

Original Article

Status of Thyroid Hormone Parameters in Hypertensive Disorders of Pregnancy

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ABSTRACT

Introduction: Hypertensive disorders of pregnancy (HDP) are the most common complications observed during pregnancy and are a leading cause of maternal and perinatal morbidity and mortality. Thyroid hormone abnormalities are prevalent in females of reproductive age group. However, the relation between thyroid hormones and hypertensive pregnant women remains unclear. This study aims to assess the status of thyroid hormone abnormalities in patients with HDP.

Materials and Methods: This is a case-control study conducted for one year in Karnali Province Hospital and Deuti Hospital, Surkhet, Nepal. Thirty hypertensive patients with singleton pregnancies in the third trimester were taken as case and 30 healthy normotensive singleton pregnant women as control and their thyroid hormone parameters were compared. Statistical analysis was done using SPSS version 21.

Results: The mean gestational age of recruited study subjects and control were 37.00 ± 3.04 weeks and 35.70 ± 3.83 weeks ($p > 0.05$). The mean value of TSH was significantly higher ($p < 0.05$) in hypertensive subjects (4.19 ± 2.95) $\mu\text{IU/L}$ when compared with the control (2.67 ± 1.71) $\mu\text{IU/L}$. There was no significant difference when the serum level of FT3 and FT4 were compared between hypertensive and normotensive pregnant women ($p > 0.05$). Subclinical hypothyroidism was found in 16.66% of hypertensive subjects.

Conclusions: HDP is associated with thyroid hormone abnormalities. An increase in TSH levels with normal FT3 and FT4 levels were found to be the most common form of thyroid dysfunction during pregnancy.

Keywords: Hypertension; Pregnancy, Thyroid hormones

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INTRODUCTION

Hypertension is the most common medical problem that affects 10% of total pregnancies and is accompanied by an increase in fetal and maternal morbidity and mortality.¹⁻³ Hypertensive disorders of pregnancy (HDP) are common and represent a range of disease ranging from chronic and gestational hypertension to eclampsia.⁴ National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy recommended and classified HDP into 4 categories: 1) chronic hypertension, 2) preeclampsia-eclampsia, 3) preeclampsia superimposed on chronic hypertension, and 4) gestational hypertension.⁵

Thyroid hormone abnormalities frequently occur during pregnancy and are associated with adverse health outcomes for both mother and child, including increased risk of miscarriage, gestational hypertension, preterm delivery, placental abruption, low birth weight, and fetal death.⁶ Both hyper and hypothyroidism can negatively affect the prognosis of pregnancy. Moreover, thyroid dysfunction is considered to be correlated with gestational hypertensive disorders. The severity of preeclampsia is positively correlated with the level of thyroid-stimulating hormone (TSH). Hypothyroidism has been confirmed to be an independent risk factor for preeclampsia and fetal growth restriction. However,

the underlying roles of thyroid function in hypertensive disorders during pregnancy are still poorly established.⁷⁻⁹ The main objective of this study was to find out the thyroid hormone abnormalities in hypertensive disorders of pregnancy.

MATERIALS AND METHODS

The present case-control observational study was conducted in the Department of Obstetrics and Gynaecology of Province Hospital, Karnali Province, and Deuti Hospital, Surkhet. This study was conducted for a period of one year from 15th March 2018 to 14th March 2019. This study was approved by the ethical committee and informed consent was taken. The study includes 30 hypertensive patients (aged between 18-40 years) with singleton pregnancies categorized in 4 subgroups (gestational hypertension, mild preeclampsia, severe preeclampsia, eclampsia) as case group and 30 healthy normotensive singleton pregnant women of same age group and gestational age of pregnancy in the third trimester constituted the control group. The diagnostic criterion for HDP was an increase in blood pressure to $\geq 140/90$ mmHg after 20 gestational weeks in previously normotensive women. Patients of the first or second trimester, multiple pregnancies, known thyroid disorders, chronic hypertensive on medication, and gestational diabetes mellitus were excluded from the study.

3 ml of whole blood was collected in a plain tube and was allowed to clot and centrifuged to separate serum. Serum concentrations of TSH free tri-iodothyronine (FT3) and free thyroxine (FT4) were measured using a highly sensitive and specific chemiluminescence immunoassay (CLIA) method. All variables were presented as number and frequency and were arranged in tables and figures. Predesigned performa was used to collect the data. Data were expressed as mean \pm standard deviation. The Independent t-test, Chi-square, and Fisher exact test were used to compare those variables with respect to case and control. Statistical analysis was done by SPSS software (Statistical Package for the Social Sciences, version 21.0, SPSS Inc, Chicago, USA). The level of significance (p-value) was set at 0.05.

RESULTS

Among the study population, the maximum study population was between the ages 21-30 years which was approximately 73.40% in both HDP subjects and normotensive pregnant women. The frequency and percentage of study participants (both case and control) were very less in age below 21 years and above 31 years. (fig. 1) There was no statistically significant difference between the mean ages of the two groups ($p > 0.05$).

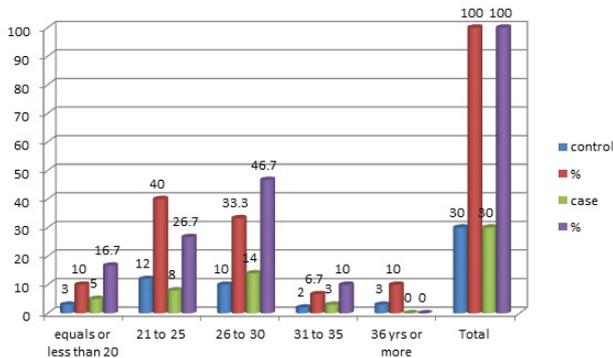


Figure 1: Distribution of HDP and normotensive pregnant women according to age group

The mean values of TSH were 4.19 ± 2.95 μ IU/L in hypertensive subjects and 2.67 ± 1.71 μ IU/L in the control subjects respectively (Table 1) which was significantly higher in hypertensive subjects when compared with the control ($p < 0.05$). There was no significant difference when the serum level of FT3, FT4, and gestation period were compared between hypertensive and normotensive pregnant women ($p > 0.05$). Among the hypertensive females, 5 (16.66%) patients had subclinical hypothyroidism and the remaining ($n = 25$; 83.33%) were euthyroid.

Table 1: Mean and standard deviation of Age, FT3, FT4, TSH, and period of gestation among the study population (n=60)

Parameters	Case		Control		p-value
	Mean	SD	Mean	SD	
Age (years)	25.57	4.36	26.00	5.60	0.739
FT3 (pg/ml)	2.85	0.46	2.98	0.17	0.157
FT4 (ng/ml)	1.08	0.99	0.93	0.10	0.425
TSH (μ IU/L)	4.19	2.95	2.67	1.71	0.018
POG (weeks)	37.00	3.04	35.70	3.83	0.15

POG: Period of gestation

Among studied populations with Preeclampsia, TSH value correlated significantly with mild preeclampsia whereas FT3 and FT4 values in mild preeclampsia women did not show any statistical difference with that of control. (Table 2) In the case of severe preeclampsia, no correlation was observed with thyroid function test findings (p -value: > 0.05) as compared to healthy normotensive pregnant women.

Table 2: Mean and standard deviation of FT3, FT4, TSH in Mild Preeclampsia, and normotensive pregnant women.

Parameters		Mean	Std. Deviation	p-value
FT3 (pg/ml)	case	2.9022	0.07311	0.191
	control	2.9803	0.16982	
FT4 (ng/ml)	case	0.8856	0.10285	0.196
	control	0.9343	0.09598	
TSH (μ IU/L)	case	4.3089	1.35093	0.013
	control	2.6747	1.71407	

DISCUSSION

Thyroid hormones play an important role in cardiovascular physiology and the regulation of blood pressure that affects ventricular remodeling.^{10,11} Alterations in maternal hemodynamic occurs during pregnancy with HDP. Peripheral vasoconstriction secondary to maternal systemic inflammation and endothelial cell activation are also considered to be responsible for hypertensive disorders during pregnancy.⁷

In our study, the mean gestational age of the study participants was found to be higher in the hypertensive group (37.00 ± 3.04 weeks) compared with normotensive pregnant women whose mean gestational age was 35.70 ± 3.83 weeks. The differences between them were not found to be statistically significant ($p > 0.05$). Our findings were supported by the study done in 2015 by Abdulslam and Yahaya in the Nigerian population in

which they observed that the differences between the period of gestation (POG) in the case and control group were not found to be statistically significant ($p > 0.05$).¹² Thus, our study participants were well matched with respect to their gestational age.

We had observed that the mean value of serum TSH (4.19 ± 2.95 $\mu\text{IU/L}$) was higher in pregnant women with HDP compared to normotensive pregnant women (2.67 ± 1.71 $\mu\text{IU/L}$). A similar result was observed in a study by Abdulslam and Yahaya where mean values of TSH in case and control were 2.1 ± 1.7 $\mu\text{IU/L}$ and 1.6 ± 1.0 $\mu\text{IU/L}$ respectively.¹² This finding is also supported by the related studies conducted in Anambra state of Nigeria and Odisha state of India in which the researchers reported significantly increased mean values of TSH in hypertensive pregnant women.^{13,14} This significant increase of TSH in hypertensive pregnant women may be recognized as thyroid hormone abnormalities known as hypothyroidism. In hypothyroidism, there is an activation of antigen-presenting dendritic cells by self-proteins which in turn stimulate the T-cells to produce cytokines that promote hypertension through vascular remodeling (increased peripheral vascular resistance).¹⁵

On the contrary, there were no significant differences in the mean serum level of FT3 and FT4 in both hypertensive and normotensive groups. The findings of our study have been supported by two different studies done in the Nigerian population. Abdulslam and Yahaya also found that the mean serum FT3 was 6.4 ± 2.7 pmol/L and 6.9 ± 2.6 pmol/L among participants in hypertensive and normotensive groups. In 2017, Maduka Ignatius et al. reported the mean value of FT4 in hypertensive pregnant women (2.1 ± 2.3 pg/dl) and compared them with the mean value of FT4 in normotensive pregnant women (2.3 ± 2.1 pg/dl).¹³ However, both Nigerian studies concluded that there was no statistically significant difference in the mean value of FT3 and FT4 between these two groups ($p > 0.05$).^{12,13} The virtual nonsignificance difference in serum level of FT3 and FT4 in both hypertensive and normotensive group may be due to the normal functioning of thyroid peroxidase enzyme as well as iodothyronine deiodinase in both subjects.¹³

We found a higher level of TSH (4.30 ± 1.35) in mild preeclampsia whereas, in normotensive control, the level of TSH was 2.67 ± 1.71 . A significant p-value ($p < 0.05$) was seen in comparing these two groups. Moreover, the p-value of FT3 and FT4 were ($p > 0.05$) which was greater than the set value of P thus, the statistical difference between case and control group has not seen in our study. These findings are also supported by the study done in 2005 by Kumar et al. in which they have shown that mean serum TSH was significantly high ($p < 0.001$) and FT3 and FT4 were without

alterations in preeclampsia women.¹⁶ Rafeinia et al. studied the thyroid hormones level in preeclampsia women in Gorgan and reported the findings similar to our study¹⁷ whereas other studies reported an increased level of TSH and decreased levels of T3 and T4 in preeclampsia women in comparison with normotensive pregnant.¹⁸⁻²⁰ Some other findings have indicated a high risk of hypertensive disorders in mothers with hypothyroidism²¹ or hyperthyroidism,²² while some of the other studies did not show any associations.^{23,24}

There was no significant correlation between serum level of FT3, FT4, and TSH in severe preeclampsia as compared to healthy normotensive pregnant women. The association between thyroid function and severe eclampsia needs further investigation because of the small number of subjects in this study. A multi-centric study may answer the association and mechanism of thyroid abnormality in severe eclamptic women in terms of geographical variation. Therefore, according to our findings, thyroid abnormalities might not be associated with severe eclampsia which is similar to the study done by Mostaghel et al. in 2008.¹⁸

Subclinical hypothyroidism was found in 16.66% of hypertensive pregnant women and was considered as the most common form of thyroid dysfunction in this study. Subclinical hypothyroidism was associated with HDP, particularly among women diagnosed with mild preeclampsia in the third trimester. However, the exact mechanism of HDP remains unknown. Besides subclinical hypothyroidism, multiple factors including hormonal disorders, angiogenic factors imbalances, and placental hypoxia also contribute to an increase in blood pressure. Moreover, in women with subclinical hypothyroidism, decreased nitric oxide secretion, and impairment of vasodilation in endothelial tissues may be the underlying mechanism involved for HDP. An increase in blood pressure may be related to hypercoagulability, increments in blood viscosity, and lipid abnormalities in patients with subclinical hypothyroidism potentially increase the risk for atherosclerosis. However, the exact mechanism remains unclear till now.^{10,11,25,26}

CONCLUSIONS

Hypertensive disorders of pregnancy are associated with thyroid hormone abnormalities. Pregnant women with HDP had a significantly higher level of TSH as compared to normotensive pregnant women. Subclinical hypothyroidism identified during pregnancy has an increased risk for HDP when compared to euthyroid pregnant women. Thus, the estimation of TSH could be a good predictor of the development of hypertension in pregnancy.

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