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Original Research Article

# Thyroid status in preeclamptic patients and in normal pregnancy: A case control study

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ABSTRACT

**Aim & Objectives:** To compare thyroid profile in pre- eclamptic patients and normal normotensive pregnant women in between gestational age of 28-40 weeks of pregnancy.
**Materials and Methods:** This case control study was done from Dec. 2015 to June 2017 in Geetanjali Medical College & Hospital, Udaipur. It was done on 50 patients of preeclampsia (case group) and 50 normal pregnant women (control group) in between gestational age of 28-40 weeks of pregnancy.
**Results:** Mean T 3 between case and control group was not statistically significant with p value = 0.844. Mean T 4 between case and control group was statistically significant with p value = 0.011. Mean TSH between case and control group was statistically significant with p value = 0.00068. Prevalence of hypothyroidism in patients of preeclampsia was 44% as compared to 16% in control group and p value was 0.00225, which was statistically significant. If the titers of TSH were above 4.04 $\mu$IU/ml in between gestational age of 28-40 weeks of pregnancy then there was 4 times higher risk of the development of preeclampsia.
**Conclusion:** Present study suggested that pathogenesis of preeclampsia is related to primary hypo-functioning of the thyroid. Severity of preeclampsia correlated with modest decreases in thyroid hormones along with increased TSH level.



## 1. Introduction

Preeclampsia complicates 3-5% of all pregnancies and it is an important cause of maternal and fetal morbidity and mortality. The risks related by preeclampsia to the mother include cerebrovascular accidents, placental abruption, postpartum haemorrhage, pulmonary edema and those to the fetus include preterm birth (iatrogenic or spontaneous), intrauterine growth restriction (IUGR), intrauterine fetal demise (IUD) and birth asphyxia. Obesity, age (women younger than 20 and older than 40), primigravidas, multiple pregnancy, renal disease, diabetes, gestational diabetes, family history and previous history of preeclampsia, certain autoimmune disorders are the risk factors for preeclampsia.[1] For reducing the morbidity and mortality associated with preeclampsia knowledge of the risk factors is important.

Preeclampsia is defined in terms of proteinuria and hypertension, it can affect multiple maternal systems also, so the presentation and progression of this disease is highly variable.[2] The most important pathogenesis of preeclampsia is endothelial cell dysfunction. Severity of preeclampsia correlated with modest decreases in thyroid hormones along with increased TSH level in maternal serum and high levels of endothelin.[3] The mechanism of

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hypothyroidism in patients of preeclampsia is not well identified but high circulation of maternal estrogens are related to changes in thyroid function. Faulty estrogen production due to placental dysfunction in preeclampsia may leads to reduced serum concentration of T3 and T4.[4] Endothelial dysfunction, hypertension, and proteinuria in preeclampsia may also related to excess placental soluble fms-like tyrosine kinase 1 (sFlt1).[5]

The present study compare thyroid profile in pre-eclamptic patients and normal normotensive pregnant women in between gestational age of 28-40 weeks of pregnancy.

## 2. Materials and Methods

After taking clearance from institutional ethical committee and proper informed consent this case control study was conducted from Dec. 2015 to June 2017 at Geetanjali Medical College & Hospital, Udaipur. It was performed on 50 patients of preeclampsia (case group) and 50 normal pregnant women (control group) in between gestational age of 28-40 weeks of pregnancy, who were admitted in the department of Obstetrics and Gynaecology.

Both groups were compared for thyroid profile.

The Inclusion criteria was: Patients of pre-eclampsia in between gestational age of 28-40 weeks of pregnancy.

The exclusion criteria for both the groups were:

1. History of any treatment that may affect thyroid function.
2. History of metabolic syndrome before or during pregnancy.
3. History of hypertensive disorder.
4. History of renal dysfunction.
5. Previous history of thyroid dysfunction in pregnancy and the post- partum period.
6. Previous history of congenitally malformed baby.

Blood pressure was recorded by standard sphygmomanometer in right arm semi reclining position at 2 occasions 6 hours apart.

Pre-eclampsia as defined by the National high blood pressure education program working group,[6] was diagnosed in hospital as a blood pressure of 140/90mmHg or more on two or more occasions, 6 hours apart, after 20 weeks of gestation and the presence of proteinuria (which was diagnosed when a reading of 1+ or more, on the uristix, found in repeated clean catch mid stream urine sample) and/or edema.

Ten ml venous blood sample was taken from preeclamptic women and each control subject. All samples were sent to the laboratory. T3, T4 and TSH serum levels were estimated by the highly sensitive and precise immunoassay technique. All women were observed for the development of the symptoms and signs of hypothyroidism during pregnancy.

Pregnancy specific and trimester specific reference levels recommended by American Thyroid Association, for TSH are as follows[7,8]

| TSH Ref. Range | Nonpregnant adult | $1^{st}$ trimester | $2^{nd}$ trimester | $3^{rd}$ trimester |
|---|---|---|---|---|
| $\mu$IU/ml | 0.34-4.25 | 0.6-3.4 | 0.37-3.6 | 0.38-4.04 |

### 2.1. Statistics

The data was tabulated and analyzed by using suitable statistical software. All the quantitative parameters were expressed as mean with standard deviation in both groups. Student's t-test was applied when the data followed the normal approximation to test the differences in the mean values between the two groups for various quantitative parameters. Chi-square test of significance were used to test differences in the proportions between different categorical variables. Significant P value was less than 0.05.

## 3. Results

Patients of preeclampsia (case group) and normal pregnant women (control group) included 50 participants each. n1 stands for patients of preeclampsia (case group) and n2 stands for normal pregnant women (control group).

The Table 1 states that mean age (± SD) in case group was 28.6 years with SD of 5.47, while mean age in control group was 28years with SD of 5.55. On statistical analysis, the p-value (p = 0.093) was not significant.

Mean T3 in case group was 1.17 ng/ml with SD 0.3 and in control group was 1.18 ng/ml with SD 0.28. On statistical analysis, the p-value (p = 0.844) was not significant.

Mean T4 value in case group was 7.7 ug/dl with SD 2.95 and in control group was 8.96ug/dl with SD 1.78. On statistical analysis, the p-value (p = 0.011) was significant.

Mean TSH in case group was 4.66 $\mu$IU/ml with SD 2.8 and in control group was 2.99 $\mu$IU/ml with SD 1.87. On statistical analysis, the p-value (p = 0.00068) was significant.

Pregnancy specific and trimester specific reference levels recommended by American Thyroid Association, for TSH in third trimester of pregnancy is 0.38-4.04 $\mu$IU/ml.

Table 2 states that out of 50 cases in our study 28 (56%) had TSH < 4.04 $\mu$IU/ml and 22 (44%) had TSH > 4.04 $\mu$IU/ml. Out of 50 controls in our study 42 (84%) had TSH < 4.04 $\mu$IU/ml and 8 (16%) had TSH > 4.04 $\mu$IU/ml. On statistical analysis (Chi square test) the p-value 0.00225 was significant.

The odds ratio related to the TSH levels >4.04$\mu$IU/ml in the patients of preeclampsia (case group) and normal pregnant women (control group) was 4. Thus, TSH was related to be a strong associating factor for the development of preeclampsia.

**Table 1:** Demographic profile of the women in case and control groups

| Variables | Cases n 1 = 50 | | Controls n 2 = 50 | | P Value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Age(years) | 28.6 | 5.47 | 28 | 5.55 | 0.093 |
| Systolic BP (mm Hg) | 153.96 | 9.84 | 112.56 | 6.16 | <0.00001 |
| Diastolic BP(mm Hg) | 95.88 | 4.91 | 74.88 | 5.79 | <0.00001 |
| T3 (ng/ml) | 1.17 | 0.3 | 1.18 | 0.28 | 0.844 |
| T4 (ug/dl) | 7.7 | 2.95 | 8.96 | 1.78 | 0.011 |
| TSH ($\mu$IU/ml) | 4.66 | 2.8 | 2.99 | 1.87 | 0.00068 |

**Table 2:** Distribution of TSH level in case and control group

| | TSH < 4.04 $\mu$IU/ml | | TSH > 4.04 $\mu$IU/ml | | P value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Case | 28 | 56% | 22 | 44% | 0.00225 |
| Control | 42 | 84% | 8 | 16% | |

Odds ratio: 4

## 4. Discussion

In the developing countries, preeclampsia and eclampsia are an important factors of maternal and perinatal morbidity and mortality. Very mild hyperthyroxinemia is usually associated with pregnancy but high incidence of hypothyroidism found in preeclamptic women that might related to the severity of preeclampsia. Various studies have sought to determine the relation between deranged thyroid function and preeclampsia.

Present study was done on 50 patients of preeclampsia and 50 normal normotensive pregnant women in between gestational age of 28-40 weeks of pregnancy at Geetanjali Medical College & Hospital, Udaipur. The purpose of study was to compare thyroid profile in pre- eclamptic patients and normal normotensive pregnant women in between gestational age of 28-40 weeks of pregnancy.

In the present study mean T3 was not statistically significant between pre- eclamptic patients and normal pregnant women, but statistically significant difference was observed in mean T4 between pre- eclamptic patients and normal pregnant women.

We found that serum TSH level was significantly higher in pre- eclamptic patients group as compared to normal pregnant women. On statistical analysis, the p-value (p = 0.00068) was significant. These findings were in accordance with Kumar et al,[9] L Harshvardhan et al,[10] Dhananjaya B.S. et al,[11] Larijani et al.[12] On the other hand Khadem et al,[13] Qublan et al.[14] observed insignificant TSH values.

It was found that there was high prevalence of hypothyroidism (44%) in patients of preeclampsia as compared to 16% in normal pregnant women group. These findings supported that patients of preeclampsia had higher incidence of hypothyroidism compared to normal pregnant women (Kumar et al. 40% v/s 12.2%),[9] (Harshvardhan L et al. 46% v/s 14%).[10]

In our study proportion of patients of preeclampsia with TSH> 4.04 $\mu$IU/ml was found to be significantly higher than that in the normal pregnant women group (p=0.00225).The severity of preeclampsia was correlated with decrease in thyroid hormones with simultaneous increase in TSH titers.[3]

The mechanism of it in these preeclamptic women is not well understood. Mild alteration in the thyroid hormones might occur due to non-thyroidal illness acting as a stress factor as well as due to decreased plasma albumin concentrations in these patients. In patients of preeclampsia in between gestational age of 28-40 weeks of pregnancy, serum total T3 and TT4 levels were decreased significantly and TSH levels was increased significantly.[3,4] Severity of preeclampsia correlated with modest decreases in thyroid hormones along with increased TSH level in maternal serum and high levels of endothelin.[3] Thyroid hormone may affect hypertensive disorders onset in pregnant women. Increased level of thyroid hormone can cause endothelial cell dysfunction, which has an important role in the pathophysiology of hypertensive disorders during pregnancy.[15]

## 5. Conclusion

Present study suggested that pathogenesis of preeclampsia is related to primary hypo-functioning of the thyroid. In this study 44% of preeclamptic women had hypothyroidism with abnormally high serum TSH when compared to 16% in control group. If the titers of TSH were above 4.04 $\mu$IU/ml, then there was 4 times higher risk of the development of preeclampsia.

This high-risk potential marker of preeclampsia needs further investigation because of the small number of subjects in this study. A multi-centric study may answer the relationship and mechanism of thyroid dysfunction in patients of preeclampsia. Identification of thyroid

dysfunction and appropriate treatment might affect the occurrence and risk of morbidity and mortality in patients of preeclampsia. Therefore thyroid function screening is recommended in first trimester of pregnancy and its follow up till the third trimester of pregnancy is necessary.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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