

## Estimation of thyroid hormones levels in preeclamptic pregnant women; an early predictor of the disease

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**Abstract:** *Background:* During normal pregnancy, changes in thyroid function are very well documented and these changes are physiological and have been considered as one of the pathophysiological causes of preeclampsia. The information regarding thyroid function in preeclampsia is scanty. *Aim:* To estimate the levels of thyroid hormones in preeclamptic pregnant women and to compare it with healthy normotensive pregnant women. *Material and methods:* Thirty five (35) pregnant women clinically diagnosed as preeclampsia were taken as subjects and an equal number of age matched, parity matched and gestation age matched healthy normotensive pregnant women were taken as controls for the study. This is the case-control hospital based study carried in the Department of Biochemistry M.G.M. Medical College and associated M.Y. Hospital. Indore (M.P.) Blood samples collected were estimated for T3, T4 and TSH by a one step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA). Comparison between both the groups was done by Student's t-test. *Results:* There were no significant differences between the two groups in age and body mass index (BMI) but significantly higher differences in gestational age, systolic and diastolic blood pressure was observed. When the levels of T3 and T4 were compared between healthy normotensive pregnant and preeclamptic pregnant women, no significant difference was observed between both the groups. The study shows highly significant increase in the TSH levels in preeclampsia as compared to normal pregnancy. *Conclusion:* The study concluded that the thyroid disorder is one of the predisposing causes for preeclampsia. Hence thyroid hormonal assay can be considered as a screening test for early diagnosis and treatment of preeclampsia to prevent further complications of it.

**Keywords:** Preeclampsia, Tri-iodothyronine (T3), Thyroxine (T4), Thyroid stimulating hormone (TSH).

### Introduction

Preeclampsia, also called as toxemia of pregnancy, is a medical condition, characterized by new onset of hypertension (SBP >140 mm of Hg or DBP >90mm of Hg) and proteinuria (>0.3g or 300mg protein in a 24 hour urine specimen or 1+ on dipstick) and also may be associated with myriad other signs and symptoms, such as pitting edema, [1] visual disturbances, headache, and epigastric pain after 20<sup>th</sup> weeks gestation in a previously normotensive and non proteinuric patients [2-3].

The clinical features usually develop in the latter part of the third trimester i.e. close to term (near 38-40<sup>th</sup> weeks gestation) and progress until delivery [4]. It continues to be a major obstetric problem in present day medical practice. It is a leading cause of maternal and fetal morbidity and mortality [5-6]. The major cause of fetal

compromise in preeclampsia is reduced utero-placental perfusion [7-8]. This disorder is unique to human pregnancy in which numerous genetic immunological and environmental factors interact [9]. In preeclampsia, the most affected organs are liver, kidney and brain and due to auto-intoxication, functional disorders in these organs system are evidential [10].

Pregnancy is a physiological process to supply adequate nutrition to the growing fetus. Many maternal physiological adjustments of different organ systems occur in pregnancy, which include circulatory, metabolic and hormonal changes [11]. During normal pregnancy, there is an increased thyroid demand and increased iodine uptake and synthesis of thyroid hormones. Changes in thyroid functions are well documented in

normal pregnancy but the information about thyroid function in preeclamptic pregnancy is scanty. The changes in thyroid function during pregnancy are accounted for by high circulating estrogens [12]. The maternal thyroid hormone excess or deficiency can influence maternal and fetal outcome at all stages of pregnancy and can interfere with ovulation and fertility [13].

Although pregnancy is usually associated with mild hypothyroidism, woman complicated with preeclampsia have high incidence of hypothyroidism that might correlates with the severity of preeclampsia [14]. Maternal hypothyroidism is the most common disorder of thyroid function in pregnancy which has been associated with fetal effects such as fetal loss, reduced intellectual function in the offsprings, premature birth, low birth weight increased neonatal respiratory distress and adverse maternal outcomes such as pregnancy induced hypertension, post partum hemorrhage, placental abruption and [15-16] Moreover hypothyroidism has been listed as one of the causes of high blood pressure i.e. the physiological changes in thyroid gland during pregnancy have been suggested as one of the pathophysiological cause of preeclampsia [17].

The above incidence may justify screening for thyroid function during pregnancy [18]. Although there are limited number of studies on the levels of thyroid hormones in preeclampsia and it is suggested that there may be mutual influence between preeclampsia and thyroid function [19]. Thus it has been suggested that preeclampsia has the effect on TSH levels thus exposing preeclamptic patients to the risk for low birth weight babies [20]. Therefore the study was undertaken to estimate the levels of thyroid hormones in preeclamptic pregnant women and its comparison with normal pregnant women for predicting the severity of preeclampsia.

### Material and Methods

This case control study was conducted in the Department of Biochemistry M.G.M. Medical College and associated M.Y. Hospital. Indore. The 35 pregnant women were taken as subjects clinically diagnosed as preeclampsia during third trimester (28-40 weeks) with the age 18-35 years visiting obstetrics OPD and wards of M.Y. Hospital. This was done on the basis of blood

pressure, (both systolic and diastolic) proteinuria and pathological edema, which are the diagnostic criteria of preeclampsia. As a control group 35 healthy normotensive pregnant women were taken who were also in the third trimester (28-40 weeks) of their pregnancy with the age 18-35 years along with the same parity and gestational age. Inclusion criteria for preeclamptic pregnant women included in the study were: should not be using any kind of oral contraceptives, anticoagulant drugs, should be non-smokers and non alcoholics and exclusion criteria was: past history of diabetes, systemic or endocrine disorder, chronic infection, chronic renal disease and hypertension women in the labor pains were excluded from the study.

Preeclampsia was diagnosed according to American college of Obstetrics and Gynecology (ACOG) criteria: a blood pressure higher than 140/90 mm Hg and proteinuria more than 300mg/24hr were observed on at least two occasions more than 6hrs apart after the 20<sup>th</sup> weeks of pregnancy.

*Sample collection:* Single samples of 10 ml of ante-cubital venous blood were obtained with aseptic measure. After clotting, the blood was centrifuged for 30 minutes and the supernatant (serum) was taken in the separate test tube. Serum for thyroid hormone estimation was ready and was measured by a one step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA) (Biomerieux, Mini Vidas, France).

*Statistical Analysis:* All the data were expressed as mean  $\pm$  SD. The statistical significance was evaluated by Student's t-test using SPSS software, version 20. The level of significance was set at  $< 0.05$ .

### Results

Table no.1 shows the Anthropometric factors of healthy normotensive pregnant women and preeclamptic pregnant women. When comparison of maternal age and body mass index was done between both the groups, no significant difference was observed between the groups ( $p > 0.05$ , Table no-1). Gestational age, systolic and diastolic blood pressures were significantly higher in preeclamptic

pregnant women as compared to healthy normotensive pregnant women ( $p < 0.001$ , Table no- 1).

**Table-1: Comparison of mean and standard deviation of Anthropometric factors of Control and Subjects**

| Anthropometric factors              | Healthy normotensive pregnant women (n=35) | Preeclamptic pregnant women (n=35) |
|-------------------------------------|--|------------------------------------|
|                                     | Mean $\pm$ SD                              | Mean $\pm$ SD                      |
| Age (yrs)                           | 23.17 $\pm$ 2.61                           | 22.94 $\pm$ 3.25 <sup>@</sup>      |
| BMI (Kg/m <sup>2</sup> )            | 23.83 $\pm$ 1.62                           | 24.13 $\pm$ 1.45 <sup>@</sup>      |
| Gestational age (wks)               | 38.54 $\pm$ 3.37                           | 35.85 $\pm$ 2.65 <sup>#</sup>      |
| Systolic blood pressure (mm of Hg)  | 114.85 $\pm$ 4.99                          | 140.0 $\pm$ 5.34 <sup>#</sup>      |
| Diastolic blood pressure (mm of Hg) | 75.42 $\pm$ 5.52                           | 92.28 $\pm$ 7.50 <sup>#</sup>      |

<sup>@</sup>  $p > 0.05$ -compared with healthy normotensive pregnant women, <sup>#</sup>  $p < 0.001$ -compared with healthy normotensive pregnant women

**Table-2: Comparison of mean and standard deviation of Thyroid profiles of Control and Subjects**

| Thyroid Profile        | Healthy normotensive pregnant women (n=35) | Preeclamptic pregnant women (n=35) |
|------------------------|--|------------------------------------|
|                        | Mean $\pm$ SD                              | Mean $\pm$ SD                      |
| Serum T3 (ng/ml)       | 1.38 $\pm$ 0.45                            | 1.39 $\pm$ 0.35 <sup>@</sup>       |
| Serum T4 ( $\mu$ g/dl) | 10.26 $\pm$ 3.67                           | 10.99 $\pm$ 3.34 <sup>@</sup>      |
| Serum TSH (mIU/mL)     | 3.35 $\pm$ 1.36                            | 6.22 $\pm$ 1.37 <sup>#</sup>       |

<sup>@</sup>  $p > 0.05$ -compared with healthy normotensive pregnant women, <sup>#</sup>  $p < 0.001$ -compared with healthy normotensive pregnant women

Table no.2 shows the comparison of Thyroid profiles between healthy normotensive pregnant women and preeclamptic pregnant women. The levels of T3 and T4 was found to be decreased in preeclamptic pregnant women when compared with healthy normotensive pregnant women and the difference was found to be not significant

between both the groups ( $p > 0.05$ , Table no.2). But the mean TSH level for preeclamptic pregnant women was higher than the healthy normotensive pregnant women with highly significant difference ( $p > 0.001$ , Table no.2).

### Discussion

Preeclampsia is a serious complication of pregnancy with unknown etiology. Although it is defined as triad of hypertension, edema and proteinuria, it can affect other maternal systems [21]. The condition correlates with deficient intravascular production of prostacyclin, a vasodilator and excessive production of thromboxane, a platelet derived vasoconstrictor and stimulant of platelet aggregation [22]. Though the effect of preeclampsia and thyroid dysfunction in pregnancy is very well studied, the relationship between the two is poorly established.

As estrogen levels during normal pregnancy increases, the increased estrogen levels cause the increased production of proteins by the liver. As a result, hepatocytes increase their production of thyroid-binding globulin, the protein that transports T4 in the circulation. High estrogen due to oligosaccharide modification reduces peripheral degradation of thyroid binding globulin so the content of thyroid binding globulin in the serum increases. Due to the elevated serum level of thyroid binding globulin the binding capacity of the plasma increases so more hormones bind to the globulin. This increases the plasma content of the thyroid hormones. In addition, in pregnancy, the stimulatory effect of serum hCG of placental origin increased metabolic demand and mental stress may increase overall thyroid activity and elevate thyroid hormone levels [23].

Preeclampsia is pregnancy-induced auto-intoxication with multisystem disorders; the most affected organs are brain, liver and kidneys where the functional disorders of these organs are evident. During preeclampsia, involvement of liver and kidney may lead on to decreased peripheral conversion of T4 to T3 hence the level of T3 decreases [24]. Impaired placental function deprives the fetus from sufficient oxygen and

nutrient supplies. This may lead to a compromised fetal condition and a “low T4 syndrome” may develop [25]. It has been suggested that reduced concentration of thyroid hormones in preeclampsia may be due to the loss of protein and protein-bound hormones in the urine [26]. Also faulty estrogen production due to placental dysfunction in preeclampsia accounts for the decreased levels of T3 and T4 [27].

Many investigators in their studies concluded that preeclamptic women may also be affected by a variety of conditions such as systemic illnesses, protein-energy malnutrition, starvation, Cushing’s syndrome, excessive steroid therapy. When the women who developed such systemic disorders, the extrathyroidal deiodination of T4 to T3 has been reduced [28].

The significant elevation in the level of TSH in preeclampsia gives a good indicator that the preeclampsia is associated with an increased level of TSH in the serum, and also the level of increment in this hormone depends on the severity of disease. Elevated levels of TSH might be associated with risk for developing preeclampsia and these patients may have the tendency to have low birth weight babies [25].

Endothelial activation/dysfunction is a central pathogenic feature in women with preeclampsia [29]. Preeclampsia is associated with decreased circulating levels of VEGF and PlGF, which are angiogenic factors. This leads to an anti-angiogenic state and causes endothelial dysfunction [30]. TSH can act as a tissue specific angiogenesis in physiological and pathological conditions [31]. Other possible explanation might be the elevation of secretion of the placental thyrotropic like peptide and increased levels of pre-delivery soluble fms-like tyrosine-kinase level [32].

Kaya E et al [26], Lao et al [27] and Kumar et al [33] observed the similar findings in preeclamptic pregnant women with high TSH levels and low thyroid hormones. Preeclamptic pregnancies are therefore associated with hypothyroidism (elevated TSH and low T3 and T4) which may cause vascular smooth muscle contraction both in systemic and renal vessels which leads to increased diastolic hypertension, peripheral vascular resistance and decreased tissue perfusion [34]. Contradictory findings was observed by Qublan et al [35] who reported no significant differences in TSH levels between two groups.

### Conclusions

In the present study TSH levels were elevated in preeclamptic pregnant women as compared to healthy normotensive pregnant women with decreased T3 and T4 levels but with no significant difference. It could indicate the possible etiology for preeclampsia. Elevated TSH levels could be used as predictor of preeclampsia. So it was concluded that identification of thyroid hormones and thyroid screening during pregnancy in the future might be helpful in predicting the occurrence of preeclampsia. Thyroid function screening should be done in first trimester of pregnancy for early diagnosis and treatment of preeclampsia to prevent further complication of it.

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