

# A Study of Thyroid Hormone Status in Pre-Eclampsia

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**Abstract:** ***Aim:** The study was done to estimate thyroid hormone status in preeclamptic women and compare to normotensive normal pregnant women. **Material and Methods:** The study comprised of 40 cases of preeclamptic women who attended in department of Obstetrics & Gynaecology, Kakathiya Medical College, Warangal from February 2017 to August 2019 and 40 normotensive healthy women as controls. Serum total Triiodothyronine (T3), Tetraiodothyronine (T4) and Thyroid Stimulating Hormone (TSH) were estimated. **Results:** In the present study the mean serum TSH in preeclampsia women were increased significantly ( $p < 0.001$ ). On the other hand serum T3 levels and Serum T4 levels were decreased significantly in preeclamptic women when compared to controls ( $p < 0.001$ ). **Conclusion:** Results observed from this study conclude that all these parameters play an important role in preeclampsia hence early detection of these parameters in preeclampsia may help to improve maternal and fetal outcome.*

**Keywords:** T3 -Total triiodothyronine, T4- Tetraiodothyronine, TSH- Thyroid stimulating hormone, preeclampsia

## 1. Introduction

Pregnancy is a physiological state associated with many alterations in metabolic, biochemical, physiological, hematological and immunological processes. If these changes are exaggerated, they can lead to complications during pregnancy.<sup>1</sup>

Preeclampsia is a multisystem disorder of unknown etiology and is a major cause of maternal and fetal morbidity and mortality.<sup>2</sup> It complicates 2-8% of pregnancies and account for more than 50,000 maternal deaths worldwide. It is a rapidly progressive condition characterized by high blood pressure, platelet aggregation, swelling of the lower extremities and protein in urine.<sup>3</sup> Typically blood pressure elevations and pre-eclampsia occur in the late second trimester or third trimester.<sup>4</sup>

It has long been recognized that maternal thyroid hormone excess or deficiency can influence maternal outcomes like miscarriages, anemia in pregnancy, preterm birth, low birth weight, increased neonatal respiratory distress, low intelligence quotient of off-springs and adverse maternal outcomes such as pregnancy induced hypertension, postpartum hemorrhage and placental abruption.<sup>5</sup>

During normal pregnancy, changes in thyroid function are well-documented, but information about thyroid function in complicated pregnancy is scanty. During pregnancy, there is an increased thyroid hormone demand and increased iodine uptake and synthesis of thyroid hormones. Estrogen induces a rise in serum TBG and the placenta releases several thyroid stimulatory factors in excess e.g. HCG. Alpha subunit of HCG is identical to that of TSH and has weak thyrotrophic activity.<sup>6</sup> In preeclampsia, there is failure of estrogen production due to placental dysfunction resulting in lowering of TBG, T3, and T4 along with growth retardation of the fetus.<sup>7</sup> Hypothyroidism has been listed as one of the causes of high blood pressure.<sup>8</sup> Experimental studies have indicated that release of nitric oxide is altered in

hypothyroidism and the resulting endothelial cell dysfunction might be a pathogenic mechanism for hypothyroidism in preeclampsia.<sup>9</sup>

The risks posed by preeclampsia to the mother include placental abruption, cerebrovascular accidents, postpartum hemorrhage, pulmonary edema etc. and those to the fetus include intrauterine growth restriction, intrauterine fetal demise, preterm birth (iatrogenic or spontaneous) and birth asphyxia.<sup>10</sup>

The present study was undertaken to evaluate the thyroid hormones and serum albumin in preeclamptic women and compared to normotensive pregnant women. Therefore this study shows that there is a need to consider the thyroid hormones (serum T3, T4, TSH), in preeclampsia in its development & management and also to prevent its complications.

## 2. Materials and Methods

**Setting:** A case control study was conducted in the Department of Biochemistry, Mahatma Gandhi Memorial Hospital, Warangal and government maternity hospital, Hanamkonda during February 2017 to August 2019.

**Source of samples and data:** 80 subjects were included in the study from Department of Obstetrics and gynecology, Government maternity hospital, Hanamkonda. Investigations were performed at the Department of Biochemistry, Mahatma Gandhi Memorial Hospital, Warangal.

In the present study the individuals included were categorized into 2 groups.

Group Number	Patient Type	No. of Patients
Group1 (controls)	Normal pregnancy	subjects 40
Group 2 (cases)	Preeclampsia	subjects 40

**Ethical considerations:** This research protocol was approved after it was reviewed by the Committee for Kakatiya Medical College. The aim and purpose of the study were well explained to the preeclampsia patients and control subjects, verbal and written consent were obtained from all the study subjects.

**Specimen collection:** Fasting venous blood samples were collected from all groups. 4ml of blood was collected into serum vacutainer (red cap) for thyroid profile.

Selected controls and cases are subjected to the following protocol with consent:

- 1) Detailed history & clinical examination.
- 2) Blood samples are collected from all the subjects and following parameters are analyzed.

Estimation of Thyroid hormones T<sub>3</sub> (Triiodothyronine), T<sub>4</sub> (Tetraiodothyronine), TSH (Thyroid Stimulating hormone) are done by Chemiluminescence immunoassay (CLIA) System.

**Inclusion Criteria**

- 1) Diagnosed patients of preeclampsia (BP ≥140/90 mm of Hg and proteinuria ;300 mg/L in 24hrs or ≥ 1+ dipstick) after 20 weeks of gestational age.
- 2) No previous history of congenitally malformed baby.
- 3) No previous history of thyroid disease in pregnancy and post partum period.

**Exclusion Criteria**

- 1) The patients with history of thyroid disorders, chronic hypertension, renal disorders cardiovascular diseases.
- 2) Any metabolic disorders before or during the pregnancy.
- 3) Gestational diabetes mellitus.

**3. Observation and Results**

The present study was undertaken in the department of biochemistry, Kakatiya medical college, MGM hospital, Warangal. A total of 80 patients were recruited for the study which included 40 preeclampsia patients as cases and 40 healthy normal pregnant women as controls.

The following parameters were analysed.

- 1) Serum T<sub>3</sub> (ng/dl)
- 2) Serum T<sub>4</sub> (µg/dl)
- 3) Serum TSH (µIU/ml)

**Statistical analyses:**

Data was collected, entered using Microsoft excel and analysed using statistical package of social science (SPSS) version 20. All the data were expressed in terms of figures, mean and standard deviation. For parametric variables independent t test and p value are done to assess the data in both the groups. p value <0.05 is taken as the level of significance.

**Table 1:** Demographic distribution for age, gestational age & parity in the groups

Groups	Age mean± SD (years)	Minimum age (years)	Maximum age (years)	Gestational age (weeks)	Nulliparity	Multiparity
Controls	23.98± 9	19	35	35±3.18	14	26
Cases	25.38 ±11	20	31	34±2.84	21	19

**Table 2:** Mean values of S.B.P and D.B.P in both the groups

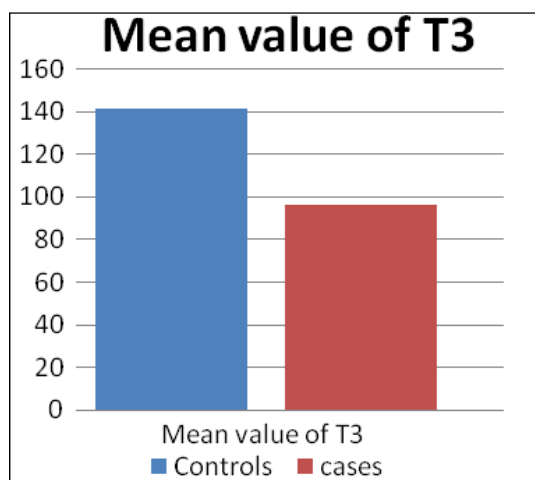
Groups	S.B.P mean± SD	D.B.P mean± SD
Controls	114.8±54.93	73.55±58.77
Cases	148.5 ±19.85	98.85 ±43.7

**Table 4:** t-Test mean values of T<sub>4</sub> in both controls and cases

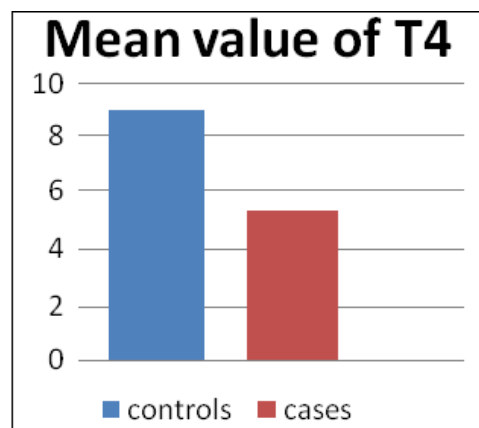
Type of sample	Mean value of T <sub>4</sub> (µIU/ml)	t value	p value
Controls	9.09	12.31	<0.001 Significant
Cases	5.3		

**Table 3:** t-Test mean values of T<sub>3</sub> in both controls and cases

Type of sample	Mean value of T <sub>3</sub> (ng/dl)	t value	p value
Controls	141.52	7.08	<0.001 significant
Cases	96.65		



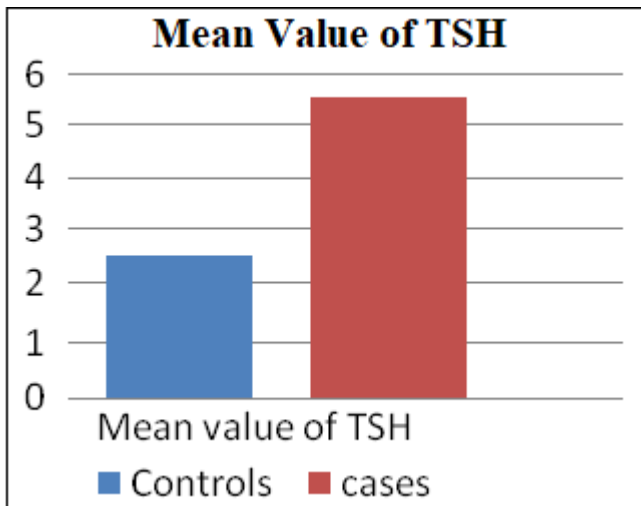
**Figure 1:** Graphical representation of t-Test means values of T<sub>3</sub> in both the groups.



**Figure 2:** Graphical representations of t-Test mean values of T<sub>4</sub> in both the groups.

**Table 5:** t-Test mean values of TSH in both controls and cases

Type of sample	Mean value of TSH (µIU/ml)	t value	p value
Controls	2.48	12.41	<0.001 Significant
Cases	5.45		



**Figure 3:** Graphical representation of t-Test means values of TSH in both the groups.

#### 4. Discussion

Pre-eclampsia remains a major cause of perinatal and maternal morbidities and mortality, and is one of the most common medical complications of pregnancy<sup>11</sup>. Preeclampsia describes a common syndrome that occurs in the second half of pregnancy and often manifesting with hypertension and proteinuria. It is the second leading cause of maternal mortality worldwide, constituting 12-18% of pregnancy related maternal deaths<sup>12</sup>.

Although the actual cause is unclear, various hypotheses link with decrease in thyroid hormones with an increase in anti-angiogenic factors associated with Preeclampsia. Hypothyroidism in preeclampsia can cause morbidities in mother and growth retardation, intrauterine death, or congenital hypothyroidism in the fetus.<sup>13</sup>

Comparison of means of different variables like total T3, total T4, T.S.H between cases and controls was done in the present study which included 40 normotensive pregnant women as controls and 40 preeclampsia cases.

According to the study done by Muraleedharan et al,<sup>14</sup> the mean age of PE patients was  $24.98 \pm 2.8$  and that of normal pregnant women was  $24.5 \pm 3$  years. There is no significant difference in age between cases and controls.

Sardana et al,<sup>15</sup> studied that the mean ( $\pm$ SD) age of the pre-eclamptic and control groups were  $23.68 \pm 4.55$  years and  $24.72 \pm 4.72$  years respectively and there was no statistically significant difference between the two groups ( $p > 0.05$ ).

Lao TT et al,<sup>16</sup> also studied the mean age  $28.40 \pm 5.20$  years and  $27.50 \pm 5.10$  years of study and control groups and there was no statistically significant difference between the two groups.

Chaudary et al,<sup>17</sup> also found mean age in the preeclampsia cases was  $23.57 \pm 2.99$  years and that in controls was  $22.90 \pm 2.96$  years.

In the present study the mean $\pm$ SD age (years) of preeclampsia group is  $25.38 \pm 11.01$  and normal pregnancy is  $23.98 \pm 9$  which is not significant and supportive to the above studies.

Khadem et al,<sup>18</sup> studied mean ( $\pm$ SD) gestational age of pre-eclamptic group was  $34.30 \pm 2.92$  weeks and  $35.10 \pm 2.82$  weeks in control group.

Larijani et al,<sup>19</sup> also found the mean ( $\pm$ SD) gestational age in weeks was  $35.67 \pm 6.88$  and  $37.16 \pm 3.62$  in preeclampsia and normal pregnancy respectively.

The mean $\pm$ SD of gestational age in weeks in the present study also found to be  $34.33 \pm 2.84$  in preeclampsia group and in normal pregnancy is  $35 \pm 3.18$  which is statistically significant and in accordance to above studies.

Pregnancy is associated with profound modifications in the regulation of thyroid function. These changes are the result of the various factors like an increase of thyroid-binding globulin due to elevated estrogens and human chorionic gonadotropin, increased renal losses of iodine due to increased glomerular filtration rate, modifications in the peripheral metabolism of maternal thyroid hormones, and modifications in iodine transfer of placenta.<sup>20,21,22</sup>

In Preeclampsia, there is an increase in anti-angiogenic factors that decrease nitric oxide production. This in turn decreases thyroid capillary flow which could lead to hypothyroidism.<sup>23</sup>

Thyroid hormone production is regulated by the pituitary through the action of thyrotropin (thyroid-stimulating hormone, TSH). TSH comprises of two subunits and it has one alpha-subunit in common with luteinizing hormone, follicle stimulating hormone and human chorionic gonadotropin (HCG).<sup>24</sup>

Human chorionic gonadotrophin hormone which is secreted by the placenta stimulates thyroid gland during pregnancy as there is structural similarity with thyrotropin. Thyroid hormones have very important role in embryogenesis and fetal development. Normal pregnancy is associated with mild hyperthyroidism on other hand preeclampsia is associated with hypothyroidism.<sup>25</sup>

Preeclampsia is a state of decreased estrogen, may be due to placental dysfunction. This decreased estrogen leads to decrease in synthesis of thyroid binding globulin. As thyroid binding globulin is decreased it might be the reason for lowering of serum T3 and T4 levels in preeclampsia.<sup>26,27</sup>

As preeclampsia is multisystem disorder, the most affected organs are kidney, liver and brain. In liver and kidney peripheral conversion of the T4 to T3 occurs. Thus due to involvement of kidney and liver in preeclampsia no conversion of T4 to T3 occurs. This might be the main factor for decreased serum T3 concentration in pre-eclamptic patients.<sup>28,29</sup>

In support to the above hypothesis the present study found that the pre-eclamptic group presented with significantly low

levels of T3 ( $96.65 \pm 15.03$ ) and low T4 levels ( $5.9 \pm 0.84$ ) compared to their normal pregnant counter parts ( $141 \pm 37.13$ ) and ( $9.09 \pm 1.83$ ) respectively, which is statistically significant i.e p value  $< 0.001$ .

These observations are in support with the study conducted by Chowdary et al,<sup>17</sup> it was found that T3 and T4 levels were significantly lower in preeclamptic group ( $92 \pm 3.8$ ), ( $5.29 \pm 2.16$ ) as compared to control group i.e. normal pregnant women ( $141 \pm 2.9$ ), ( $9.46 \pm 1.96$ ) respectively ( $p < 0.05$ ).

Similar results were seen in study conducted by Farah et al,<sup>31</sup> in which there was significant decrease in T3 and T4 levels and significant increase in TSH levels in preeclamptic women.

Chowdary et al,<sup>17</sup> found TSH levels mean ( $\pm$ SD) are significantly higher in preeclamptic group ( $6.19 \pm 2.32$ ) as compared to control group ( $2.22 \pm 0.84$ ) ( $p < 0.001$ ). Similar observations are also seen in studies done by Kumar et al,<sup>9</sup> Larijani et al,<sup>19</sup> Tolino et al,<sup>31</sup> Das S et al,<sup>32</sup> Dhananjaya BS et al.<sup>33</sup>

In concordance with the above studies the present study also observed that the preeclamptic group presented with significantly higher levels of TSH ( $4.85 \pm 0.65$ ) when compared to their normal pregnant counter parts ( $2.48 \pm 0.8$ ) which is statistically significant i.e p value  $< 0.001$ .

## 5. Limitations of the study

The current study has important strengths and limitations. The major strength is the randomized controlled nature of the study. On the other hand, the major limitation is the small sample size in both groups may limit the possibility of generalization of the findings in the present study. Finally, within the limit of this study, low thyroid hormone status is associated with preeclampsia.

## 6. Conclusion

Results observed in the present study suggest that decreased thyroid hormones itself might be a predisposing factor for the development of preeclampsia on the other hand hypothyroidism is more pronounced in preeclampsia.

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