Original Research Paper

"A STUDY ON MATERNAL THYROID HORMONAL STATUS IN PREECLAMPSIA IN A TERTIARY CARE INSTITUTE"

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ABSTRACT:

Background: Preeclampsia (PE) is a pregnancy-specific illness characterized by new-onset or worsening hypertension (BP>140/90 mm Hg), substantial proteinuria (> 300 mg/24 h), and/or maternal end-organ damage after 20 weeks of gestation [1]. In low-resource countries, hypertensive disorders of pregnancy (HDP), particularly preeclampsia, continue to be a leading cause of maternal and perinatal morbidity and mortality [2].

OBJECTIVES:

1. To know the prevalence of thyroid disorders in cases of preeclampsia
2. To compare the serum levels of T3, T4 and TSH in normal pregnancy and preeclampsia.

MATERIAL & METHODS: Study Design: Hospital-based case-control study. **Study area:** Department of Obstetrics & Gynecology / Medical College, Kolkata. **Study Period:** 1st February 2023 to 31st January 2024 (1 year). **Study population:** All consecutively diagnosed unbooked cases of preeclampsia (blood pressure ≥140/90mmHg and proteinuria≥300mg/24h after 20th week of gestation) with gestational age>28 weeks and singleton pregnancy. **Sample size**: The study consisted of a total of 200 subjects. (100 cases and 100 controls) **Sampling Technique:** Simple Random technique.

Results: 69 out of 100 cases had a T3 level (<1.23ng/ml), 50 out of 100 controls had a T3 level <1.23, and 31% of cases and 50% of controls had a T3 level (>1.23ng/ml). The observed difference was significant according to the chi-square test.

CONCLUSION: In the present study, TSH levels were higher in preeclampsia subjects compared to normal pregnant women, which could indicate the possible aetiology for preeclampsia. The prevalence of thyroid disorders in preeclampsia was 34%.

Keywords: TSH, FT3, FT4, Preeclampsia, thyroid dysfunction, gestational hypertension

INTRODUCTION:

Preeclampsia (PE) is a pregnancy-specific illness characterized by new-onset or worsening hypertension (BP>140/90 mm Hg), substantial proteinuria (> 300 mg/24 h), and/or maternal end-organ damage after 20 weeks of gestation [1]. In low-resource countries, hypertensive disorders of pregnancy (HDP), particularly preeclampsia, continue to be a leading cause of

maternal and perinatal morbidity and mortality [2]. Preeclampsia is the most severe type of HDP, affecting about 3-8% of pregnant women [2,3].

Although preeclampsia appears with the characteristic symptoms of hypertension and proteinuria, the pathogenic process that causes this disease begins early in the first trimester. Currently, clinical predictions of preeclampsia and its outcome are poor and incorrect. Thyroid dysfunction is one of the most frequent endocrine problems during pregnancy, following diabetes mellitus [4], and has been linked to preeclampsia. Changes in T4 and T3 levels during pregnancy are primarily caused by a variety of factors, including an increase in thyroid-binding globulin (TBG) due to estrogen stimulation and human chorionic gonadotropin (HCG), increased renal iodine losses due to increased glomerular filtration rate, changes in the peripheral metabolism of maternal thyroid hormones, and changes in placental iodine transfer [5].

Because maternal T3 does not cross the placenta, the fetus relies on the transplacental transfer of maternal T4, particularly during the first trimester of pregnancy [6]. Adverse fetal outcomes at any stage of pregnancy, such as prematurity, low birth weight, increased newborn respiratory distress, and fetal thyroid abnormalities, may justify thyroid function screening during pregnancy. The cause of thyroid dysfunction in preeclampsia is unknown, however, it has been linked mostly to an imbalance of vasoactive hormones and the resulting oxidative stress at the uteroplacental implantation site [7,8].

As a result, the case-control research described below was conducted to better understand the link between pregnancy-induced hypertension and maternal serum TSH levels.

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MATERIAL & METHODS:

Study Design: Hospital-based case-control study.

Study area: Department of Obstetrics & Gynecology / Medical College, Kolkata.

Study Period: 1st February 2023 to 31st January 2024 (1 year).

Study population: All consecutively diagnosed unbooked cases of preeclampsia (blood pressure ≥140/90mmHg and proteinuria≥300mg/24h after 20th week of gestation) with gestational age>28 weeks and singleton pregnancy.

Sample size: The study consisted of a total of 200 subjects. (100 cases and 100 controls)

Sampling Technique: Simple Random technique.

Inclusion Criteria: All consecutively diagnosed unbooked cases of preeclampsia (blood pressure ≥140/90mmHg and proteinuria≥300mg/24h after 20th week of gestation) with gestational age>28 weeks and singleton pregnancy and no history of thyroid disease before and throughout pregnancy.

Exclusion criteria:

Patients with

1. History of hypertension,
2. History of Renal disorders,
3. History of cardiovascular diseases
4. Any metabolic disorder before or during the pregnancy, and

5. History of intake of any medication such as levothyroxine that may affect thyroid function.

Ethical consideration: Institutional Ethical committee permission was taken before the commencement of the study.

Study tools and Data collection procedure:

An equal number of age-matched, parity-matched and gestation-age-matched pregnant women without any previous disorders or pregnancy-induced complications were selected as controls. Written informed consent was obtained from all patients participating in the study and they were assured about the privacy of the data. Preeclampsia was defined as mild when blood pressure (BP) exceeded 140/90 mmHg on two more occasions at least 6-h apart and proteinuria exceeded 300 mg/24-h, and as severe when BP was at least 160/110 mmHg and proteinuria exceeded 5 g/24-h. After hospitalization, 3 CC of cubital venous blood samples were obtained from each woman (cases and controls), after the diagnosis was made before the initiation of the antihypertensive treatment, and before delivery40. Blood pressure values were recorded in a sitting position every 4 h. The right arm was used in a roughly horizontal position at heart level. For diastolic blood pressure measurements, both phases (muffling sound and disappearance sound) were recorded. This is very important since the level measured at phase IV is about 5 to 10 mmHg higher than that measured at phase V. Blood pressure measurements were obtained with random-zero sphygmomanometers and were recorded in a sitting position.

Blood samples from both groups were assayed by immunoassay for Thyroxine (T4), Triiodothyronine (T3) & Thyroid stimulating hormone (TSH).

TABLE NO 1: Normal values of T3, T4 & TSH

	1st trimester	**2nd trimester**	**3rd trimester**
TSH (mIU/ml)[42,43]	0.60 -3.40	0.37 -3.60	o.38 -4.04
T4(µg/dl)	6.5 -10.1	7.5 -10.3	6.3 -9.7
T3(ng/ml)	0. 97 -1.49	1.17 -1.69	1.23 -1.62

Statistical analysis:

Statistical analysis was performed by using the STATISTICAL PACKAGE OF SOCIAL SCIENCE Version 20.0 (SPSS). The data was tabulated and analysed. All the quantitative parameters were expressed as mean with standard deviation (mean ± SD) in both groups. Z-the test was applied when the data followed the normal approximation to test for the differences in the mean values between the two groups for various quantitative parameters. Differences in the proportions between different categorical variables (mode of delivery, dichotomous levels of TSH <4.04mIU/ml and >5m IU /ml) were tested through the Chi-square test of significance. Statistical significance was considered as $p < 0.05$. To quantify the association between TSH and preeclampsia, the odds ratio along with 95% CI (confidence interval) were estimated for TSH levels. The prevalence of thyroid disorders in preeclampsia was calculated.

OBSERVATIONS & RESULTS:

A total of 200 pregnant women were recruited in this case-control study. Of these, 100 women were with preeclampsia taken as cases and 100 were normal pregnant women taken as controls.

TABLE 2: DISTRIBUTION OF AGE IN CASES AND CONTROLS

AGE	CASES	CONTROLS	P- value
< 20 years	36(36%)	47(47%)	0.246
21 – 25years	48(48%)	46(46%)	
26 – 30years	12(12%)	5(5%)	
>30years	4(4%)	2(2%)	

Out of 100 cases 36% cases were under 20 years of age, 48% belonged to the age group 21-25,12% were between 26 – 30 years, 4% of cases were above 30 years of age, and out of 100 controls age under 20 years and 21 -25 years, was 47% and 46% respectively,5% are between 26 -30 years, only 2% are above 30 years of age. The observed difference between the two groups is not significant.

TABLE 3: COMPARISON OF PARITY BETWEEN CASES AND CONTROLS

Parity	CASES	CONTROLS	P-value
Primi gravida	67(67%)	51(51%)	0.01
Second gravida	23(23%)	43(43%)	
≥G3	10(10%)	6(6%)	

67% of cases and 51% of the control group were primi gravidae,23% of cases and 43% of controls were second gravidae, and 10% of cases and 6% of controls were multi gravidae. The observed difference is statistically significant according to the chi-square test. ($p < 0.05$)

TABLE 4: COMPARISON OF T3 BETWEEN CASES AND CONTROLS

T3	CASES	CONTROLS	P – value
<1.23(ng/ml)	69(69%)	50(50%)	0.007
>1.23(ng/ml)	31(31%)	50(50%)	
Total	100	100	

69 out of 100 cases had a T3 level (<1.23ng/ml), 50 out of 100 controls had a T3 level <1.23, and 31% of cases and 50% of controls had a T3 level (>1.23ng/ml). The observed difference was significant according to the chi-square test.

TABLE 5: COMPARISON OF T4 BETWEEN CASES AND CONTROLS

T4 LEVELS	CASES	CONTROLS	P – value
<6.3 µg/dl	19(19%)	7(7%)	0.0001
>6.3 µg/dl	81(81%)	93(93%)	
TOTAL	100(100%)	100(100%)	

19% 0f cases and 7% of controls have T4 level (<6.3 µg/dl),81% 0f cases and 93% of controls have T4 level >6.3µg/dl. The observed difference is statistically significant.

TABLE 6: COMPARISON OF TSH BETWEEN CASES AND CONTROLS

TSH LEVELS	CASES	CONTROL	P – value
<4.04 (mIU/ml)	66(66%)	89(89%)	0.000
>4.04 (mIU/ml)	34(34%)	11(11%)	

High TSH (>4.04mIU/ml) was seen in 34% of pre-eclamptic and 11% of controls, while 66% of cases and 89% of controls had TSH levels <4.04mIU/ml. This difference was significant when the Chi-square test was applied. (p =0.000).

TABLE 7: MEAN T3, T4, TSH LEVELS BETWEEN CASES AND CONTROLS

	CASES	CONTROLS	P – value
Mean T3 (ng/ml)	1.10 ±0.36	1.39 ±0.97	0.005
Mean T4 (µg/dl)	8.17 ±2.04	9.66 ±2.76	0.001
Mean TSH (mIU/ml)	3.84 ±2.29	2.50 ±1.25	0.000

Mean T3 (ng/ml) of cases was 1.10 ± 0.36 which was significantly lower than that of controls (1.39 ±0.97). MeanT4 (µg/dl) of cases was 8.17 ± 2.04 which was lower than the controls (9.66 ± 2.76) which was significant. The mean TSH (mIU/ml) of cases is 3.84 ±2.29 was significantly higher than controls (2.50 ± 1.25). Z– test was applied and the difference was statistically significant.

21% of cases and 9% in the control group were delivered before 37 weeks, 70% of cases and 50% of controls were delivered at 37 to 40 weeks of gestation, and 9% of cases and 41% of controls were delivered after 40 weeks. The observed difference was statistically significant. (p = 0.000).

In total 100 preeclamptic cases, 21 cases are delivered before 37 weeks in those 21 cases 71.4% have TSH levels >4.04 mIU /ml. In the total of 100 controls, 9 were delivered before 37 weeks in which 55.5% of cases had TSH levels>404mIU/ml.

Out of 100 pre-eclamptic pregnant women, 46% have mild preeclampsia, 20% have moderate and 34% of women have severe preeclampsia.

Out of 100 cases, 46 had MAP <100mmHg in that 37(80.4%)cases had TSH <4.04,9(19.5%) cases had TSH >4.04, and 12 cases had MAP 110 - 115 mmHg in that 7(58.3%) cases had TSH <4.04, 5(41.6%) cases had TSH >4.04, and in 42 cases having MAP >115 mmHg, 22(52.3%) had TSH <4.04,20(47.6%) cases had TSH >4.04.

50% of cases and 75% of controls had a normal vaginal delivery, whereas 50% of cases and 25% of controls underwent caesarean section. The difference is statistically significant according to the Chi-square test ($p < 0.05$).

Out of 100 cases, 32% had a birth weight <2.5 kg, and 68% had a birth weight >2.5 kg. Out of 100 controls, 13% had birth weight <2.5kg, and 87% had birth weight >2.5kg. The observed difference is statistically significant.

TABLE 8: FETAL OUTCOME

	CASES (n = 100)	**CONTROLS (n =100)**	**P – value**
LIVE	93	99	0.03
DEAD	7	1	
TOTAL	100	100	

93% of cases and 99% of controls had live babies with good perinatal outcomes, whereas 7% of cases and one control had perinatal deaths. The observed difference is statistically significant according to the Chi-square test.

DISCUSSION:

The current investigation was a case-control study carried out in the Department of Obstetrics and Gynaecology. This study enrolled 200 pregnant women with gestational ages greater than 28 weeks and singleton pregnancies who had no prior or ongoing history of thyroid disease. The goal was to compare the thyroid hormonal status of healthy pregnant women to those with preeclampsia. Of these, 100 women diagnosed with preeclampsia were used as cases, whereas 100 normal pregnant women served as controls.

Though the effects of pre-eclampsia and thyroid dysfunction in pregnancy have been extensively investigated, the link between the two remains poorly understood. As a result, this study was conducted to determine the impact of pre-eclampsia on thyroid profile parameters in euthyroid pregnant women.

Most of the women in the present study were in the age group of 21-25 years, which might be probably due to early marriages in the study population which is taken from rural areas of south India. The mean age of cases and control group in the present study was 22.87 ± 3.768years and 21.61±2.651years respectively and the difference between the two groups is statistically significant ($p < 0.05$). It is similar to a study conducted by Deshpande S. et al[9] in which the mean age of the cases is 23.08 ± 0.301 and the controls are 22.78 ± 0.281.

In the present study, 67% of preeclamptic women were primi gravida compared to 49% in the control group which is comparable with the above studies. The mean parity of the cases was 1.48 ± 0.82 and the controls were 1.56 ± 0.64 and the difference was not significant (p

=0.44). Muraleedharan et al[10], found 65% of cases and 57.5% of controls are primigravida and rest were multigravida. Parveen M. Aabida et al[11], found 52% of preeclampsia patients are primi gravida, and 20% are second gravida. Nulliparity is widely reported as a risk factor for hypertensive disorders in pregnancy due to first-time exposure to chorionic villi. Parity has followed the similar pattern reported in most existing literature with preeclampsia being common among the primigravida.

In the present study, there were low mean T3 and T4 levels in the women affected with preeclampsia. Mean T3 and T4 of cases was 1.100 ± 0.36and 8.17±2.04, mean T3 and T4 of controls was 1.39±0.97 and 9.66±2.76 and This difference was significantT3 (p =0.005), T4(p =0.001). The mean TSH of cases was 3.84±2.29, control was 2.50 ± 1.25 which was statistically significant (p = 0.000). Similar results were seen in the following studies. P Jain et al.[12], in their study, showed that serum TSH increased significantly(p<0.05) while TT4 and TT3 decreased significantly in preeclampsia as compared to normal pregnancy (p <0.05). Tadas SA et al.[13], reported that levels of total T3 in preeclamptic women (1.51±0.86) were significantly lower than that of controls (1.95±0.67). Similarly, a significant difference in the levels of total T4(11.33±1.02) versus (14.56±0.9) (p <0.001) was observed in the preeclamptic group compared with the normotensive group. The mean level of TSH was significantly higher in the preeclamptic group (3.75±0.43) than in controls (2.33±0.24).

Muraleedharan et al[10] reported a significant decrease in both total and free thyroid hormones. The mean TSH level in preeclampsia patients was significantly higher than in normal pregnant (p <0.001). There was a significant percentage of cases (55%) with high TSH. Preeclampsia patients have 11 times greater risk for hypothyroidism.

Manjunatha S et al,[14] reported there was no significant difference in the T4 (p=0.08) and T3 (p=0.49) levels in normal pregnancy and preeclampsia. TSH levels in preeclampsia were increased significantly (p =0.0001). Satyanarayana et al.[15], (2015) reported no difference between the normal pregnancy (9.03±1.18, 1.21±0.3) and preeclampsia patients (10.16±1.13,1.25±0.11), but the TSH levels in preeclampsia patients were increased (7.22±1.3) when compared to normal pregnancy (p =0.0001). Kumar Ashok et al[16], observed that more preeclamptic women had abnormally high TSH levels at the time of diagnosis when compared to normotensive women. A statistically significant higher number of cases with preeclampsia (76.7%) were also observed in pregnant women with abnormally high TSH.

Khanam M et al[17], reported that the mean (±SD) TSH of the study group and control group were 4.14±2.24 and 2.75±1.73 respectively and there was a highly significant difference between the two groups (p=0.0007). There was no significant difference between T3 and T4 levels. Kaya E et al[18], reported that serum T3, T4 and TBG values were significantly lower and TSH was significantly higher in preeclamptic and eclamptic women compared to the value of the control group Their findings suggest that preeclamptic women had a higher incidence of biochemical hypothyroidism compared with normotensive pregnant women.

In the present study as the MAP increases the percentage of the patients having elevated TSH becomes increased. Which shows a strong association between preeclampsia and thyroid disorders. The odds ratio corresponding to TSH level >4.04 mIU/ml in the study group compared to the control group, was 4.16 with (a 95% confidence interval of 1.96 – 8.83). Thus, TSH was found to be a strong associating factor for the occurrence of preeclampsia. If

the titers of TSH are above 4.04mIU/ml, then there is a 4.1 times higher risk of the development of preeclampsia. This is comparable to the study conducted by Kumar Ashok et al[16] with an odds ratio of 4.8. Deshpande et al.[9] found that the preeclampsia group have a chance of higher TSH by 2.19 times. Muraleedharan et al[10], found that preeclampsia patients have 11 times greater risk for hypothyroidism.

In the present study, the prevalence of thyroid disorders in preeclampsia was 34%. Kumar et al[16] had a prevalence of 40%. This is comparable with the present study. Muraleedharan et al[10] found that the prevalence of thyroid disorders in preeclampsia is 55%. During preeclampsia, there is involvement of the liver and kidney that may lead to decreased peripheral conversion of T4 to T3, hence decreasing the T3 levels. Also, "low T3 syndrome" has been reported in preeclampsia. In addition to this, there is a loss of proteins and protein-bound hormones in the Urine in preeclampsia which may also contribute to low TT3 levels in preeclampsia as compared to controls. Also, it may be a reflection of an inability to compensate for increased fetal demand, increased thyroid break-down by the placenta and transfer of maternal T4 to the fetus.

In the present study, 50% of preeclamptic women underwent caesarean section compared to 25% in controls and the difference is statistically significant. Similar findings are seen in a study conducted by Rusha Halder et al.[19] most common indications for caesarean section in the present study is previous caesarean section followed by fetaldistress.50% of cases and 75% of controls had a normal vaginal delivery.

In the present study, TSH levels were elevated in pre-eclamptic patients compared to normal pregnant women, which could be the possible aetiology for pre-eclampsia. Elevated TSH levels could be used as a predictor of pre-eclampsia. Hence, thyroid hormonal assay in the first trimester may be considered as a screening test for early diagnosis and treatment of preeclampsia and prevention of its complications. According to the present study, the prevalence of thyroid disorders in preeclampsia is 34%. However, this cannot apply to the general population as the study was conducted on a small population, which is a hospital-based study.

CONCLUSION:

In the present study, TSH levels were higher in preeclampsia subjects compared to normal pregnant women, which could indicate the possible aetiology for preeclampsia. The prevalence of thyroid disorders in preeclampsia was 34%. Women who develop preeclampsia are more like to have decreased thyroid function. Thyroid function screening should be done in the first trimester of pregnancy for early diagnosis and treatment of preeclampsia to prevent further complications.

REFERENCES:

1. Brown MA, Magee LA, Kenny LC, International Society for the Study of Hypertension in Pregnancy (ISSHP), et al. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. Hypertension. 2018;72(1):1–4.

2. Abalos E, Cuesta C, Grosso AL, et al. Global and regional estimates of preeclampsia and eclampsia: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2013;170(1):1–7.

3. Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol. 2009;33(3):130–137.

4. Negro R, Formoso 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(7):2587–2591.
5. Hod T, Cerdeira AS, Ananth Karumanchi S. Molecular mechanisms of preeclampsia. ColdSpring Harbor Perspect Med. 2015;5(10):1–21.
6. Pappa T, Ferrara AM, Refetoff S. Inherited defects of thyroxine-binding proteins. Best practice and research. Clin Endocrin Metabol. 2015;29(5):735–747.
7. Redman CW, Sargent IL. Latest advances in understanding preeclampsia. Sci. 2005;308(5728):1592–1594.
8. Lorentzen B, Henriksen T. Plasma lipids and vascular dysfunction in preeclampsia. Semin Reprod Endocrinol. 1998;16(1):33–39.
9. Deshpande S, et al. Maternal thyroid hormone status in pre-eclampsia: a tertiary care hospital-based study. Int J Reprod Contracept Obstet Gynecol. 2015;4(6):1853–1857.
10. Muraleedharan N, Janardhanan J. Thyroid hormone status in preeclampsia patients: A case-control study. Muller J Med Sci Res. 2017;8(2):68–68.
11. Qublan HS, Al-Kaisi IJ, Hindawi IM, Hiasat MS, Awamleh I, Hamaideh AH, et al. Severe pre-eclampsia and maternal thyroid function. J Obstet Gynaecol. 2003; 23: 244-6.
12. Jain P, Devi R. Thyroid hormonal status in pregnancy and pre-eclampsia and its correlation with maternal age and parity. Int J Basic Appl Med Sci. 2017;7(1):1–7.
13. Tadas S, Tadas A. Thyroid hormone alteration in women with pre-eclampsia. Int J Res Med Sci. 2016;4(10):4520–4523.
14. Manjunatha S et al, Sch. J. App. Med. Sci.,2014;2(6F):3297 -3299.
15. Satyanarayan AK, et al. Maternal thyroid profile in pre-eclampsia. Int J Med Sci Public Health. 2015;4(10):1401–1403.
16. Kumar A, Ghosh BK, Murthy NS. Maternal thyroid hormonal status in preeclampsia Indian J Med Sci 2005; 59: 57-63.
17. Khanam M, Ilias M. Study of thyroid hormonal status in preeclamptic patients. Med Today. 2013;25(2):63–66.
18. Kaya E, et al. Relation between birth weight and thyroid function in preeclampsia-eclampsia. Gynecol Obstet Invest. 1994;37(1):30–33.
19. Haldar R, et al. Correlation Between Maternal Serum Thyroid Profile And Preeclampsia At or Above 36 wks Gestation A Prospective Comparative Observational Study. IOSR J Dental Med Sci. 2017;16(3):41–45.