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 (TT₃) and total thyroxine (TT₄) were decreased significantly (P<0.001) and TSH was increased significantly (P<0.001) in pre-eclampsia as compared to normal pregnancy. There was no influence of parity and maternal age on thyroid functions. TT₃ and TT₄ decreased significantly (P<0.001) with increase of serum albumin, while there was no correlation of TT₄ 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 autoimmune 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 (TT₄) and FT₄) and subnormal tri-iodothyronine (TT₃) and free tri-iodothyronine (FT₃) concentrations have been reported in pre-eclamptic patients. (5, 6). On the other hand low TT₃, FT₃ and thyroxine binding globuline (TBG), high thyroid stimulating hormone (TSH) and no change in TT₃ concentrations was reported in proteinuric pre-eclamptic women (7).

The present study has examined the thyroid function in pre-eclamptic and normal pregnant women in the third trimester.
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 protienuria 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°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 TT₃, TT₄ & 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 μl lit of albumin standard was added to ‘standard’ test tube by means of a microlitre pipette. 50 μl lit of serum was added to the ‘test’ test tube and 50 μl 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)

\[
\text{Albumin (gm/dl)} = \frac{\text{Absorbance of test} - \text{Absorbance of blank}}{\text{Absorbance of standard} - \text{Absorbance of blank}} \times 4.06
\]
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 TT4 and TT3 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, T3 and T4 in the two age groups.

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

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

*P<.001

The subjects were grouped according to level of mean B.P. into two (i) between 110–115 mmHg (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 TT3 and TT4 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.

<table>
<thead>
<tr>
<th>Mean Blood Pressure (mmHg)</th>
<th>&lt;110 mmHg</th>
<th>110-115 mmHg</th>
<th>&gt;115 mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Normal)</td>
<td>TSH (μIU/ml)</td>
<td>TT3 (ng/ml)</td>
<td>TT4 (μg/ml)</td>
</tr>
<tr>
<td>(PET)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.34 ± .24</td>
<td>3.45 ± .57</td>
<td>4.02 ± .33 **</td>
</tr>
<tr>
<td>T3 (ng/ml)</td>
<td>195.6 ± 7.41</td>
<td>156.82 ± 10.08</td>
<td>145.83 ± 7.55 *</td>
</tr>
<tr>
<td>T4 (μg/ml)</td>
<td>14.36 ± 1.11</td>
<td>11.82 ± .97</td>
<td>10.86 ± .71 *</td>
</tr>
</tbody>
</table>

*P<.01
**<.001

Serum albumin decreased significantly from 3.95 ± 0.49 gm/dl in normal pregnancy to 2.86 ± 0.34 in preeclampsia (P<.001). The correlation of serum albumin with TT3 was significant and direct while with TSH was significant and inverse (P<.001), while there was no correlation between serum albumin and TT4.

DISCUSSION

In the present study the result shows that T4 and T3 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>115mmHg) 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 T4, T3 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 T3 was reported in toxaemic patients but T3 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 T₃ is mostly the peripheral conversion of T₄, the decrease in T₃ level associated with T₄ value is a normal consequence besides involvement of liver and kidneys in toxemia of pregnancies. This may be the main factor determining decreased serum T₃ concentration in pre-eclamptic patients since liver and kidneys are important organs in peripheral conversions of T₄ to T₃ (5).

Patients with severe systemic illness and starvation often have low T₃ concentration in the presence of normal or even raised T₄ concentration, condition known as the “low T₃ syndrome” (9). This low T₃ syndrome has also been noted in pre-eclampsia (5, 6). But in the present study no such finding was observed.

The decreased T₃ & T₄ 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 µ 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 FT₃ concentration suggest that disturbed plasma albumin concentration could be responsible for the lower FT₃ concentration but there was no correlation between FT₄ concentration and albumin, thus hypoalbuminemia is unlikely to account for a decreased concentration of FT₄ which together with a significant higher TSH concentration suggest the presence of genuine hypothyroidism (10).

The low T₃ and T₄ level reflect the severity of preeclampsia and these patients tend to have low birth weight babies (10). The significant correlation between T₄, T₃ with plasma albumin and urate concentrations are further evidence that thyroid hormones reflect the severity of preeclampsia, 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 TT₃ and albumin is significant and direct, as most of T₃ is bound to plasma proteins, proteinuria accounts for its increased loss. While the correlation of albumin with TT₄ is not significant as is shown in previous studies (10). The difference in T₃ and T₄ 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.
REFERENCES


