

**Original Article****Serum Thyroxine & Triiodothyronine Levels in Normal Pregnancy and Pre-Eclampsia**M Hafizur Rahman¹, Mahbub Ara Chowdhury², M Towhidul Alam³**Abstract**

To evaluate the thyroid hormone levels in pre-eclampsia and normal pregnancy, a study was undertaken among 54 women of age ranged from 18 to 35 years without present or past history of thyroid diseases. Among the study subjects, 32 women were patients of pre-eclampsia, 12 women were in their normal third trimester pregnancy and 10 women were married but non-pregnant (without having hormonal contraceptives at least for 6 months). We have measured serum levels of total and free thyroxine (TT₄ & FT₄) and total and free triiodothyronine (TT₃ & FT₃) by using RIA. The mean serum TT₄ and TT₃ in normal pregnancy were significantly higher compared to that of non-pregnant women when mean FT₄ and FT₃ were similar in both normal pregnancy and non-pregnant women. In pre-eclampsia, mean serum TT₄ and TT₃ were significantly higher than that of non-pregnant women but compared to that of normal pregnancy, TT₄ was clearly higher but not significant when TT₃ was significantly lower. The mean serum FT₄ was significantly higher in pre-eclampsia compared to non-pregnant women and not significantly higher compared to normal pregnancy. The mean serum FT₃ was similar in both non-pregnant and normal pregnancy but significantly lower in pre-eclampsia compared to normal pregnancy. In pregnancy i.e. in both normal pregnancy and pregnancy with pre-eclampsia, the increased serum thyroid hormone levels might result from increased stimulatory effect of placental hormones (hCG),^{1,2} increased metabolic demands in pregnancy³ and mental stress in pregnancy as mentioned by other investigators. Decreased TT₃ and FT₃ associated with higher TT₄ in pre-eclampsia might be due to reduced conversion of T₄ to T₃ in the liver and kidneys.⁴

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Introduction

Pregnancy is a physiological process. To supply adequate nutrition to the growing fetus, maternal physiological adjustment of different organ systems occur in pregnancy which includes circulatory, metabolic and hormonal changes.⁵ Now it is established that thyroid gland increases its size as well as secretion during gestation.^{6,7}

In normal pregnancy increased serum level of thyroxine binding globulin (TBG) results in increased serum concentration of total thyroxine (TT₄) and to a lesser extent of total triiodothyronine (TT₃).^{8,9,10} There is controversy in different studies regarding alterations in serum free hormone levels in pregnancy i.e. FT₄ and FT₃ which are the biological active forms.^{11,12}

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In pre-eclampsia, the most affected organs are liver, kidneys and brain and due to auto-intoxication, functional disorders in these organ systems are evidential.¹³ As liver, kidneys and muscles are the main organs of peripheral deiodination of T₄ to T₃, the serum concentration of T₄ and T₃ may differ in pre-eclampsia than that of normal pregnancy.⁴

In Bangladesh little works have been done in this regards where pre-eclampsia/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 pre-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 Obs/Gynae., Rajshahi Medical College Hospital. The total duration of this study was 12 months from January, 2005 to December, 2005. Age ranged from 18 to 35 years and the total 54 subjects were studied and divided in to 3 groups. The group I included 10 apparently healthy non-pregnant women without having hormonal contraceptive at least for 6 months. The group II included 12 women in their normal pregnancy of third trimester. The group III included 32 women (patients) of pregnancy associated with pre-eclampsia. The objectives of the study were explained and a written concept was taken from each subject. Detailed case history was obtained and bed-side urine examination for sugar was done. Those giving present or past history of thyroid disease, diabetes mellitus or glycosuria were excluded from the study.

Single sample of 10 ml. ante-cubital venous blood was obtained with all aseptic measure. After let to clot, the blood 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). FT₄ and FT₃ were measured by two-step magnetic FT₄ -RIA and FT₃-RIA respectively. The kits used were manufactured by Beijing Atomic High-tech. co. Ltd. China.

The obtained data was analyzed in computer using soft ware 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 were expressed in nmol/L and serum FT₄ and FT₃ were expressed in pmol/L. The results were presented as mean ± SE (standard error of mean).

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

Group	T T ₄ (nmol/L) mean±SE	T T ₃ (nmol/L) mean±SE	F T ₄ (pmol/L) mean±SE	F T ₃ (pmol/L) mean±SE
Group I n=10	105.5±8.7	1.4±0.1	18.5±1.6	4.8±0.4
Group II n=12	148.9±12.6	3.0±0.2	20.4±2.7	4.6±0.3
Group III n=34	179.8±9.5	2.3±0.1	26.6±2.2	3.8±0.2

Serum total thyroxine (TT₄)

The mean serum TT₄ was significantly higher in normal pregnancy and in pre-eclampsia than that of non pregnant women (Table 1 and 2).

Table-2: Showing statistical comparison between non-pregnant and normal late pregnancy.

Parameters	Group I n=10 (mean±SE)	Group II n=12 (mean±SE)	Significance (P value)
TT ₄ (nmol/L)	105.5±8.7	148.9±12.6	S (p=.011)
TT ₃ (nmol/L)	1.4±0.1	3.0±0.2	HS (p=.000)
FT ₄ (pmol/L)	18.5±1.6	20.4±2.7	NS (p=.011)
FT ₃ (pmol/L)	4.8±0.4	4.6±0.3	NS (p=.011)

S = significant. HS = highly significant. NS = non significant.

Tabl-3: Showing statistical comparison between non-pregnant and pre-eclampsia.

Parameters	Group I n=10 (mean±SE)	Group III n=12 (mean±SE)	Significance (P value)
TT ₄ (nmol/L)	105.5±8.7	179.8±9.5	HS (p=.000)
TT ₃ (nmol/L)	1.4±0.1	2.3±0.1	HS (p=.001)
FT ₄ (pmol/L)	18.5±1.6	26.6±2.2	S (p=.006)
FT ₃ (pmol/L)	4.8±0.4	3.8±0.2	NS (p=.047)

S = significant. HS = highly significant. NS = non significant.

The mean serum TT₄ in pre-eclampsia was higher than that of normal pregnancy but was not statistically significant (Table IV).

Table -4: Showing statistical comparison between normal late pregnancy and pre-eclampsia.

Parameters	Group II n=12 (mean±SE)	Group III n=32 (mean±SE)	Significance (P value)
TT ₄ (nmol/L)	148.9±12.6	179.8±9.5	NS (p=.063)
TT ₃ (nmol/L)	3.0±0.2	2.3±0.1	S (p=.016)
FT ₄ (pmol/L)	20.4±2.7	26.6±2.2	NS (p=.096)
FT ₃ (pmol/L)	4.6±0.3	3.8±0.2	S (p=.045)

S = significant. HS = highly significant. NS = non significant

Serum free thyroxine (FT₄)

The mean serum FT₄ was higher in normal pregnancy than that of non pregnant women but the difference was not statistically significant (Table 2).

The mean serum FT₄ was significantly higher in pre-eclampsia than that of non pregnant women (Table 3).

The mean serum FT₄ was higher in pre-eclampsia than that of normal pregnancy but the difference was not statistically significant (Table 4).

Serum total triiodothyronine (TT₃)

The mean serum TT₃ in this study was significantly higher both in normal pregnancy and in pre-eclampsia than that of non pregnant women (Table 2 and 3).

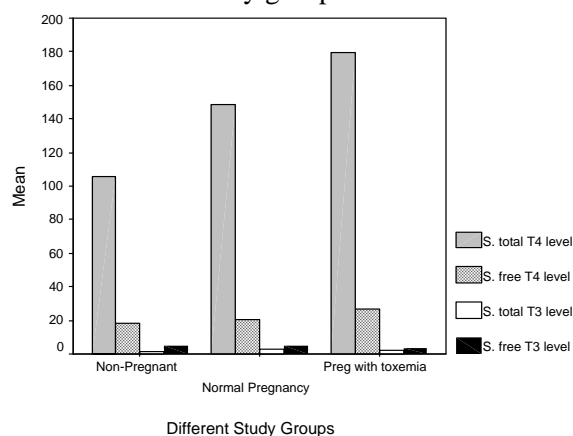
The mean serum TT₃ was significantly lower in pre-eclampsia than that of normal pregnancy (Table 4).

Serum free triiodothyronine (FT₃)

There was no significant difference in mean serum FT₃ between normal pregnancy and non-pregnant women but the value was significantly lower in pre-eclampsia than that of non pregnant women (Table 2 and 3).

In this study the mean serum FT₃ in pre-eclampsia was also significantly lower than that of normal pregnancy (Table 4).

Fig. 1. Bar diagram of thyroid hormone levels of different study groups



Discussion

The present study represents an evaluation of thyroid hormone levels in normal pregnancy and pre-eclampsia without detectable thyroid abnormalities. Elevation in serum thyroid hormone levels in pregnancy indicates important modification of thyroid activity in pregnancy. In this study, serum TT₄ and TT₃ were significantly higher in pregnancy than that of non-pregnant control whereas the free forms i.e. FT₄ and FT₃ were similar in both groups. The increase in serum binding forms of thyroid hormones may be due to the marked increase in circulating level of the major T₄ binding protein (TBG), which is induced by high estrogen level in pregnancy. In addition of this stimulatory effect of serum hCG of placental origin, increased metabolic demand 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 proteins by the liver, consequently TBG production by hepatocytes is also increased.¹⁴ High estrogen, on the other hand reduces peripheral TBG degradation due to oligosaccharide modification.¹⁵ As a result the TBG content in the serum is increased.

As the binding capacity of the plasma is increased due to elevated TBG level 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 occur.

There is controversy in different studies regarding free hormone levels during 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 this study, we also compared the thyroid hormone levels in pre-eclampsia to that of normal pregnancy. In pre-eclampsia mean serum total and free T_4 were non-significantly higher when total and free T_3 were significantly lower than that of normal pregnancy. As the cause of this non-significant higher T_4 associated with significantly lower T_3 levels in pre-eclampsia, we held responsible the reduced extrathyroidal conversion of T_4 to T_3 .

Pre-eclampsia is pregnancy induced auto-intoxication with multisystem disorder when the most affected organs are brain, liver and kidneys. Functional disorder in these organ systems is evidential in pre-eclampsia. On the other hand liver and kidneys are the important organs in peripheral deiodination (conversion of T_4 to T_3) and in maintenance of normal blood levels of T_4 and T_3 , that is why involvement of liver and kidneys is likely to change serum T_4 and T_3 levels in pre-eclampsia.

In some other studies, the investigators observed that in variety of systemic illness, protein-energy malnutrition (PEM), starvation, anorexia nervosa, Cushing's syndrome, excessive steroid therapy etc.

when systemic disorder developed, the extrathyroidal deiodination of T_4 to T_3 had been reduced.^{4,16} Due to wide range of normal limits, these differences usually neither exceed normal limit nor produce significant change on metabolism.

Pre-eclampsia is a major health problem in developing countries like Bangladesh. Poverty, low socioeconomic condition, poor nutritional status and early marriage 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 rates of morbidity and mortality in pre-eclampsia in this country.

Though the exact cause of change in serum levels of thyroid hormone in pre-eclampsia is difficult to explain, this 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, HCG and estrogen level.
2. Estimation of plasma proteins including TBG.
3. Inclusion of subjects during normal pregnancy and pre-eclampsia of all terms (first, second and third trimester).
4. Increase in number of sample size.

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