

## ASSOCIATION BETWEEN HYPERTENSIVE DISORDERS OF PREGNANCY AND MATERNAL THYROID STIMULATING HORMONE LEVELS-A CASE CONTROL STUDY

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### Abstract

**Background:** With rise in occurrence of hypertensive disorders of pregnancy particularly pre-eclampsia, there is a necessity to study its association with other comorbid conditions like thyroid disorder which may have shared pathophysiology. The objective is to study the association between thyroid hormone status with preeclampsia and correlate it with severity of pre-eclampsia. **Materials and Methods:** It was a case control study, 278 women attending tertiary care hospital between the study period September 2020 to August 2021 were recruited in the study in which 139 women were cases (diagnosed as preeclampsia) and 139 were taken as control (healthy normotensive women). Assessment of thyroid status of cases and control was done. Association was studied between thyroid hormone status and pre-eclampsia and co-related with severity of preeclampsia. SPSS was used for analysis. **Result:** There was a significant association between pre-eclampsia and thyroid hypofunction (overt and sub clinical hypothyroidism) with P-value being 0.04. Odds-ratio indicates that preeclampsia group have chance of higher TSH (>4.8 mIU/L) by 2.19 times. The association between severity of pre-eclampsia and thyroid hypofunction (subclinical and overt hypothyroidism) was found to be statistically significant (p= 0.02). Odds ratio indicates that severe preeclampsia group have 2.87 times more chance of thyroid hypofunction. However the correlation coefficient for the entire study population was (-0.0532) between serum albumin and serum TSH, which suggests both values were independent of each other. Serum uric acid was significantly higher in cases as compared to controls (p<0.01). **Conclusion:** A positive association was found between thyroid hypofunction and pre-eclampsia and it was found to be statistically significant. However Serum TSH values need to be adjusted to the population and hospital for cut offs for reliable diagnosis.

## INTRODUCTION

Thyroid dysfunction establishes one of the commonest endocrine disorders during pregnancy after diabetes mellitus.<sup>[1]</sup> Pregnancy is related with profound modifications in the regulation of thyroid function. These variations are the result of the various factors like an increase of thyroid-binding globulin (TBG) due to raised estrogens and human chorionic gonadotropin (HCG), increased renal losses of iodine due to increased glomerular filtration rate, alterations in the peripheral metabolism of maternal thyroid hormones, and

modifications in iodine transfer of placenta. It has long been documented that maternal thyroid hormone excess or deficiency can effect maternal outcomes like miscarriages, anaemia in pregnancy, preeclampsia, abruption of placenta and postpartum hemorrhage and fetal consequence at all stages of pregnancy like prematurity, low birth weight, increased neonatal respiratory distress and fetal thyroid abnormalities which may validate screening for thyroid functions in pregnancy. In India incidence of pre-eclampsia as recorded from hospital statistics fluctuate widely from 5-15%.<sup>[2]</sup> This disorder is exceptional to human pregnancy in

which abundant genetic, immunological and environmental factors interrelate.<sup>[3,4]</sup> Therefore, it is a foremost cause of maternal and fetal morbidity and mortality throughout the world and still is one of the most complex problems in obstetrics. Women complicated with preeclampsia have high incidence of hypothyroidism that might correlate with the severity of preeclampsia.<sup>[4]</sup> The mechanism of hypothyroidism in pre-eclamptic women is not well identified but changes in thyroid function are due to high circulation of estrogens.<sup>[5]</sup> There are limited number of studies on thyroid function in preeclampsia and it has been recommended that there may be a reality of mutual effects between preeclampsia and thyroid function. Therefore the rationale behind this study has been undertaken to evaluate the association between thyroid hormone status and pre-eclampsia and co-relate it with the severity of pre-eclampsia.

## MATERIALS AND METHODS

A case control study was carried out in tertiary care hospital. 278 women were recruited in the study in which 139 women were cases and 139 were taken as controls between the study period September 2020 to August 2021

### Inclusion Criteria

Diagnosed cases of preeclampsia.

### Exclusion Criteria

H/o heart diseases, pregnancy induced hypertension without proteinuria, H/o pre-eclampsia already on antihypertensive drugs, H/o thyroid disease, H/o any metabolic disorder before or during pregnancy, Medical disorders like RHD, Epilepsy, H/o Molar pregnancy, H/o Multiple pregnancy, H/o congenitally malformed fetus.

### Case

Defined on the basis of inclusion and exclusion criteria i.e. diagnosed cases of pre-eclampsia characterized by elevation of blood pressure of more than 140 mmHg systolic or more than 90 mm of Hg diastolic with proteinuria (more than 300 mg/l in 24 hours specimen) after 20 weeks of gestation in previously normotensive non proteinuric pregnant women.

### Control

The control constituted of equal number of matched age, parity, socio-demographic status, gestational age; healthy normotensive pregnant women visiting the labour ward.

### Methodology

This study was approved by Institutional Ethical Committee. Written informed consent was obtained from all participants recruited in study after they had been made aware of purpose of study. Details of the women were noted such as name, age, symptoms,

menstrual history for menarche. Past obstetric history was asked for duration of marriage, infertility, gravidity and parity status, recurrent abortions, pre-eclampsia, growth restriction and mental retardation in previous pregnancy. Past medical history was asked for any associated medical disorders like diabetes, thyroid disorders, exposure to radiation or autoimmune disorders. Significant surgical history, family history was also asked. A thorough clinical examination including height, weight, pulse, blood pressure, pedal oedema, thyroid enlargement, etc. was done followed by systemic examination. In obstetrical examination gestational age, presentation and amount of liquor was noted and fetal heart sounds were auscultated with stethoscope. All investigations pertaining to complications of preeclampsia like liver and kidney function tests, serum uric acid were also done. Assessment of thyroid status of cases and controls were done with serum Free T3, T4 and TSH for which 10ml venous blood sample was taken from the cubital vein irrespective of NBM status. (i) In cases, after the diagnosis of pre-eclampsia was made but before the initiation of the antihypertensive treatment and before the delivery and (ii) In controls, after admission.

### Statistical Analysis

Study group (cases vs control) was considered as primary explanatory variable. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Categorical outcomes were compared between study groups using Chi square test /Fisher Exact test. P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

## RESULTS

[Table 1] shows the distribution of cases and controls according to age, parity and gestational age. The two groups were comparable in age, parity, socio-demographic and clinical characteristics since they are not significant. ( $p>0.05$ ).

As per [Table 2] the distribution according to mean levels of thyroid hormone, the difference in Mean TSH level and Mean FT3 levels in cases and controls was found to be statistically significant ( $p<0.001$ ). For Mean FT4 it was not significant.

According to [Table 3] there was a significant association between pre-eclampsia and thyroid hypofunction (overt and sub clinical hypothyroidism) with P-value being 0.04. Odds-ratio indicates that preeclampsia group have chance of higher TSH ( $>4.8$  mIU/L) by 2.19 times. (95% confidence intervals= 1.02–4.69).

As per [Table 4] shows the correlation of Thyroid hormone status with severity of Pre-eclampsia. The association between severity of pre-eclampsia and thyroid hypofunction (subclinical and overt

hypothyroidism) was found to be statistically significant (p= 0.02). Odds ratio indicates that

severe preeclampsia group have 2.87 times more chance of thyroid hypofunction.

**Table 1: Age, parity and gestational age wise distribution of cases and controls**

Mean	Cases	Controls	p-value
Age in years	23.18+0.30	22.38+0.2	0.46
Parity	0.66+0.11	0.85+0.13	0.21
Gestational age in weeks	36.79+0.26	38.17+0.22	0.12

**Table 2: Distribution according to mean levels of thyroid hormone**

Mean	Cases	Controls	tvalue	pvalue
Mean TSH (μIU/ml)	3.13+0.18	1.92 +0.12	5.370	P<0.001
MeanFT3 Level(pg/ml)	3.07 +0.04	3.49 +0.04	6.298	P<0.001
MeanFT4 Level(pg/ml)	0.89+ 0.01	0.86 +0.01	1.197	P=0.23

**Table 3: Distribution of cases and controls according to thyroid status**

Thyroid Status	Cases		Controls		Total		Test of Significance
	(n=139)	%	(n=139)	%	(n=278)	%	
Euthyroid	116	77	126	88	242	82.5	X <sup>2</sup> =4.31 P=0.04 OR=2.19
Sub Clinically Hypothyroid	20	20	10	10	30	15	
Overt Hypothyroid	3	3	3	2	6	2.5	
Total	139	100	139	100	278	100	

**Table 4: Correlation of thyroid status with severity of pre-eclampsia**

Thyroid status	Cases				Test of Significance
	Severe Pre-eclampsia		Non-Severe Pre-eclampsia		
	(n=59)	%	(n=80)	%	
Euthyroid	52	64.86	76	84.13	X <sup>2</sup> =4.81 P=0.02OR=2.87
Subclinical hypothyroid	6	29.73	3	14.29	
Overt Hypothyroid	1	5.41	1	1.59	
Total	59	100	80	100	

## DISCUSSION

Pre-eclampsia is a serious complication of pregnancy with unknown etiology that may occur at any stage of second or third trimester. With the case and control group having comparable age and gestational age, hypothyroidism in hypertensive pregnant women was found to be significantly very high with 22% of cases with serum TSH > 3.5 mIU/ml than in normotensive pregnant women with only 14% patients with hypothyroidism. Earlier studies have also shown higher number of preeclamptic patients with hypothyroidism. Serum albumin levels were significantly lower in the hypertensive group with 21.33 % cases as compared to normotensive group with 11% patients having serum albumin < 3.0g/dL.<sup>[6,7]</sup> we also found that the decrease in serum albumin correlated with the severity of pregnancy induced hypertension.<sup>[7,8]</sup>

It was found that the mean serum TSH level increased as the pathology of pregnancy induced hypertension progressed along the spectrum of gestational hypertension to non-severe to severe preeclampsia which showed a stronger association of hypothyroidism with severity of pregnancy induced hypertension based on odds ratio.<sup>[7,9,10]</sup>

The negative correlation between the serum TSH and serum albumin levels showed both values were independent of each other. There has been no correlation found at all between the two values in certain studies before. Some of the earlier studies did not find any significant association between

hypertension and serum TSH levels.<sup>[11,12]</sup> Other blood parameters were also compared between the case and control groups. The albumin to globulin ratio was significantly higher in the hypertensive group. The effect of hypertension on birth weight of babies was seen as a fetal outcome with significantly lower birth weights in hypertensive patients as compared to normotensive patients. Nahid Mostaghel et al reported no significant difference in cases and controls in thyroid levels.<sup>[13]</sup> This may be due to the fact that the blood sample was taken just at the time of diagnosis of pre-eclampsia. It is possible that low titers of T3 and T4 along with high TSH titers would be observed at a later stage of pre-eclampsia with severe disease and low plasma albumin levels.

## CONCLUSION

The results of the study suggest there may be a higher chance of hypothyroidism in hypertensive patients as the spectrum of severity of hypertension advances. The need for trimester specific reference range of thyroid hormone levels for study population also represents a prospective area of further research. This study recommends that a multicentric study with large population is needed to support the hypothesis that thyroid hormone abnormalities are associated with pre-eclampsia. Identification of one may help in anticipation of existence of the other condition which may further

prevent maternal mortality and morbidity along with adverse fetal outcomes.

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