology, KAP Viswanatham Medical College, Tiruchirappalli, Tamil Nadu, India

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Corresponding Author:

**Dr. Prasanna Lakshmi,**  
Email: prasanand01@gmail.com

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### Abstract

**Background:** Gestational hypertension (GH) is characterised by an increase in blood pressure (BP) that occurs at or after the 20th week of pregnancy, without the presence of proteinuria, in women who were previously normotensive. Hypertensive complications during pregnancy, which occur in approximately 10% to 17% of all pregnancies, are primarily attributed to this particular cause. Some of the complications that can arise from inadequate management include pre-eclampsia, eclampsia, and mortality. Although gestational hypertension (GH) is a significant cause of maternal and perinatal morbidity and mortality, the precise mechanisms responsible for its development have not been completely understood. The purpose of this study is to assess the relationship between thyroid function and the severity of hypertension during pregnancy. **Materials and Methods:** The study group consisted of 100 hypertensive pregnant women, ranging in age from 18 to 40 years. The control group consisted of 100 pregnant women who were normotensive and matched in age to the study group. The determination of gestational age for each participant was made using the last menstrual period. The study included individuals who were diagnosed with hypertension after 20 weeks of gestation, specifically during the second and third trimesters. **Result:** Majority of women with pregnancy induced hypertension were having mild preeclampsia 63% followed by severe preeclampsia 23% and GHTN 14%. The prevalence of clinical hypothyroidism was found to be 13.04% among individuals diagnosed with severe preeclampsia, whereas no cases of clinical hypothyroidism were observed among those with gestational hypertension. The prevalence of subclinical hypothyroidism was found to be 47.83% in cases of severe preeclampsia and 19.05% in cases of gestational hypertension. **Conclusion:** The present study revealed a significant correlation between thyroid hypofunction and pregnancy induced hypertension.

## INTRODUCTION

Hypertension is a prevalent medical issue that impacts approximately 10% of pregnant individuals, often leading to increased rates of hospitalisation and mortality for both the foetus and the mother.<sup>[1,2]</sup> Hypertensive disorders of pregnancy encompass a range of distinct conditions, such as chronic hypertension, gestational hypertension, and eclampsia.<sup>[1]</sup> As per the findings of the National High Blood Pressure Education Programme Working Group on High Blood Pressure in Pregnancy, hypertension during pregnancy can be classified into four distinct categories: (1) chronic hypertension, (2) preeclampsia-eclampsia, (3) preeclampsia superimposed on chronic hypertension, and (4) gestational hypertension.<sup>[3]</sup> The available evidence regarding the risk of thyroid dysfunction in relation to maternal and neonatal health is currently limited,

despite the significant burden it poses. Hypertension, also known as high blood pressure, is a medical condition characterised by elevated arterial pressure that exceeds the normal range. This abnormal elevation in blood pressure can potentially result in detrimental consequences such as organ damage and the development of serious illnesses. Hypertension, characterised by a blood pressure reading equal to or greater than 140/90 mmHg, has been identified as one of the most prevalent chronic conditions.<sup>[4]</sup> The occurrence of elevated blood pressure during pregnancy has been documented to have various physiological consequences and can increase the maternal susceptibility to complications prior to, during, or subsequent to childbirth. The development of the placenta may be impacted, leading to insufficient provision of nutrients and oxygen to the foetus.<sup>[5]</sup> The incidence of hypertensive disorders during pregnancy varies between 10% and 21%

among expectant mothers. Thyroid dysfunctions, specifically hyperthyroidism and hypothyroidism, occurring during pregnancy have the potential to induce hypertension and other related negative health consequences for both the foetus and the mother. The adverse health outcomes associated with this condition encompass a heightened likelihood of experiencing miscarriage, pregnancy induced hypertension, preterm delivery, placental abruption, low birth weight, and foetal death.<sup>[6]</sup> Moreover, it is worth noting that hypothyroidism could potentially serve as a standalone risk factor for the development of preeclampsia and foetal growth restriction. Nevertheless, there is still limited understanding regarding the fundamental roles of thyroid dysfunction in hypertensive disorders that occur during pregnancy.<sup>[7]</sup>

## MATERIALS AND METHODS

A sample size of 200 individuals was selected through a random sampling method for the purpose of this study. The study group consisted of 100 hypertensive pregnant women, ranging in age from 18 to 40 years. The control group consisted of 100 pregnant women who were normotensive and matched in age to the study group. The determination of gestational age for each participant was made using the last menstrual period. The study included individuals who were diagnosed with hypertension after 20 weeks of gestation, specifically during the second and third trimesters. Control subjects were selected from apparently healthy pregnant women attending antenatal clinic, who were of similar age and trimester as the hypertensive group. Subjects who had hypertension prior to the current pregnancy, individuals with diabetes mellitus, and those with a pre-pregnancy weight exceeding 90 kg were excluded from the study. Additionally, all patients with proteinuria equal to or greater than 0.3 gm were also excluded from the study.

### Methodology

The researchers employed a random sampling technique in the process of collecting the samples. A volume of 3 millilitres of whole blood was obtained by employing a plain specimen container. The centrifuged serum was subsequently stored at a temperature range of 2-8°C until it was subjected to analysis. The demographic information of all participants in the study was collected through the utilisation of a standardised questionnaire

administered by trained interviewers. The questionnaire had undergone pretesting to ensure its reliability and validity. The blood pressure of each participant was assessed utilising an Accoson mercury sphygmomanometer. The utilisation of Korotkoff's sound phases I and V was employed in order to ascertain the systolic and diastolic blood pressures (SBPs and DBPs) correspondingly. Values exceeding 140 mmHg for systolic blood pressure (SBP) and 90 mmHg for diastolic blood pressure (DBP) were deemed to be outside the normal range.

## RESULTS

The demographic and anthropometric parameters were analysed to determine any differences between hypertensive pregnant women and normotensive subjects. The mean age of hypertensive pregnant women (28.11±3.15 years) was found to be statistically similar to that of normotensive subjects (27.15±3.74 years) (P=0.11). There were no statistically significant differences observed in the mean levels of height (1.63 ± 0.04 m), weight (69.44 ± 3.58 kg), body mass index (26.21±2.48 m/kg<sup>2</sup>), and gestational age (29.19±2.13 weeks) between hypertensive subjects and normotensive subjects (1.65 ± 0.04 m, 68.24 ± 3.66 kg, 25.77±2.29 m/kg<sup>2</sup>, and 29.11±2.37 weeks, respectively) (P>0.05). In hypertensive individuals, the average values of systemic blood pressure (SBP) and diastolic blood pressure (DBP) were found to be significantly higher (P=0.001) compared to the control group. Specifically, the mean SBP was 160.52±4.59 mmHg in hypertensive subjects, while it was 116.89±3.78 mmHg in the control group. Similarly, the mean DBP was 94.53±3.99 mmHg in hypertensive subjects, whereas it was 70.11±3.67 mmHg in the control group.

The average TSH value was found to be significantly higher (P<0.05) among pregnant women with hypertension (4.11 ± 1.25 µIU/ml) in comparison to pregnant women without hypertension (2.23 ± 1.26 µIU/ml). The serum mean level of FT3 was found to be significantly lower (P<0.05) in the test subjects (3.33 ± 1.44 pg/ml) compared to the control subjects (4.99 ± 1.41 pg/ml). Nonetheless, the study findings revealed no statistically significant disparity (P=0.36) in the average FT4 levels between hypertensive pregnant individuals (2.22 ± 1.10 pg/dl) and normotensive pregnant individuals (2.33 ± 1.56 pg/dl).

**Table 1: Demographic and anthropometric profile of the study participants.**

Parameters	Study Group	Control group	T-test	P-Value
Age (years)	28.11±3.15	27.15±3.74	2.11	0.11
BMI (kg/m <sup>2</sup> )	26.21±2.48	25.77±2.29	3.64	0.23
Gestational age (weeks)	29.19±2.13	29.11±2.37	4.77	0.19
SBP (mmHg)	160.52±4.59	116.89±3.78	25.19	0.001
DBP (mmHg)	94.53±3.99	70.11±3.67	26.45	0.001

**Table 2: TSH, FT3 and FT4 in hypertensive and normotensive pregnant women**

Parameters	study group	Control group	T-test	P-Value
TSH ( $\mu$ IU/ml)	4.11 $\pm$ 1.25	2.23 $\pm$ 1.26	5.89	0.001
FT3 (pg/ml)	3.33 $\pm$ 1.44	4.99 $\pm$ 1.41	-6.44	0.001
FT4 (ng/dl)	2.22 $\pm$ 1.10	2.33 $\pm$ 1.56	-0.05	0.36

**Table 3: Severity of hypertension**

Severity of hypertension	Number	Percentage
Gestational hypertension (GHTN)	14	14
Mild preeclampsia	63	63
Severe preeclampsia	23	23

Majority of women with pregnancy induced hypertension were having mild preeclampsia 63% followed by severe preeclampsia 23% and GHTN 14%.

**Table 4: Correlation of thyroid status with severity of hypertension**

Thyroid status	Study group			Total
	GHTN	Mild PE	Severe PE	
EU	12(85.71%)	50(79.37%)	9(39.13%)	71(71%)
SCH	2(14.29%)	12(19.05%)	11(47.83%)	25(25%)
CH	0(0%)	1(1.58%)	3(13.04%)	4(4%)
Total	14(100%)	63(100%)	23(100%)	100(100%)

**Table 5: Correlation between SBP, DBP, TSH, FT3 and FT4 among the hypertensive pregnant women.**

Parameters	SBP mmHg	DBP mmHg	TSH ( $\mu$ IU/ml)	FT3 (pg/ml)	FT4 (ng/dl)
SBP (mmHg)	--	1.31a	0.85 a	0.04	0.02
DBP (mmHg)	1.31a	--	1.21a	0.05	0.03
TSH ( $\mu$ IU/ml)	0.85a	1.21a	--	-0.61b	-0.41b
FT3 (pg/ml)	0.04	0.05	-0.61b	--	0.01
FT4 (ng/dl)	0.02	0.03	-0.41b	0.01	--

a = marked positive significance and b = marked negative significance.

The data presented in the aforementioned table indicates a positive correlation between the severity of hypothyroidism and the severity of hypertension. A notable disparity was observed in the incidence of clinical hypothyroidism cases and subclinical hypothyroidism cases among individuals with gestational hypertension and severe preeclampsia, respectively. The prevalence of clinical hypothyroidism was found to be 13.04% among individuals diagnosed with severe preeclampsia, whereas no cases of clinical hypothyroidism were observed among those with gestational hypertension. The prevalence of subclinical hypothyroidism was found to be 47.83% in cases of severe preeclampsia and 19.05% in cases of gestational hypertension. [Table 4]

The results indicate a statistically significant positive correlation between systolic blood pressure (SBP) and diastolic blood pressure (DBP) ( $R=1.31a$ ,  $P=0.001$ ), as well as between SBP and thyroid-stimulating hormone (TSH) ( $R=0.85a$ ,  $P=0.001$ ). Furthermore, notable inverse relationships were observed between TSH and FT3 ( $R= -0.61b$ ,  $P=0.001$ ), as well as between TSH and FT4 ( $R= -0.41b$ ,  $P=0.001$ ). Nevertheless, the analysis revealed that there was no statistically significant positive relationship ( $P>0.05$ ) observed between the mean values of systolic blood pressure (SBP) and free triiodothyronine (FT3) ( $R=0.04$ ), SBP and free thyroxine (FT4) ( $R=0.02$ ), diastolic blood pressure (DBP) and FT3 ( $R=0.05$ ), DBP and FT4 ( $R=0.03$ ), as well as FT3 and FT4 ( $R=0.01$ ) [Table 5].

## DISCUSSION

Gestational hypertension, which is recognised as a temporary condition, represents the prevailing manifestation of hypertension during pregnancy. The majority of researchers have directed their attention towards pre-eclampsia due to its significant implications for the health of both the mother and the foetus. In contrast, there is a dearth of information regarding the consequences associated with a diagnosis of gestational hypertension (GH). There is evidence indicating that thyroid-associated endocrinopathies are prevalent among women of maternal age, making them one of the most common endocrine disorders.<sup>[8]</sup> Based on the findings of Klein et al. (2007), it was observed that a significant proportion, specifically 30%, of pregnant women who were diagnosed with gestational hypertension (GH) also exhibited pre-eclampsia and other hypertensive complications during their pregnancy. Consequently, it is plausible that thyroid dysfunction could serve as the fundamental pathological condition in growth hormone (GH) and various other endothelial vascular disorders. In this study, we aim to assess thyroid function in pregnant women with hypertensive disorders, with the goal of obtaining current insights into the underlying causes, mechanisms, and consequences of thyroid dysfunction in the development of gestational hypertension. There was a statistically significant difference ( $P=0.001$ ) observed in the mean value of TSH between hypertensive pregnant women and normotensive subjects. The observed notable

increase in thyroid-stimulating hormone (TSH) levels among pregnant women with hypertension can be attributed to a condition of thyroid dysfunction referred to as hypothyroidism. Hypothyroidism is primarily an autoimmune disorder characterised by the activation of antigen presenting dendritic cells through self-proteins. Nevertheless, the antigen presenting dendritic cells that have been activated can subsequently induce the T-cells to generate cytokines that facilitate the development of hypertension via vascular remodelling, leading to an increase in peripheral vascular resistance.<sup>[9]</sup> This discovery aligns with previous research conducted in Australia, India, and Kano, Nigeria, as well as in Australia.<sup>[10-12]</sup> These studies have consistently reported notable elevations in the average levels of thyroid-stimulating hormone (TSH) among pregnant women with hypertension in their respective regions. However, it should be noted that this particular finding contradicts the results reported by Pasupathi et al,<sup>[13]</sup> who found no significant difference between Indian hypertensive and normotensive pregnant individuals. The current study found that the average TSH level ( $4.11 \pm 1.25$ ) falls within the acceptable reference range (0.4–6.0  $\mu\text{IU/ml}$ ) for the population under investigation.

In contrast, the average serum concentration of FT3 was found to be significantly lower in pregnant women with hypertension compared to pregnant women without hypertension. However, there was no notable difference in the average serum concentration of FT4 when comparing both hypertensive and normotensive cases. FT4 and FT3 refer to the free circulating thyroid hormones, specifically Thyroxine (T4) and Triiodothyronine (T3). These hormones are synthesised by thyroid follicular cells in the thyroid gland through the action of thyroperoxidase, an enzyme that facilitates the binding of iodine to tyrosine residues. T4 is considered a pro-hormone and serves as a storage form for the active and primary thyroid hormone, T3.<sup>[14]</sup> Moreover, the conversion of T3 is facilitated by iodothyronine deiodinase in the tissues [14]. Hence, the observed lack of significant variation in serum levels of FT4 between hypertensive and normotensive pregnant women may be attributed to the normal enzymatic activity of thyroperoxidase in both groups. Conversely, the apparent decrease in FT3 levels in hypertensive individuals compared to normotensive individuals may be attributed to the relative inhibition of iodothyronine deiodinase in hypertensive pregnant women. T3 is a thyroid hormone that is metabolically active and may potentially induce vasodilation in vascular smooth muscle cells.<sup>[15]</sup> There is also existing documentation indicating that hypertension is an autoimmune disorder that results in the compromised synthesis of vasodilators, including endothelin, nitric oxide (NO), and T3. Hence, the notable reduction in the serum concentration of FT3 may be attributed to the relative suppression of FT3 release, which is a consequence of thyroid dysfunction linked to heightened peripheral

vasoconstriction, a factor implicated in the elevation of blood pressure. This observation is consistent with the findings reported by other researchers.<sup>[10,12,16]</sup> The observed values deviated from the values reported by Pasupathi et al,<sup>[13]</sup> in their study on pregnant women in India. Furthermore, the prevalence of thyroid disorders among the individuals involved in the study exhibited a noteworthy disparity in subclinical hypothyroidism ( $P < 0.05$ ), while no substantial variances were observed in euthyroid, overt hypothyroidism, subclinical hyperthyroidism, and overt hyperthyroidism ( $P > 0.05$ ).

The majority of women diagnosed with pregnancy-induced hypertension exhibited mild preeclampsia, accounting for 63% of cases. Severe preeclampsia was the second most prevalent condition, affecting 23% of women, while gestational hypertension (GHTN) was observed in 14% of cases. A study conducted by Manjusha et al. reported a comparable occurrence of gestational hypertension and preeclampsia, with rates of 19.2% and 78.8%, respectively.<sup>[17]</sup> Our study found a positive correlation between the severity of hypothyroidism and hypertension, indicating that as the severity of hypertension increased, so did the severity of hypothyroidism. There was a higher prevalence of euthyroid cases observed in gestational hypertension (85.71%) compared to severe preeclampsia (39.13%). A notable disparity was observed in the incidence of clinical hypothyroidism between individuals with gestational hypertension and those with severe preeclampsia. The prevalence of clinical hypothyroidism in women with severe Preeclampsia was 13.04%, whereas no instances of clinical hypothyroidism were observed in women with gestational hypertension. In a similar vein, a notable disparity was observed in the prevalence of subclinical hypothyroidism between individuals with gestational hypertension (14.29%) and those with severe preeclampsia (47.83%). In a study conducted by Khaliq et al,<sup>[18]</sup> it was observed that there is a notable distinction between severe and mild cases of Preeclampsia in women. Specifically, the severe group exhibited a significant elevation in serum Thyroid-Stimulating Hormone (TSH) levels compared to the mild group. In a study conducted by Osathanordh and colleagues,<sup>[19]</sup> it was observed that there was a notable reduction in thyroid hormone levels among individuals with severe Preeclampsia when compared to those with mild Preeclampsia. In a study conducted by Minire et al,<sup>[20]</sup> it was found that among women with preeclampsia, there were incidences of complications such as eclampsia, abruptio placenta, HELLP syndrome, renal failure, and DIC. The reported percentages for these complications were 3.3%, 6.9%, 4.2%, 12.3%, and 2.79% respectively. The study yielded outcomes that were largely comparable. In a study conducted by Khanaam et al,<sup>[21]</sup> it was observed that there was a significant increase in the prevalence of hypothyroidism among individuals diagnosed with preeclampsia. Das et al,<sup>[22]</sup> discovered a statistically

significant association between elevated levels of thyroid-stimulating hormone (TSH) and thyroid disorders in women with preeclampsia.

In addition, there was a significant correlation observed between the serum concentration of thyroid-stimulating hormone (TSH) and both systolic blood pressure (SBP) and diastolic blood pressure (DBP) among pregnant women with hypertension. There was no statistically significant correlation observed between serum levels of FT3 and FT4 and both systolic blood pressure (SBP) and diastolic blood pressure (DBP) when these variables were examined in relation to each other. Consequently, the serum concentration of thyroid-stimulating hormone (TSH) rises as hypertension progresses. This discovery suggests that the presence of hypothyroidism is linked to the occurrence of hypertension during pregnancy, as evidenced by the notable disparity in subclinical hypothyroidism rates between pregnant women with hypertension and those without. In a study conducted in India, Nanda et al,<sup>[23]</sup> observed a comparable outcome among pregnant women with hypertension.

## CONCLUSION

The present study revealed a significant correlation between thyroid hypofunction and pregnancy induced hypertension. Further investigation is warranted to explore the relationship between thyroid function and preeclampsia due to limitations such as a small sample size, geographical variation, diverse racial backgrounds, and disparate dietary patterns within the study population. It is recommended that thyroid function be screened in all pregnant women, with a particular emphasis on those experiencing pregnancy induced hypertension.

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