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A STUDY TO EVALUATE THYROID HORMONES STATUS IN CASES OF PRE ECLAMPSIA

Debasish Char [1], Priyadarshi Mandal [2], Shuvankar Halder [3], Sucheta Biswas [4]

1. Assistant Professor, Department of Obstetrics & Gynaecology, NRS Medical College, Kolkata.

2. Assistant Professor, Department of Obstetrics & Gynaecology, NRS Medical College, Kolkata.

3. Post graduate trainee, Department of Obstetrics & Gynaecology, NRS Medical College, Kolkata.

4. Assistant Professor, Department of Physiology, IPGME&R, Kolkata.

Corresponding author: Dr Sucheta Biswas, Email Id: mantibiswas.8@gmail.com

ABSTRACT:

Background: The objective of this study is to establish association between thyroid hormone status & pre-eclampsia and also the level of thyroid hormone concentration with severity of pre-eclampsia.

Methods: In this observation based descriptive cross sectional study, 100 pregnant women including 50 cases of pre-eclamptic mothers and 50 control ie normotensive pregnant women attending tertiary care hospital during one year were recruited in the study. Serum FT3, FT4 and TSH were measured in both cases & control. Association between thyroid hormones status with pre-eclampsia as well as with its severity was noted.

Result: Significant association between pre-eclampsia and thyroid hormone levels was found between the normotensive group and pre-eclamptic group (p value<0.001 for FT3, 0.0345 for FT4 & <0.0001 for TSH). The association between severity of pre-eclampsia and thyroid hormone status was also found to be statistically significant (p value 0.0001 for FT3, <0.0001 for FT4 and TSH). Sub-clinical hypothyroidism was more common in mild pre-eclampsia group but overt hypothyroidism more commonly seen in severe pre-eclamptic group (chi-square value<0.0001).

Conclusion: Positive correlation was seen between thyroid dysfunction & pre-eclampsia. Thyroid hormone concentration may reflect the severity of pre-eclampsia. The association may be useful in understanding the pathological process of pre-eclampsia as well as criteria for early prediction of pre-eclampsia.

Key words: FT3, FT4, TSH, Pre-eclampsia.

INTRODUCTION:

Pre eclampsia is one of the common complications in obstetrics associated with increased feto-maternal morbidity and mortality in the developing countries including India accounting for 1.5% of its incidence. Thyroid hormone status alters during pregnancy leads to altered Nitric oxide as well as vascular endothelial growth factor levels, as a result of this there is increased chance of vasoconstriction, stiffness of arterioles and diastolic hypertension.

Hypothyroidism and hyperthyroidism both may be associated with pre eclampsia. Though the association of hyper thyroxinemia is mild but the incidence of hypothyroidism in pre eclampsia mothers are high which might correlate with its severity. It is seen that 16.7%

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cases of sub clinical hypothyroidism and 43.7% cases of overt hypothyroidism during pregnancy are associated with pre eclampsia[1]. Hypothyroidism in pre eclampsia can cause maternal morbidity and fetal growth restrictions, intrauterine death or congenital hypothyroidism[2].

The mechanism of hypothyroidism in pre eclampsia mothers is still unidentified but high circulating estrogens may account for changing thyroid factors during pregnancy[3]. Low thyroid hormone concentrations in pre eclampsia is still controversial which is related to decreased concentration of plasma protein and high endothelin levels which is a potent vasoconstrictor produced after vascular endothelial injury[4,5]

So the objective of our study is to establish association between thyroid hormones status and pre eclampsia and also level of thyroid hormones with severity of preeclampsia; so that thyroid hormone status may be a good predictor of preeclampsia.

MATERIALS AND METHODS:

This observation based on descriptive cross sectional study was conducted in the department of Obstetrics and Gynaecology, NRS Medical College and Hospital, Kolkata. The study was carried out in 100 pregnant women including 50 cases of preeclampsia mothers and 50 control i.e. normotensive pregnant women from March 2020 to September 2021. The study was conducted after approval of institutional ethics committee. All pregnant women fulfilling the eligibility criteria were included in the study sample. Serum FT3, serum FT4 and Serum TSH were measured. Then association between thyroid hormones status and preeclampsia were evaluated and also level of thyroid hormones with severity of preeclampsia were evaluated.

INCLUSION CRITERIA INCLUDES:

All pregnant women from 20 weeks of gestation up to termination of pregnancy who has blood pressure 140/90mmHg or more with additional criteria like proteinuria 1+ or more and patients with features suggestive of severe preeclampsia.

EXCLUSION CRITERIA INCLUDES:

Gestational hypertension
Chronic hypertension
Pre existing renal disease
Diabetes mellitus
Pre existing thyroid disease
Normotensive pregnant women

Statistical analysis was done by Chi square technique using spss vs 27.0 and graphpad prism version 5 statistical software. A p value of <= 0.05 was considered statistically significant.

RESULT:

During our study period 50 cases of pre eclampsia mothers and 50 cases of controls ie. normotensive pregnant women were taken for study.

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Table 1 shows demographic characteristics of the studied groups. There was no statistical difference in maternal age and weeks of gestation between two groups. Mean maternal age in both groups were slightly more than 26 years (mean 26.66 +/- 3.66 in cases vs 26.72 +/- 3.34 in control groups). The mean gestational age during sample collections in cases was 28.50 +/- 5.30 vs 28.40 +/- 4.64 in control groups. There is no statistical significance in maternal age or gestational age between two groups. In normotensive, the mean SBP of patients was 122.56 +/- 7.45 whereas in pre eclampsia group the mean SBP of patients was 148+/-9.41(p value< 0.001).

The mean DBP in normotensive patients was 81.24+/-3.72 and in pre eclampsia patients was 97.48+/- 8.64(p value<0.0001). In normotensive patients the mean 24 hours urinary protein was 0.1946+/-0.413. Whereas in pre eclampsia the mean 24 hours urinary protein was 0.2434+/- 0.1143(p value<0.0055).

Table 1: Demographic characteristics of the studied group:

Characteristics	normotensive group (n=50)	preeclampsia group(n=50)	p value
mean maternal age	26.66+/-3.66	26.72+/-3.54	0.932
period of gestation during sampling	28.50+/-5.30	28.40+/-4.64	0.919
SBP(mmHg)	122.56+/-7.45	148.48+/-9.41	<0.0001
DBP(mmHg)	81.24+/-3.72	97.48+/-8.64	<0.0001
urinary protein(24hrs)	0.1946+/-0.413	0.243+/-0.1143	0.0055

Table 2 compares the thyroid hormones level between normotensive and pre eclampsia group. In normotensive the mean FT3 was 3.142+/-0.0324 and in pre eclampsia patients the mean FT3 was 3.56+/-0.047, which is statistically significant.(p value <0.001). The mean FT4 in normotensive groups was 0.93+/-0.11 and in pre eclampsia group the mean was 0.83+/-0.33 which is statistically significant (p value<0.0345). In normotensive the mean TSH was 1.54+/-0.69. It in pre eclampsia group the mean TSH was 3.42+/- 2.19. Distribution of mean TSH between two groups was statistically significant (p value<0.0001).

Table 2: Comparison of thyroid hormone levels between normotensive and pre eclampsia group:

	normotensive group(n=50)	preeclampsia group(n=50)	p value
free T3	3.142+/-0.0324	3.56+/-0.047	<0.001
free T4(ng/dl)	0.93+/-0.11	0.83+/-0.33	0.0345

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TSH(micro IU/ml)	1.54+/-0.69	3.42+/-2.19	<0.0001

Table 3 correlates thyroid hormones level with the severity of pre eclampsia. In mild pre eclampsia the mean FT3 was 3.26+/-0.42. But in pre eclampsia with severe features FT3 was 4.01+/-0.76 (P value 0.001). In case of FT4, the mean was 0.96+/- 0.20 in mild cases of pre eclampsia and mean was 0.32+/-0.22 in severe case of pre eclampsia (p value<0.0001). Distribution of both mean FT3 and FT4 with pre eclampsia group was statistically significant. In patients with mild pre eclampsia the mean TSH was 2.64+/-1.64, but in patients with severe features the mean was 6.51+/-1.04(p value<0.0001). This distribution of mean TSH with pre eclampsia group was statistically significant.

Table 3: Comparison of FT4 and TSH levels between mild preeclampsia and severe preeclampsia groups

	mild preeclampsia (n=40)	severe preeclampsia (n=10)	p value
free T3	3.26+/-0.42	4.01+/-0.76	0.001
free T4(ng/dl)	0.96+/-0.20	0.32+/-0.22	<0.0001
TSH(micro IU/ml)	2.64+/-1.64	6.51+/-1.04	<0.0001

Table 4 shows distribution of patients according to thyroid status.In normotensive, 48(96%) patients had euthyroid and 2(4%) patients had sub clinical hypothyroidism in thyroid disorders. But in mild pre eclampsia group, 24(60%) patients had euthyroid and 16(40%) patients had sub clinical hypothyroidism. In severe pre eclampsia group 8(80%) patients had overt hypothyroidism and 2(20%) patients had sub clinical hypothyroidism in thyroid disorders.

Table 4: Distribution of patients according to thyroid status

Thyroid status	normotensive group (n=50)	mild preeclampsia (n=40)	severe preeclampsia (n=10)
Euthyroid	48(96%)	24(60%)	0
Subclinical hypothyroidism	2(4%)	16(40%)	2(20%)
Overt hypothyroidism	0	0	8(80%)

Chi-square value < 0.0001

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Discussion:

Thyroid dysfunction associated with pre-eclampsia carries a higher risk of poor feto-maternal outcome. Increase angiogenic factors which decrease nitric acid production in pre-eclampsia. This may result in decrease in the thyroid capillary blood flow, may lead to hypothyroidism in pre-eclampsia. In this current research, we studied the status of thyroid hormones in pre-eclampsia as well as the level of thyroid hormones with the severity of pre-eclampsia.

In normotensive mothers, the mean age was 26.66+/-3.66 years, but in mothers with pre-eclampsia, the mean age was 26.72+/-3.34 years. Distribution of mean age with hypertensive disorders of pregnancy was not statistically significant (p 0.932). Mean age during sampling were 28.50+/-5.30 weeks & 28.40+/-4.64 weeks in normotensive and pre-eclampsia group respectively. During our study 14% patients were nulliparous in normotensive group & 12% patients were nulliparous in pre-eclamptic group. There was no significant difference in relation to age, period of gestation during sampling and parity between the two groups. These findings are similar with the study done by Banik P et al in respect to age but not correlate with the study done by Singh A et al, who reported that nulliparity is a risk factor to develop pre-eclampsia.[6,7]

During our study we found that the mean SBP was higher (148.48+/-9.41 mm of Hg) in pre-eclampsia patients compared to normotensive mothers (122.56+/-7.45 mm of Hg) **,** which was statistically significant. We also found that the mean DBP of patients were increased in patients with pre-eclampsia (97.48+/- 8.64 mm of Hg) compared to normotensive patients (81.24+/-3.72 mm of Hg), which was also statistically significant. Similar study was conducted by Nilima Vivek patil who had also found raised SBP & DBP in pre-eclampsia patients compared to normal pregnancy (p <0.0001).

In this study the mean 24 hours urinary protein excretion was increased in patients with pre-eclampsia (0.2434+/-0.1143) compared to normotensive patients (0.1946+/-0.413), which was statistically significant (p = 0.0055)**.** Urinary protein excretion was more common in pre-eclamptic patients as shown by Nilima vivek patil et al.[8]

Present study suggests that the mean SBP, DBP & 24 hours urinary protein excretion was increased in patients with severe features of pre-eclampsia (166.6+/-3.19, 113.8+/-2.90 & 0.4270+/-0.1297) respectively compared to patients with its mild variety (144.05+/-2.88, 93.4+/-2.52 & 0.1975+/-0.416) respectively (p <0.0001). Blood pressure & proteinuria were used as parameters for severity of pre-eclampsia in various literature.[8]

In this current study women with pre-eclampsia had higher FT3 level but lower FT4 level compared to normotensive Pregnant women (FT3: p <0.001, FT4: p= 0.0345). We found that the mean TSH of patients was decreased in normotensive patients (1.54+/-0.69) compared to pre-eclamptic patients (3.42+/-2.19) , which was statistically significant (p <0.0001). Ashok Kumar & his associates in their study found that mean FT3 & FT4 levels were not statistically significant difference between the two groups (FT3: p= 0.24,FT4= 0.25). Significantly higher TSH value was seen in pre-eclamptic mothers compared to the normotensive one (p <0.0001).[9,10]

It was found that the mean TSH was reduced in patients with mild pre-eclampsia (2.64+/-1.64) compared to severe pre-eclampsia (6.51+/-1.04) & this was statistically significant (p<0.0001). Patients with severe features of pre-eclampsia higher mean FT3 level was found

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compared to mild pre-eclamptic patients (4.01+/-0.76 vs 3.26+/- 0.42), which was statistically significant (p= 0.0001), but lower mean FT4 level was found in severe pre- eclampsia compared to its mild variety (0.32+/-0.22 vs 0.96+/-0.20, p <.0001). But in contrary to the study done by others statistically no significant differences were found in respect to FT3, FT4 & TSH levels when comparing patients between mild pre- eclampsia and severe pre-eclampsia.[11,12]

A total of 50 patients of pre-eclampsia were studied in in this current research, out of these patients 26 (52%) were diagnosed as having thyroid dysfunction. Among these 26 patients 18 (36%) having sub clinical hypothyroidism & 8 (16%) overt hypothyroidism (p <0.0001). Bankowska EM et al found that 78.2% of patients with pre-eclampsia had thyroid dysfunction and most common cause of thyroid dysfunction was sub clinical hypothyroidism in their study, supporting the findings of the present study.[13] Fifty five percent patients of pre-eclampsia had hypothyroidism in a study done by Kharb S et al.**[14]** However, contrary to the present study, thyroid dysfunction was not observed in pre- eclampsia patients by Khadem M et al.[15]

Statistically significant association was found between severity of pre-eclampsia & dysfunction of thyroid (both subclinical & overt hypothyroidism) (p <.0001) in our study. In a similar study chance of dysfunction of thyroid was 2.87 times higher in severe pre-eclampsia group.[16]

Conclusion: Positive correlation was seen between thyroid dysfunction and pre-eclampsia. Thyroid hormone concentration may reflect the severity of pre-eclampsia. The association may be useful in understanding the pathological process of pre-eclampsia as well as criteria for early prediction of pre-eclampsia. However association between pre-eclampsia and thyroid function needs further investigation due to small sample size, single centre based study & hospital bias can't be ruled out.

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