



Original Article

Functional Status of Maternal Thyroid Gland in Eclampsia

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Abstract

Marked changes in maternal thyroid activity occur in pregnancy. During pregnancy bodily hormonal changes and metabolic demands result in complex alteration in the bio-chemical parameters of thyroid activities. Besides these, thyroid enlargement, increased thyroid capability for iodine uptake and increase in basal metabolic rate are evidential though these findings are not usually associated with symptoms of hyperthyroidism in pregnancy. Serum concentration of thyroid hormone thyroxine and triiodothyronine in complicated pregnancy like eclamptic toxemia is another field of controversy. To evaluate the changes in thyroid function in normal pregnancy and eclamptic toxemia, a study was undertaken in Rajshahi Medical College Hospital. We collected serum specimens from non pregnant but married women, normal 3rd trimester pregnant women and patients with eclampsia at 3rd trimester of pregnancy and measured serum concentrations of total and free thyroxine (TT₄ & FT₄) and total and free triiodothyronine (TT₃ & FT₃) by using RIA. Among the study subjects, 10 women were married but non pregnant, 12 women were in their 3rd trimester of normal pregnancy and 32 patients of eclamptic toxemia with 3rd trimester of pregnancy. In normal pregnancy, FT₄ and FT₃ levels remained normal while TT₄ and TT₃ levels were elevated. In patients with toxemia of pregnancy, the mean serum TT₃ concentration was significantly lower than that of normal pregnancy and the serum FT₃ concentrations were below the normal pregnancy range. The mean serum TT₄ and FT₄ concentrations in patients with eclampsia were however, significantly higher than those in normal pregnant women.

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Introduction

In pregnancy maternal physiological adjustment of different organ systems occur which includes circulatory, metabolic and hormonal changes to supply adequate nutrition to the growing fetus.¹ There is evidence for presence of other thyroid stimulators like human chorionic gonadotropin hormone (hCG) besides thyroid stimulating hormone (TSH) in pregnancy. There is also evidence for increase concentration of thyroxine binding globulin (TBG) which is induced by increased estrogen production in pregnancy.^{2,3,4} In normal pregnancy increased serum concentration

of TBG results in increased serum concentration of total T₄ and to a lesser extend of total T₃. There is different opinion in different studies regarding alterations in serum free hormone levels in pregnancy.⁵

In normal pregnancy, FT₄ and FT₃ levels remained normal while total T₄ and T₃ levels were elevated. In patients with toxemia of pregnancy, the mean serum total T₃ concentration was significantly lower than that of normal pregnancy and the serum FT₃ concentrations were below the normal pregnancy range. The mean serum TT₄ and FT₄ concentrations in patients with eclampsia

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were however, significantly higher than those in normal pregnant women.

In Bangladesh little works have been done in this regards where eclampsia is among major health problems. The present study has been designed to compare the total and free thyroxine and triiodothyronine in normal pregnancy, in eclampsia and in non pregnant (control) subjects.

Materials and Methods

The study was conducted in the department of physiology, Rajshahi Medical College with collaboration of department of Gynae and Obstetrics, Rajshahi Medical College Hospital. The total duration of the study was 12 months. The age of the subjects were ranged from 18 to 35 years. Those having present or past history of any kind of thyroid disease, diabetes mellitus or glycosuria were excluded from the study.

A total of 54 subjects were selected as study subject in this study. The study subjects were divided into 3 groups. The group I includes 10 apparently healthy non pregnant women without having hormonal contraceptives at least for 6 months. The group II includes 12 women in their normal 3rd trimester of pregnancy. The group III

includes 32 women (patients) of 3rd trimester pregnancy with eclamptic toxemia. The objectives of the study were explained to the subjects and a written concept was taken from each of them. Detailed case history was obtained and bed-side examination of blood for random blood sugar (RBS) and urine for urine sugar were done carefully. Single sample of 10ml ante cubital venous blood was obtained with all aseptic measures. After let it be clotted, it was centrifuged for 30 minutes and the supernatant (serum) was taken in a separate test tube. Thus the serum was ready and used for hormone analysis in the laboratory of the Center for Nuclear Medicine and Ultrasound (CNMU), Rajshahi. TT₄ and TT₃ were measured by conventional RIA (Radioimmunoassay) method. FT₄ and FT₃ were measured by two-step magnetic FT₄-RIA and FT₃-RIA respectively. The kits used for the tests were manufactured by Beijing Atomic High Tech. Co. Ltd. China.

The obtained data was analyzed in computer using software SPSS for window version 11.5. Test of probability for significant difference was conducted by T-test (unpaired) for two independent means.

Results:

Serum TT₄ and TT₃ are expressed in nmol/L and serum FT₄ and FT₃ are expressed in pmol/L. The results are presented as mean \pm SE (standard error of mean). The bio-chemical parameters of thyroid function of study subjects are given in Table 1

Table 1 : Showing mean \pm SE of TT₄, TT₃, FT₄ & FT₃ of study subjects.

Parameters	Group I n =10 non pregnant	Group II n =12 3 rd trimester	Group III n =32 eclampsia
TT ₄ (nmol/L) mean \pm SE	105.5 \pm 8.7	148.9 \pm 3.6	179.8 \pm 9.5
TT ₃ (nmol/L) mean \pm SE	1.4 \pm 0.1	3.0 \pm 0.2	2.3 \pm 0.1
FT ₄ (pmol/L) mean \pm SE	18.5 \pm 1.6	20.4 \pm 2.7	26.6 \pm 2.2
FT ₃ (pmol/L) mean \pm SE	4.8 \pm 0.4	4.6 \pm 0.3	3.8 \pm 0.2

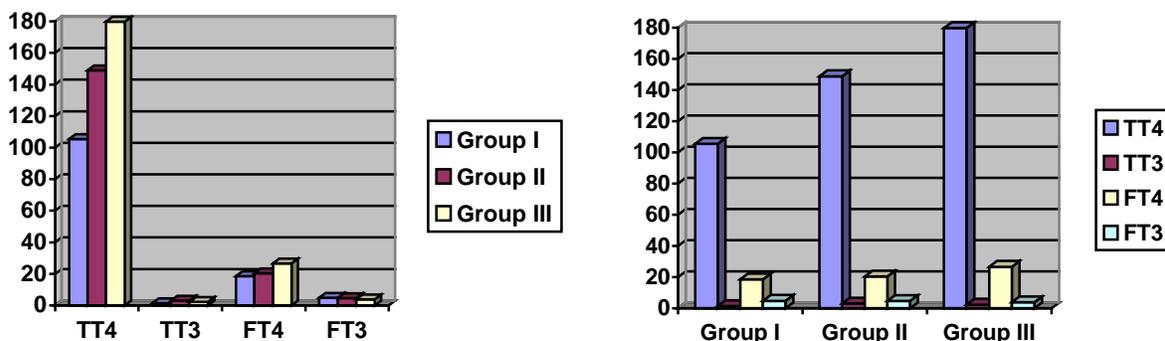


Fig 1: Bar diagram showing thyroid hormone levels Of different study groups

Serum total thyroxine (TT₄):

The mean serum TT₄ is significantly higher in normal pregnancy and in eclampsia than that of non pregnant women (Table 2 and 3). The mean serum TT₄, though higher in eclampsia than that of normal 3rd trimester pregnancy but the difference is not significant (Table 4). Out of 32 patients of eclampsia, serum concentrations of TT₄ in 3 patients in this study are higher than normal range. The mean serum TT₄ is 21% higher in eclampsia than that of normal pregnancy.

Table 2: Showing statistical comparison between non pregnant and normal 3rd trimester of pregnancy.

Parameters	Group I n =10 non pregnant	Group II n =12 normal 3 rd trimester	Significance
TT ₄ (nmol/L) mean ± SE	105.5 ± 8.7	148.9 ± 3.6	Significant (P = 0.011)
TT ₃ (nmol/L) mean ± SE	1.4 ± 0.1	3.0 ± 0.2	Highly significant (P =0.000)
FT ₄ (pmol/L) mean ± SE	18.5 ± 1.6	20.4 ± 2.7	Non-significant (P =0.001).
FT ₃ (pmol/L) mean ± SE	4.8 ± 0.4	4.6 ± 0.3	Non-significant (P =0.001).

Serum total triiodothyronine (TT₃):

The mean serum TT₃ in this study is significantly higher both in normal pregnancy and in eclampsia than that of non pregnant women. In contrast to TT₄, the rise of TT₃ is pronounced in normal pregnancy than non pregnant women. The mean serum TT₃ is significantly lower in eclampsia than that of normal pregnancy.

Table 3: Showing statistical comparison between non pregnant and 3rd trimester of pregnancy with eclampsia.

Parameters	Group I n =10 non pregnant	Group III n =32 eclampsia	Significance
TT ₄ (nmol/L) mean ± SE	105.5 ± 8.7	179.8 ± 9.5	Highly significant (P=0.000)
TT ₃ (nmol/L) mean ± SE	1.4 ± 0.1	2.3 ± 0.1	Highly significant (P =0.001)
FT ₄ (pmol/L) mean ± SE	18.5 ± 1.6	26.6 ± 2.2	significant (P =) 0.006
FT ₃ (pmol/L) mean ± SE	4.8 ± 0.4	3.8 ± 0.2	Non-significant (P =0.047).

Serum free thyroxine (FT₄):

The mean serum FT₄ is higher in normal pregnancy than that of non pregnant women but the value is not significantly (Table 2). The mean serum FT₄ is significantly higher in eclampsia than that of non pregnant women (Table 3). The mean serum FT₄ is higher in eclampsia than that of normal pregnancy but the value is not significantly (Table 4).

Table 4: Showing statistical comparison between normal 3rd trimester of pregnancy and 3rd trimester of pregnancy with eclampsia.

parameters	Group II n =12 normal 3 RD trimester	Group III n =32 eclampsia	Significance
TT ₄ (nmol/L) mean ± SE	148.9 ± 3.6	179.8 ± 9.5	Non significant (P =0,046)
TT ₃ (nmol/L) mean ± SE	3.0 ± 0.2	2.3 ± 0.1	Significant (P =0.016)
FT ₄ (pmol/L) mean ± SE	20.4 ± 2.7	26.6 ± 2.2	Non-significant (P ≤ 0.05).
FT ₃ (pmol/L) mean ± SE	4.6 ± 0.3	3.8 ± 0.2	Non-significant (P ≤ 0.05).

Serum free triiodothyronine (FT₃):

There were no significant differences in mean serum FT₃ between normal pregnancy, eclampsia and non pregnant women (Table 2, 3 & 4). In 12 of the 32 patients of eclampsia, the serum concentrations of FT₃ are slightly below normal range and 26 of them show their serum FT₃ concentrations lower than that of normal pregnancy.

Discussion

The present study represents an evaluation of thyroid hormones level in normal pregnancy and pregnancy with eclampsia without detectable thyroid abnormalities. The result of this study indicates an important modification in thyroid activity in pregnancy. We have focused our attention on both total and free T_4 and T_3 in 3rd trimester of normal pregnancy and 3rd trimester pregnancy with eclampsia and on comparing them with non pregnant control subjects. In normal pregnancy, mean serum concentration of both TT_3 and TT_4 are increased significantly and the elevations remain significant in eclampsia than that of control subjects. The mean serum FT_4 and FT_3 though elevated but are not significant in normal pregnancy than the control. In eclampsia, the mean serum FT_4 is significantly different than that of non pregnant women when difference is nonsignificant in case of FT_3 . Similar results have been observed in the findings of previous investigators that is, in normal pregnancy, while the serum concentrations of total thyroxine and triiodothyronine are elevated, the absolute serum concentrations of free thyroxine and triiodothyronine remain within the range of non pregnant women.

The increase in serum binding forms of thyroid hormones may be due to the marked increase in circulating level of the major thyroxine binding protein (TBG), which is induced by high estrogen level in pregnancy.⁶ In addition, stimulatory effects of human chorionic gonadotropic hormones of placental origin, increased metabolic demand of the body and mental stress in pregnancy may have important role for over all thyroid activity and elevated thyroid hormone levels in pregnancy. During pregnancy increased estrogen level causes increase production of protein by the liver, consequently TBG production by hepatocytes is also increased.⁶ High estrogen level on the other hand reduces peripheral degradation due to oligosaccharide modification.⁷ As a result the TBG content in the plasma is elevated in pregnancy. As the binding capacity of the plasma is increased due to elevated TBG in the serum, more hormones bind to TBG and the total

plasma content of thyroid hormones is increased but free hormone levels remain unchanged and hyperthyroidism does not likely.

The mean serum FT_4 difference is significant and FT_3 difference is nonsignificant between eclampsia and non pregnant women in this study. The mean serum FT_3 in eclampsia is even reduced than that of non pregnant and pregnant women. As the cause of this reduced FT_3 associated with significant rise of TT_4 in eclampsia, we held responsible the reduced extrathyroidal conversion (peripheral deiodination) of T_4 to T_3 .

Eclampsia is a pregnancy induced auto-intoxication with multi system disorder when the most affected organs are brain, livers and kidneys. Functional disorder in these organ systems is evidential in eclampsia.¹¹ On the other hand, liver, kidneys and muscles are the important organs of peripheral deiodination (conversion of T_4 to T_3)⁵ and in maintenance of normal serum level T_4 and T_3 , that is why involvement of liver and kidneys is likely to change T_4 and T_3 levels in eclampsia.

There is controversy in different studies regarding free hormone levels in pregnancy. Different investigators showed free hormone levels remain unchanged, decreased or even increased in pregnancy compared to non pregnant control. The present study shows no significant change in free hormone levels between non pregnant and pregnant women and may be another addition of the ongoing controversy.

In some other studies, the investigators observed that in variety of systematic illness, protein-energy malnutrition (PEM), prolonged starvation, anorexia nervosa, Cushing's syndrome, excessive steroid therapy etc. when systemic disorder developed, the extra thyroidal deiodination of T_4 to T_3 had been reduced.^{5,8} Due to wide range of normal limits, these differences usually neither exceed normal limit nor produce significant change on metabolism.

Eclampsia is a major health problem in developing countries like Bangladesh. Poverty, low socioeconomic condition, poor nutritional status, early marriage and late pregnancy are common in Bangladeshi population. Illiteracy, ignorance and

fanaticism badly affect their life style. Lack of awareness, inadequate antenatal care and poor obstetrical facilities predispose to high rate of morbidity and mortality in eclampsia in this country.

Though the exact mechanism of change in thyroid function in pregnancy is difficult to explain, the present study may be helpful to resolve the debate. For further studies, the following may be helpful to explain the exact mechanism:-

1. Estimation of serum TSH, beta-hCG and estrogen level.
2. Estimation of plasma proteins including TBG.
3. Inclusion of subjects during pregnancy and eclampsia of all terms (1st, 2nd, and 3rd trimester of pregnancy).
4. Increase in number of sample size.

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