

## Research Article

# Thyroid hormone alteration in women with pre-eclampsia

Swati A. Tadas<sup>1\*</sup>, Arun K. Tadas<sup>2</sup>

<sup>1</sup>Department of Physiology, Government Medical College, Nagpur, Maharashtra, India

<sup>2</sup>Department of Biochemistry, Shri Vasant Naik Government Medical College, Yavatmal, Maharashtra, India

**Received:** 07 August 2016

**Revised:** 08 August 2016

**Accepted:** 06 September 2016

### \*Correspondence:

Dr. Swati A. Tadas,

E-mail: [swatitadas@rediffmail.com](mailto:swatitadas@rediffmail.com)

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## ABSTRACT

**Background:** Preeclampsia and eclampsia are major causes of maternal and perinatal morbidity and mortality. The obstetricians are increasingly becoming aware of the potential or adverse effects of hypothyroidism on the outcome of pregnancy.

**Methods:** This analytical, cross sectional, case control study is designed to compare the levels of thyroid hormone in women with preeclampsia and in normal pregnant women in the third trimester.

**Results:** Levels of total T3 and T4 in preeclamptic women were significantly lower than that of controls whereas the mean level of TSH was significantly higher in preeclamptic group than controls.

**Conclusions:** Primary hypo-functioning of the thyroid can accompany mild preeclampsia. Estimation of thyroid hormone levels in first and the third trimester of pregnancy are recommended.

**Keywords:** Preeclampsia, Thyroid

## INTRODUCTION

The physiological changes in the thyroid gland during pregnancy are well understood but only a few reports provide information about thyroid function in complicated pregnancies. In the developing countries, Preeclampsia and eclampsia are major causes of maternal and perinatal morbidity and mortality.<sup>1</sup>

Preeclampsia is defined by the National High Blood Pressure Education Program Working Group, as a blood pressure of 140/90 mmHg or more on two or more occasions, 6 hours apart, after 20 weeks of gestation and the presence of protein (which was diagnosed when a reading of 1+ or more, on the uristick, was found in repeated clean catch midstream urine sample) and / or edema.

Although pregnancy is usually associated with very mild hyperthyroxinemia, pre-eclamptic women have high incidence of hypothyroidism which might co-relate with

the severity of preeclampsia.<sup>2</sup> There are controversies about the mechanism and clinical significance of low concentrations of thyroid hormones in preeclampsia.<sup>3</sup> High concentration of total and free thyroxine and subnormal total triiodothyronine and free triiodothyronine have been reported in some studies in preeclamptic patients, while in some studies, low TT4 and FT4 and thyroxine binding globulin, high TSH and no change in total T3 was reported in proteinuric preeclamptic women.<sup>2,4,5</sup>

The obstetricians are increasingly becoming aware of the potential or adverse effects of hypothyroidism on the outcome of pregnancy. The present study is designed to compare the levels of thyroid hormone in women with preeclampsia and in normal pregnant women in the third trimester.

## METHODS

The study was approved by the ethical committee.

Normal pregnant women of age group 20 to 36 years from central India attending ANC clinic at Government Medical College Nagpur comprised the reference group.

This is analytical, cross sectional, case control study conducted at antenatal clinic of Government Medical College and Hospital Nagpur. Study period was from January 2015 to December 2015. Fifty pregnant women admitted with the diagnosis of preeclampsia in the third trimester were recruited for the study after obtaining informed consent.

An equal number of age and gestation matched healthy normotensive pregnant women in the third trimester attending the antenatal clinic during the study period, constituted the control group. The development of hypertension any time during antenatal follow-up excluded them from the control group.

4 ml venous blood sample was taken from the cubital vein of (i) preeclamptic women, after the diagnosis was made but before the initiation of the antihypertensive treatment, and before the delivery and (ii) each control subject as mentioned above. Sera was separated and assessed immediately for total T3 (triiodothyronine), total T4 (thyroxine) and TSH (thyroid-stimulating hormone) using ELISA.

The data was tabulated and analyzed. All the quantitative parameters were expressed as mean with standard deviation (mean±SD) in both groups.

#### Inclusion criteria

- High blood pressure equal or higher than 140/90 mm/Hg in the sitting position and a proteinuria of equal or greater than 300 mg within 24 - hour urine collection or persistent (1+dipstick) in two random urine sample with an interval of 6 hour.
- Written consent for participating in the study.

#### Exclusion criteria

- Any history of thyroid disease such as hyper or hypothyroidism or thyroid surgery.
- Consumption of thyroid related medications
- Any known systemic disorder or ones which diagnosed during study such as hypo or hyperthyroidism.
- History of renal disease
- History of hypertension

#### Statistical analysis

To test for the differences in the mean values between the two groups for various quantitative parameters, Student's unpaired t-test was applied when the data followed the normal approximation. Statistical significance was considered as  $P < 0.05$ .

## RESULTS

In the case group, age ranged from 20 to 34 years and the range for the control group was from 20 to 36 years. The mean(±SD) age of the study group and control group was 27.8±5.24 years and 26.6±6.91 years respectively and there was no statistically significant difference between the two groups ( $P > 0.05$ ) (Table 1).

In the preeclamptic women the gestational age was between 28 to 41 weeks compared with 28 to 40 weeks in control group. The mean of systolic blood pressure was 148±16.22 mmHg (140 to 220 mm Hg) and the mean for diastolic blood pressure was 92.4±6.16 mmHg (80 to 130 mmHg) in the preeclamptic women. In control group, mean systolic and diastolic blood pressure was 112±11.14 and 78±4.64 respectively.

**Table 1: Mean age and gestational age in normal pregnant and preeclamptic women.**

	Normal pregnant women (Mean ±SD)	Preeclamptic women (Mean±SD)
Age	26.6±6.91	27.8±5.24
Gestational age	35.5±4.2	34.6±3.8

N=50 in normal pregnant women; N=50 in preeclamptic women. Unpaired 't' test was applied; P value was  $> 0.5$  in both groups.

Levels of total T3 in preeclamptic women (151.34±8.68ng/dl) were significantly lower than that of controls (195.66±6.71ng/dl). Similarly a significant difference in the levels of Total T4 (11.33±1.02 µgm/dl) versus (14.56±0.9 µgm/dl), ( $p < 0.001$ ) was observed in the preeclamptic group compared with the normotensive group. The mean level of TSH was significantly higher in preeclamptic group (3.75±0.43) than controls (2.33±0.24) (Table 2). The values of Total T3, Total T4 and TSH in the two groups are shown in (Table 2). The mean values of thyroid hormones were within the normal laboratory reference ranges in both the groups.

**Table 2: Comparison of total T3, total T4 and TSH levels in normal pregnant and pre-eclamptic women.**

	Normal Mean±SD N=50	Pre-eclamptic Mean±SD N=50	P value
Total T3 (ng/dl)	195.66±6.71	151.34±8.68	$P < 0.001$
Total T4 (µgm/dl)	14.56±0.96	11.33±1.02	$P < 0.001$
TSH (µIU/ml)	2.33±0.24	3.75±0.43	$P < 0.001$

N=50 in normal pregnant women; N=50 in preeclamptic women; Unpaired 't' test was applied, levels  $P < 0.05$  was considered statistically significant; T3 in ng/dl, T4 in µgm/dl and TSH in µIU/ml.

## DISCUSSION

In the present study, we observed  $T_3$  and  $T_4$  levels were significantly lower and TSH was significantly higher in preeclamptic patients. Similar findings were reported by Kaya E et al that serum  $T_3$ ,  $T_4$  and TBG values significantly lower and TSH was significantly higher in pregnancy and eclamptic women compared to value of control group.<sup>6</sup>

Other studies are also in agreement with our observation showing lower total  $T_3$  and  $T_4$  values and higher TSH value in pre-eclamptic women in third trimester.<sup>2,3,6,7</sup> Modest decrease in thyroid hormones with concomitant increase in TSH level in maternal serum correlated with severity of pre-eclampsia and eclampsia and high levels of endothelin.<sup>3</sup> Kumar Ashok et al, observed that more member of 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 woman with abnormally high TSH.<sup>8</sup>

It was suggested that, for reduced serum concentration of thyroid hormone in toxemia may in part be explained by the loss of Protein and hence protein bound hormone.<sup>6</sup> Since  $T_3$  is mostly peripheral conversion of  $T_4$ , decrease in  $T_3$  associated  $T_4$  is a normal consequence besides involvement of liver and kidney in toxemia of pregnancy.<sup>4</sup> Reduced serum concentration of TBG,  $T_3$  and  $T_4$  may also be explained by the faulty estrogen production due to placental dysfunction in pre-eclamptic women.<sup>7</sup>

Raofi Z et al, observed that  $FT_4$  conc. in pre-eclamptic patients was lower significantly ( $P < 0.001$ ) in comparison with normal pregnancies. TSH level in these patients was not significantly different although it was higher in comparison with normal pregnant women. It was concluded that women who develop preeclampsia are more likely to have lower normal limits of thyroid function during final weeks of pregnancies.<sup>9</sup>

Zhou Jia any et al concluded that severe preeclamptic pregnant women are often accompanied by hypothyroidism and is more common in Asia.<sup>10</sup> Some studies reported higher levels of free and  $TT_4$  along with lower levels of  $TT_3$  and  $FT_3$  in toxemic patients, compared to normal pregnant women.<sup>11</sup> Khadem compared 40 normal pregnant women and 40 cases of preeclampsia in third trimester of pregnancy, Her study does not support the hypothesis that changes in  $FT_3$ ,  $FT_4$  and TSH levels could be a possible etiology of preeclampsia.<sup>12</sup>

Khaliq F et al, found a correlation between  $TT_3$  and albumin, which was significant and direct, and concluded that as most of  $T_3$  is bound to plasma protein, proteinuria accounts for its increased loss. They found that correlation between  $TT_4$  and albumin was not significant

and can be because of different degree of saturation with TBG. Correlation between TSH and albumin was significant and inverse because the pre-eclamptic patients are in a state of mild hypothyroidism.<sup>13</sup> One case report by Inversetti A et al concluded that recognizing preeclampsia like syndrome caused by hypothyroidism from other form of pregnancy induced hypertension is essential for choosing correct treatment.<sup>14</sup>

Akiibimu MO et al studied, metabolic dysfunctions in Nigerian pre-eclamptics concluded that hypothyroidism, hyper cholesterolemia oxidative stress and deranged inflammatory responses are possible features of preeclampsia.<sup>15</sup> Mechanism of altered thyroid hormonal levels in preeclamptic women is not well understood, some alteration in the thyroid hormone might occur due to non-thyroidal illness acting as a stress factors as well as due to decreased plasma albumin concentration in these patients.<sup>16,17</sup>

It is well established that, there is a big increase in concentration of TBG during pregnancy due to influence of high levels of circulating estrogen and as approximately 97-99% of total thyroxine is protein bound, the interpretation of serum total thyroxine value is difficult.<sup>18</sup> It is unlikely that pre-eclamptic patients had auto immune hypothyroidism because the abnormal  $T_3$  and  $T_4$  titres were not very high and all of them were normal when examined 6 weeks postpartum.

## CONCLUSION

Present findings suggest that primary hypo-functioning of the thyroid can accompany mild preeclampsia and possibly contribute to the pathogenesis. Identification of thyroid abnormalities and appropriate measures might affect the occurrence and severity of morbidity and mortality associating with preeclampsia. Therefore in addition to recommended thyroid function screening in first trimester of pregnancy, its follow up within the third trimester of pregnancy is recommended.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Tadas SA, Tadas AK. Thyroid hormone alteration in women with pre-eclampsia. *Int J Res Med Sci* 2016;4:4520-3.