

## Study of Thyroid Hormonal Status in Preeclamptic Patients

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### Abstract

*The physiological changes in the thyroid gland during pregnancy were well understood. Serum TSH levels were significantly increased without changes in free T<sub>3</sub> and T<sub>4</sub> in preeclamptic patient compared to normal pregnancy. This study tried to find out a possible relationship between preeclampsia and thyroid profile.*

*The present study determines thyroid hormonal levels in cases of preeclampsia in the third trimester of pregnancy. TSH level were significantly higher in preeclamptic group as compared to control.*

*A prospective case control study was conducted in the Department of Obstetrics and Gynecology, Chittagong Medical College Hospital, Chittagong.*

*Thyroid hormone, namely Triiodothyronine (Free T<sub>3</sub>), Thyroxine (Free T<sub>4</sub>) and Thyroid Stimulating Hormone (TSH) were evaluated by radioimmunoassay. In this case control study pregnant women with preeclampsia were recruited after the diagnosis were made and compared with equal number of healthy normotensive pregnant women in third trimester.*

*The data were analyzed using unpaired 't' test and chi-square test. When P value were <0.05, the result were accepted as significant.*

*Increase TSH level were associated with a risk for occurrence of preeclampsia.*

**Key Words:** Hypothyroidism, preeclampsia, pregnancy and thyroid hormones

### Introduction

Hypertensive disease in pregnancy is a major cause of maternal and fetal morbidity and mortality<sup>1</sup>. PE adversely affects the maternal and fetal outcome due to its wide spread multi organ involvement. PE is a complication in approximately 5% of all pregnancies<sup>1</sup>.

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The incidence in primigravida is about 10% and in multigravida 5%. PE is one of the most common causes of perinatal morbidity and mortality resulting in an estimated 35 ~ 300 deaths per 1000 births depending on neonatal support<sup>1</sup>.

PE usually occurs in women at both extremes of reproductive age however the risk of PE is greatest in women younger than 20 years<sup>1</sup>. PE is more prevalent in developing countries like Bangladesh where poverty, malnutrition, micronutrient deficiencies, early marriage, early child birth and lack of antenatal care are more common.

In Bangladesh the incidence of PE is very high. It is about 10 ~ 15% of all deliveries and it remains one of the commonest (about 16%) cause of maternal death being in the third position of all MMR<sup>2</sup>.

So preeclampsia is a matter of great concern for the obstetrician as well as pregnant women and for the nation. The exact cause of preeclampsia has not been identified. Numerous theories of potential causes exist including genetic, dietary, vascular and auto immune factors<sup>3</sup>. The causes of PE remains unknown however placental dysfunction many initiate the systematic vasospasm, ischemia and thrombosis that eventually damages maternal organs.

The mechanism of hypothyroidism in preeclamptic women has not been identified but the changes in thyroid function during pregnancy are accounted for high circulating oestrogen<sup>4</sup>. There are different views about the mechanism and clinical significance of low concentrations of thyroid hormones in PE, which are attributed to decrease plasma protein concentrations and high levels of endothelin, a potent vasoconstrictor produced by vascular endothelium after a vascular injury<sup>5,6</sup>.

There is a relationship between PE and thyroid profile. Serum TSH level significantly increased without concomitant changes in T<sub>3</sub> and T<sub>4</sub> in PE compared to normal pregnancy<sup>7</sup>. Thus TSH was found to be strong associating factor for the occurrence of PE.

### Materials and Methods

This was a descriptive cross sectional study. The study period was from January 2005 to December 2005 was conducted at in-patient department of Obstetrics & Gynaecology, CMCH. Fifty-two pregnant women

consecutively admitted with the diagnosis of preeclampsia in the third trimester were recruited for the study.

The inclusion criteria were: (a) Preeclamptic patients in the third trimester of pregnancy, (b) Healthy pregnant women in the third trimester of pregnancy.

The exclusion criteria for both the groups were: (a) The patient with pregnancy induced hypertension (PIH) without proteinuria, (b) the pregnant women with previous history of thyroid diseases or metabolic disorders, maternal history of taking antithyroid drugs, (c) History of thyroid surgery or treatment with RAI, (d) Pregnancy with chronic renal disease, (e) History of multiple pregnancies, (f) Pregnancy with chronic hypertension, (g) Chronic liver disease and (h) Medication with diuretics, steroids and anti-HTN drugs.

10 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. All samples were sent to the laboratory with different code numbers. Sera was separated and stored at  $-20^{\circ}$  C until assayed. Free  $T_3$  (triiodothyronine), free  $T_4$  (thyroxine) and TSH (thyroid-stimulating hormone) were measured using radioimmunoassay. All women were followed up through their antenatal, intrapartum and postpartum period. They were especially observed for the development of the symptoms and signs of hypothyroidism. Data were statistically analyzed by computer with SPSS (Version 11.5). Mean values were calculated to see the central tendency, standard deviation, standard error were calculated to assess the dispersion of the data and the Student's 't' test, Chi-square test were performed to detect statistical significance of the observations. A probability value ( $p$  - value) of  $< 0.05$  was considered significant with 95% CI.

## Results

A total 104 pregnant women were included in this study. Among them 52 women with the diagnosis of preeclampsia selected as Case and 52 were normal pregnant women as control.

### Age, parity and gestational age of participant group:

The mean ( $\pm$ SD) age of the study group and control group were  $26.15 \pm 4.17$  years and  $26.19 \pm 4.20$  years respectively and there was no statistically significant difference between the two groups ( $p > 0.05$ ).

The mean ( $\pm$ SD) parity of the study group and control group were  $1.28 \pm 0.90$  years and  $1.30 \pm 0.88$  years respectively and there was no statistically significant difference between the two groups ( $p > 0.05$ ).

The mean ( $\pm$ SD) gestational age at the time of taking the blood sample for thyroid hormonal level was  $34.30 \pm 2.92$  weeks in the study group and  $35.10 \pm 2.82$  weeks was in the control group. The difference between the two groups was not statistically significant ( $p = 0.55$ ). The results are shown in Table-I.

**Table -I: Age, parity and gestational age of participant groups**

Parameters	Control	Case	t- value	p- value	dF
Age in years (Mean $\pm$ SD)	26.19 $\pm$ 4.20	26.15 $\pm$ 4.17	0.05	0.9618	102
Parity (Mean $\pm$ SD)	1.30 $\pm$ 0.88	1.28 $\pm$ 0.90	0.044	0.0670	102
Gestational age in weeks (Mean $\pm$ SD)	35.10 $\pm$ 2.82	34.30 $\pm$ 2.92	0.35	0.5500	102

### Thyroid function tests

The mean ( $\pm$ SD) TSH of the study group and control group were  $4.14 \pm 2.24$  mIU/L and  $2.75 \pm 1.73$  mIU/L respectively and there was highly significant difference between the two groups ( $p = 0.0007$ ).

The mean ( $\pm$ SD)  $T_3$  of the study group and control group were  $1.95 \pm 0.64$  nmol/L and  $1.98 \pm 0.57$  nmol/L respectively and there was no significant difference between the two groups ( $p > 0.05$ ).

The mean ( $\pm$ SD)  $T_4$  of  $128.38 \pm 33.43$  nmol/L was in the study group and  $126.37 \pm 34.70$

nmol/L was in the control group. The difference between the two groups was not statistically significant ( $p > 0.05$ ). The results are shown in Table-II.

**Table -II: Thyroid function tests of participants groups**

Parameters	Control	Case	t- value	p- value	dF
TSH (mIU/L) (Mean $\pm$ SD)	2.75 $\pm$ 1.73	4.14 $\pm$ 2.24	3.51	0.0007	102
$T_3$ (nmol/L) (Mean $\pm$ SD)	1.98 $\pm$ 0.57	1.95 $\pm$ 0.64	0.267	0.7900	102
$T_4$ (nmol/L) (Mean $\pm$ SD)	126.37 $\pm$ 34.70	128.38 $\pm$ 33.43	0.30	0.7664	102

### TSH levels of both case and control groups

Out of 52 pregnant women in study group, 21 (40.40%) had higher TSH titers ( $> 4.8$  mIU/L) and 52 pregnant women in control group, 9 (17.30%) had higher TSH titers ( $> 4.8$  mIU/L). Twenty one (70.00%) of the 30 pregnant women with abnormal TSH titers, had the diagnosis of preeclampsia whereas 31 (41.90%) of the 74 pregnant women with normal TSH titers, had preeclampsia in the third trimester. This difference between the two groups was statistically significant ( $p = 0.009$ ), degrees of freedom was 1. Odds ratio indicates that preeclampsia group have chance of higher TSH ( $> 4.8$  mIU/L) by 3.24 times. The results are shown in Table-III.

**Table -III: Distribution of normal and increased TSH levels in both preeclamptic and control groups**

Group	TSH Group		Total	Odds ratio (95% confidence interval)	$\chi^2$ -value	p-value	dF
	TSH $< 4.8$ mIU/L	TSH $> 4.8$ mIU/L					
Control	43 82.70%	9 17.30%	52	1.00	6.75	0.009	1
Case	31 59.60%	21 40.40%	52	3.24 (2.18-10.54)			
Total	74	30	104				

## Discussion

This study was conducted in the Obstetrics and Gynecology Department of CMCH, Chittagong with the intention to determine the thyroid hormonal levels in case of 52 preeclamptic patients and 52 matched controls in the third trimester.

In this study the mean ( $\pm$ SD) age of the study group and control group were  $26.15 \pm 4.17$  and  $26.19 \pm 4.20$  years respectively and there was no statistically significant difference between the two groups ( $p > 0.05$ ).

It was also similar to other findings, Kumar et al found in 2005 the mean ( $\pm$ SD) age of the study group and control group were  $28.40 \pm 6.24$  years and  $27.50 \pm 5.91$  years respectively<sup>7</sup>. Larijani et al observed the mean ( $\pm$ SD) for the age of the study group and control group were  $27.09 \pm 5.24$  and  $27.04 \pm 4.42$  years respectively<sup>10</sup>. Lao TT et al studies the mean age  $28.40 \pm 5.20$  and  $27.50 \pm 5.10$  years of study and control groups and there was no significant difference between the two groups<sup>5</sup>.

In this study the mean ( $\pm$ SD) gestational age at the time of taking blood sample for thyroid hormonal levels was  $34.30 \pm 2.92$  weeks in the study group and  $35.10 \pm 2.85$  weeks was in the control group. The difference between the groups was not statistically significant ( $p = 0.55$ ). The mean ( $\pm$ SD) parity of the study group and control group were  $1.28 \pm 0.90$  and  $1.30 \pm 0.88$  respectively and there was no difference between the two groups ( $p > 0.05$ ).

It was also similar to the other studies, Larijani et al found the mean ( $\pm$ SD) gestational age was  $35.67 \pm 6.88$  weeks was group and the mean ( $\pm$ SD) parity was  $2.51 \pm 1.43$  in the study group and  $2.98 \pm 1.75$  was in the control group<sup>10</sup>.

In this research work, the mean ( $\pm$ SD) TSH of the study group and control group were  $4.14 \pm 2.24$  mIU/L and  $2.75 \pm 1.73$  mIU/L respectively and there was highly significant different between the two groups ( $p = 0.0007$ ). The mean ( $\pm$ SD)  $T_3$  of the study group and control group were  $1.95 \pm 0.64$  nmol/L and  $1.98 \pm 0.57$  nmol/L respectively and there was no difference between the two groups ( $p > 0.05$ ). The mean ( $\pm$ SD)  $T_4$  of  $128.38 \pm 33.43$  nmol/L was in the study group and  $126.37 \pm 34.70$  nmol/L was in the control group. The difference between the two groups was not statistically significant ( $p > 0.05$ ).

The mean values of thyroid hormones were within normal laboratory ranges in both the group. The mean  $T_3$  and  $T_4$  titres were not significantly different in the two groups ( $T_3$ ,  $p = 0.79$  and  $T_4$ ,  $p = 0.76$ ). The mean TSH value was significantly higher in the problematic women than the control ( $p < 0.0007$ ) degree of freedom was 102).

These results were similar to the findings of Kumar et al in the antenatal clinic of a public hospital of Delhi where they found the mean ( $\pm$ SD) TSH of the study group and control group were  $4.6 \pm 3.64$  mIU/L and  $2.5 \pm 2.01$  mIU/L respectively and there was highly significant difference between the two groups ( $p < 0.001$ )<sup>7</sup>.

Lao TT et al in their study found that normotensive women and preeclamptic patients had ignorantly higher TSH ( $p < 0.001$ ) while  $T_4$  and  $T_3$  concentration were slightly low but not significantly lower in the third trimester of pregnancy<sup>5</sup>.

There were similar studies, Larijani reported that the observed reduced serum concentration regarding the  $T_4$  and  $T_3$  reflect the severity of PE. Confirmatory to these report in their study mild cases of PE had lower level of  $T_3$  and  $T_4$  than healthy controls. It had been suggested that the reduced concentration of  $T_3$  and  $T_4$  levels might be explained by the loss of protein and protein bound hormones. Since  $T_3$  is mostly the product of peripheral conversion of  $T_4$ , the involvement of organs such as the liver and kidneys contributes to low level of  $T_3$ <sup>8</sup>.

In the present study, only TSH is significantly increased in preeclamptic patients at the time of diagnosis as compares to control subjects. The researches findings was also similar to the findings for the reports that preeclamptic women had higher incidence of biochemical hypothyroidism compares with normotensive pregnant women<sup>6</sup>. 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 concentration in these patients<sup>9</sup>. Serum  $T_3$  and  $T_4$  were decreases significantly and TSH was increased significantly in preeclamptic women in their third trimester<sup>11</sup>. The titres of  $T_3$  are reported to be significantly related to the decreased plasma albumin concentration in preeclamptic women<sup>5</sup>. It has been suggested that reduced serum concentrations of thyroid hormones in toxemia may be due to the loss of protein and protein-bound hormones in the urine. Modest decreases in thyroid hormones with concomitant increases in TSH levels in maternal serum correlated with severity of PE or eclamptic and high levels of endothelin<sup>6</sup>. The endothelial cell dysfunction plays an important role in the pathogenesis of PE.

In this study TSH levels of both case and control groups were: Out of 52 pregnant women in study group, 21 (40.40%) had higher TSH titers ( $> 4.8$  mIU/L) and 52 pregnant women in control group, 9 (17.30%) of the 30 pregnant women with abnormal TSH titres, had the diagnosis of PE whereas 31 (41.90%) of the 74 pregnant women with normal TSH titers, had PE in the third trimester. This difference between the two groups was found statistically significant ( $p = 0.009$ ), degrees of freedom was 1. Odds Ratio indicates preeclamptic group had change of higher TSH by 3.24 times than the normal group.

The difference in the number of pregnant women of the two groups, having high TSH titres was also significant. More number of preeclamptic women had increased TSH levels at the time of diagnosis when compares with normotensive pregnant women. Kumar et al also observed statistically significant higher number of cases with PE (76.7%) in pregnant women with abnormally high levels of TSH<sup>7</sup>. Diseases of the thyroid gland itself are a predisposing factor for the development of PE<sup>12</sup>.

In this study serum TSH level was significantly increased, but there was no alteration in serum level of  $T_3$  and  $T_4$ . Further study with larger sample is suggested to see whether the serum TSH level could be made as a predictor of development of preeclampsia in pregnancy.

## References

1. Brooks, M.B., 2005. Pregnancy, Preeclampsia [online]. Available from: <http://www.emedicine.com/EMERG/topic480.htm> [Accessed 24 May 2005].
2. Khatoon, M.S. Clinical Profile and Management of eclampsia in SSMCH and MF, Dhaka. Dissertation (FCPS, Obstetrics & Gynaecology). Bangladesh College of Physicians and Surgeons, Dhaka, Bangladesh, 1992.
3. Gaudier, F.L., 2003. Preeclampsia [online]. Available from: <http://nlm.nih.gov/medlineplus/ency/article/000898> [Accessed 24 May 2005].
4. Brent, G.A. Maternal thyroid function: Interpretation of thyroid function tests in pregnancy. *Clin Obstet Gynecol*, 1997;40:3-15.
5. Lao, T.T. Maternal thyroid hormones and outcome of pre-eclamptic pregnancies. *Br J Obstet Gynecol*, 1990;97:71-74.
6. Basbug, M. Correlation maternal thyroid function tests and endothelin in preeclampsia-eclampsia. *Obstetrics & Gynaecology*, 1999;94:551-555.
7. Kumar A., Ghosh, B.K. and Murthy, N.S. Maternal Thyroid Hormonal Status in Preeclampsia. *Indian Journal of Medical Sciences*. Feb, 2005;59:57-63.
8. Khaliq F. Thyroid functions in pre-eclampsia and its correlation with maternal age, parity, severity of blood pressure and serum albumin. *Indian J Physiol Pharmacol*, Apr, 1999;43:193-8.
9. Davis, L.E., Leveno, K.J. and Cunningham, F.G. Hypothyroidism complicating pregnancy. *Obstet Gynecol*, 1988;72:108-112.
10. Larijani, B. Thyroid hormone alteration in pre-eclamptic women. *Gynecol Endocrinol*, 2004;18:97-100.
11. Tolino, A., De Concillis, B. and Montemagno, U. Thyroid hormones in the human pregnancy. *Acta Obstet Gynecol Scand*, 1985;64:557-9.
12. Vojvodic, L.J. The effect of pre-eclampsia on thyroid gland function. *Spr Arh Celok Lek*, 1993;121: 4-7.