

## THYROID FUNCTIONS IN PRE-ECLAMPSIA AND ITS CORRELATION WITH MATERNAL AGE, PARITY, SEVERITY OF BLOOD PRESSURE AND SERUM ALBUMIN

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**Abstract :** Maternal thyroid function was investigated in 32 pre-eclamptic women and 10 normal pregnant women in their third trimester. Serum total tri-iodothyronine (TT<sub>3</sub>) and total thyroxine (TT<sub>4</sub>) were decreased significantly (P<0.001) and TSH was increased significantly (P<.001) in pre-eclampsia as compared to normal pregnancy. There was no influence of parity and maternal age on thyroid functions. TT<sub>3</sub> and TT<sub>4</sub> decreased significantly (P<.001) with increase of serum albumin, while there was no correlation of TT<sub>4</sub> with serum albumin.

**Key words :** thyroid functions      pre-eclampsia      maternal age  
parity      blood pressure      serum albumin

### INTRODUCTION

The study of thyroid disease in pregnancy is important due to the fact that, common thyroid diseases have a strong female predominance and auto immune and neoplastic thyroid diseases often occur in young adults. It was found in a large survey that 0.8% of American women who carried pregnancies for at least 20 weeks had hyperthyroidism or hypothyroidism (1). Secondly, obstetricians are increasingly aware of the potential or adverse effects of hyper or hypothyroidism on the outcome of pregnancy and have a high index of suspicion.

In normal pregnancy, changes in thyroid

function are well documented (2, 3, 4) but information about thyroid function in complicated pregnancies is scanty. High concentrations of total and free thyroxine (TT<sub>4</sub>) and FT<sub>4</sub>) and subnormal tri-iodothyronine (TT<sub>3</sub>) and free tri iodothyronine (FT<sub>3</sub>) concentrations have been reported in pre-eclamptic patients. (5, 6). On the other hand low TT<sub>4</sub>, FT<sub>4</sub> and thyroxine binding globuline (TBG), high thyroid stimulating hormone (TSH) and no change in TT<sub>3</sub> concentrations was reported in protienuric pre-eclamptic women (7).

The present study has examined the thyroid function in pre-eclamptic and normal pregnant women in the third

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trimester of pregnancy. The influence of parity, maternal age and mean arterial B.P. on thyroid functions is studied. The thyroid functions are also correlated with serum albumin levels.

## METHODS

The present study was conducted on the proved cases of pre-eclampsia. Thirty two pre-eclamptic women in third trimester of pregnancy were selected from Gynaecology & Obstetrics inpatient department of J.N. Medical College Hospital. A.M.U., Aligarh, between July 1996 and September 1997. Exclusion criteria were associated renal, hepatic, cardiac disease, metabolic disorder like diabetes mellitus and past history of hypertension.

Previously healthy normotensive women were considered to have pre-eclampsia if their blood pressure after 20 weeks of gestation was raised to 140/90 mmHg or more or had mean B.P. (Diastolic + 1/3rd pulse pressure) of more than 110 mmHg. The increase in B.P. had to be present on at least two occasions 6 hours apart along with proteinuria of more than 300 mg/day or 100 mg/dl. Ten women with normal pregnancy in their third trimester were matched on an individual basis for the same parameters and were taken as controls.

Subjects were between 20–40 yrs of age (mean–26 yrs) were having singleton pregnancy and were not on any medication during pregnancy (except vitamins, iron and calcium).

### Hormonal estimation

Intracubital venous blood was collected

early morning on empty stomach, with the patient in supine position for at least 10 mins. The blood was allowed to coagulate and the serum obtained was frozen at  $-20^{\circ}\text{C}$  until required for measurement. All estimations were carried out in single batch in duplicate by UBI MAGIWELL™ enzyme immuno assay kit. (ELISA). It provides quantitative measurement of  $\text{TT}_3$ ,  $\text{TT}_4$  & TSH in human serum.

*Estimation of serum albumin: B.C.G. Method (Kaplan and Szabo 1983)*

*Principle:* Under acidic condition, albumin present in the serum sample binds to bromocresol green to form a green coloured albumin BCG complex which is photometrically measured at 630 nm. Intensity of the colour formed is directly proportional to the sample.

*Procedure:* Three dry clean test tubes were taken serving as blank B, standard S test T. 2.5 ml of working reagent was added to each of the three test tubes by means of a clean dry pipette. 50  $\mu$  lit of albumin standard was added to 'standard' test tube by means of a microlitre pipette. 50  $\mu$  lit of serum was added to the 'test' test tube and 50  $\mu$  lit of distilled water was added to the 'blank' test tube. The contents of test standard and blank were read after 1 min and within 10 min at 628 nm or with red filter against distilled water.

*Calculation :*

Albumin (gm/dl)

$$\frac{\text{Absorbance of test} - \text{Absorbance of blank}}{\text{Absorbance of standard} - \text{Absorbance of blank}} \times 4.06$$

**Data Analysis**

Values were presented as mean ± SD. Hormonal levels were compared between the different sets by student 't' test. The corresponding value of 'P' was obtained from the standard table of critical 't' values at the appropriate degree of freedom. Statistical significance was considered as P<.05.

Thyroid functions were correlated with serum albumin by the coefficient of correlation (r).

**RESULTS**

The comparison of thyroid function in normal and pre-eclamptic pregnancy is shown in Table I. Serum TSH increased significantly while TT<sub>4</sub> and TT<sub>3</sub> decreased significantly in pre-eclampsia as compared to normal pregnancy.

The thyroid function in the two age groups (below 25 yrs. and above 25 yrs.) in normal and pre-eclamptic pregnancy is shown in Table II. There was no significant change in the levels of TSH, T<sub>3</sub> and T<sub>4</sub> in the two age groups.

TABLE I : Thyroid functions and serum albumin levels in normal and pre-eclamptic pregnancies.

	Normal pregnancy Mean ± SD N = 10	Pre-eclamptic pregnancy Mean ± SD N = 32
Albumin (gm/dl)	3.95 ± 0.49	2.86 ± 0.34*
T.S.H. (µ.I.U./ml)	2.34 ± 0.24	3.77 ± 0.53*
TT3 (ng/dl)	195.6 ± 7.41	150.62 ± 10.32*
TT4 (µgm/dl)	14.36 ± 1.11	11.31 ± 0.94*

\*P<.001

TABLE II : Thyroid Function in Normal and Pre-Eclamptic Women-Below 25 yrs. and Above 25 yrs.

		Age	
		Below 25 yrs.	Above 25 yrs.
T.S.H.	Normal	2.37 ± .26	2.29 ± .20
(µ.I.U./ml)	PET	3.63 ± .70	3.84 ± .40
T3	Normal	193.5 ± 8.30	198.75 ± 4.20
(ngm/dl)	PET	153.54 ± 12.16	149.09 ± 8.84
T4	Normal	14.11 ± 1.05	14.72 ± 1.09
(µm/dl)	PET	11.43 ± 1.09	11.20 ± .88

TABLE III : Thyroid Function in Normal and Pre-Eclamptic Women in the Two Parity Groups.

		Primiparous	Multiparous
T.S.H.	Normal	2.25 ± .27	2.47 ± .09
(µ.I.U./ml)	PET	3.57 ± .66	3.94 ± .28
TT <sub>3</sub>	Normal	197.66 ± 6.94	192.5 ± 7.01
(ngm.dl)	PET	153.6 ± 12.61	148. ± 6.76
TT <sub>4</sub>	Normal	14.81 ± .81	13.67 ± 1.15
(µgm/dl)	PET	11.64 ± 1.10	10.96 ± .69

The thyroid functions were compared for both the subjects and controls in the primiparous and multiparous women (Table III). There was no significant change in TSH, T<sub>3</sub> and T<sub>4</sub> in the two parity groups.

The subjects were grouped according to level of mean B.P. into two (i) between 110–115 mgHg (ii) above 115 mmHg. The controls had mean B.P. of less than 110 mmHg (Table IV).

It was observed that TSH increased significantly, while TT<sub>3</sub> and TT<sub>4</sub> decreased significantly with increase in mean B.P.

TABLE IV : Thyroid Function in Normal and Pre-Eclamptic Women With Three Levels of Mean B.P.

	Mean Blood Pressure (mmHg.)		
	<110 mmHg. (Normal)	110-115 mmHg. (PET)	>115 mmHg. (PET)
TSH ( $\mu$ I.U./ml)	2.34 $\pm$ .24	3.45 $\pm$ .57	4.02 $\pm$ .33**
TT <sub>3</sub> (ngm/dl)	195.6 $\pm$ 7.41	156.82 $\pm$ 10.08	145.83 $\pm$ 7.55*
TT <sub>4</sub> ( $\mu$ gm/dl)	14.36 $\pm$ 1.11	11.82 $\pm$ .97	10.86 $\pm$ .71*

\*P&lt;.01

\*\*&lt;.001

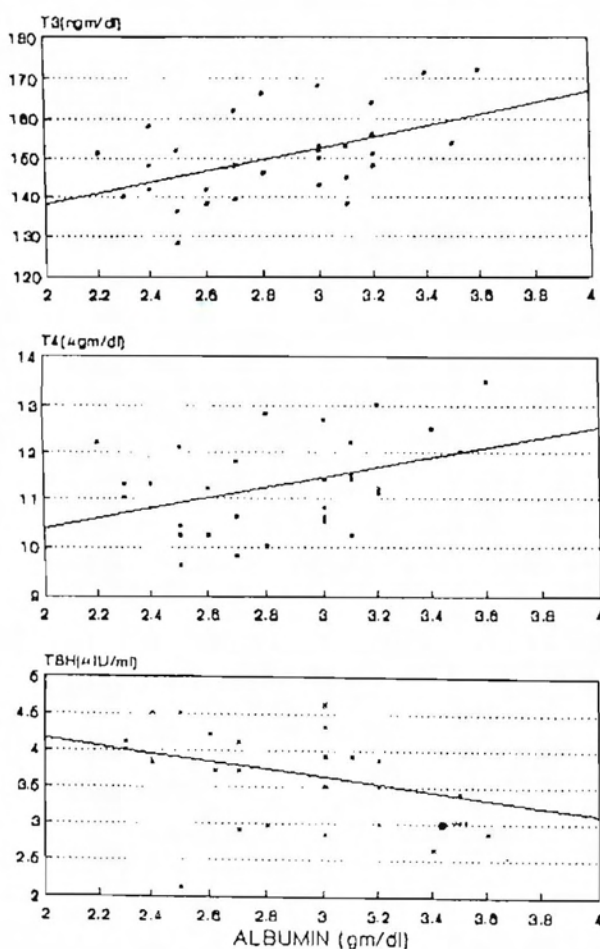


Fig. 1 : Correlation of Albumin with T3, T4, and TSH

Serum albumin decreased significantly from  $3.95 \pm 0.49$  gm/dl in normal pregnancy to  $2.86 \pm 0.34$  in preeclampsia ( $P < .001$ ). The correlation of serum albumin with TT<sub>3</sub> was significant and direct while with TSH was significant and inverse ( $P < .001$ ), while there was no correlation between serum albumin and TT<sub>4</sub>.

## DISCUSSION

In the present study the result shows that T<sub>4</sub> and T<sub>3</sub> are significantly lower and TSH is significantly increased in pre-eclamptic patients compared to the value of control group. There is no effect of maternal age in the patients, neither there is any difference in the two parity groups. Severe hypertensive pre-eclamptic patients (BP > 115 mmHg) show significant differences from less severe hypertensive pre-eclamptic patients. This signifies the positive correlation between the thyroid hormones and severity of hypertensive pregnancy.

It is well established that there is a big increase in concentration of thyroid binding globulin (TBG) during pregnancy due to influence of high levels of circulating oestrogens and as approximately 99.97% of thyroxine is protein bound the interpretation of serum total thyroxine value is difficult (2).

Serum T<sub>4</sub>, T<sub>3</sub> and TBG were reported to be significantly decreased and TSH was significantly increased in pre-eclamptic and eclamptic patients compared to the value of the control group (8). In another study higher levels of T<sub>4</sub> was reported in toxæmic patients but T<sub>3</sub> level was below that

observed in normal pregnancy (6). 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 hormones in the urine (10). Since  $T_3$  is mostly the peripheral conversion of  $T_4$ , the decrease in  $T_3$  level associated with  $T_4$  value is a normal consequence besides involvement of liver and kidneys in toxemia of pregnancies. This may be the main factor determining decreased serum  $T_3$  concentration in pre-eclamptic patients since liver and kidneys are important organs in peripheral conversions of  $T_4$  to  $T_3$  (5).

Patients with severe systemic illness and starvation often have low  $T_3$  concentration in the presence of normal or even raised  $T_4$  concentration, condition known as the "low  $T_3$  syndrome" (9). This low  $T_3$  syndrome has also been noted in pre-eclampsia (5, 6). But in the present study no such finding was observed.

The decreased  $T_3$  &  $T_4$  level and higher TSH level in comparison to normal pregnant patient suggests the presence of mild hypothyroidism in pre-eclamptic patients (10).

Although thyroid antibodies were not measured in these pre-eclamptic patients, autoimmune hypothyroidism was unlikely because the highest TSH value was only 12.3  $\mu$  IU/lit and all of them were normal when examined at their postnatal visit (10).

Measurement of free thyroid hormones using radioimmuno assay with analogue kits

tends to give low results in non-thyroidal illness and is related to the decreased plasma albumin concentration in these patients (11). The significant correlation between plasma albumin and  $FT_3$  concentration suggest that disturbed plasma albumin concentration could be responsible for the lower  $FT_3$  concentration but there was no correlation between  $FT_4$  concentration and albumin, thus hypoalbuminemia is unlikely to account for a decreased concentration of  $FT_4$  which together with a significant higher TSH concentration suggest the presence of genuine hypothyroidism (10).

The low  $T_3$  and  $T_4$  level reflect the severity of preeclampsia and these patients tend to have low birth weight babies (10). The significant correlation between  $T_4$ ,  $T_3$  with plasma albumin and urate concentrations are further evidence that thyroid hormones reflect the severity of pre-eclampsia, since low birth rate was related to low serum albumin and serum albumin was reduced in proteinuric pre-eclampsia (12).

In the present study the correlation between  $TT_3$  and albumin is significant and direct, as most of  $T_3$  is bound to plasma proteins, proteinuria accounts for its increased loss. While the correlation of albumin with  $TT_4$  is not significant as is shown in previous studies (10). The difference in  $T_3$  and  $T_4$  can be because of different degree of saturation with thyroid binding globulins. The correlation between TSH and albumin is significant and inverse because the pre-eclamptic patients are in a state of mild hypothyroidism.

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