

## Review Article

# Thyroid Function in Normal Pregnancy

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### Abstract

*Hormonal changes and metabolic demands during pregnancy result in alteration in the physiological and biochemical parameters of thyroid function. Among the many physiological alterations which may occur during pregnancy are thyroid enlargement, increased thyroid capability for iodine uptake and increase in serum thyroxine and tri-iodothyronine concentration. However these findings are not usually associated with symptoms of hyperthyroidism. To clarify the changes, a study was undertaken in Rajshahi Medical College Hospital when serum specimens were collected from individual woman at different stages of normal pregnancy and women married but non pregnant. Among the study subjects, 22 women were in their 1st trimester, 20 women were in their 2nd trimester, 32 women were in their 3rd trimester of normal pregnancy and 10 women were married but non pregnant. We have measured serum levels of total and free thyroxine (TT4 & FT4) and total and free tri-iodothyronine (TT3 & FT3) by using RIA. During the 1st trimester of pregnancy serum FT4 and FT3 concentrations are significantly higher than in non pregnant women and women in 3rd trimester. The concentration of FT4 and FT3 progressively declined as the pregnancy advanced and are to control level in the 3rd trimester. The mean serum TT4 and TT3 are significantly elevated throughout pregnancy in comparison to control.*

**Keywords:** Pregnancy, Thyroid gland, Iodine uptake.

### Introduction

To supply adequate nutrition to the growing fetus in pregnancy, maternal physiological adjustment of different organ system occur which includes circulatory, metabolic and hormonal changes<sup>1</sup>. Besides normal thyroid stimulating hormone (TSH), there is evidence for presence of other thyroid stimulators like human chorionic gonadotropin hormone (hCG). There is also evidence for increase concentration of thyroxine binding globulin (TBG) which is induced by increased estrogen production in pregnancy<sup>2,3,4</sup>. 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. Free T4 and T3 though elevated in 1st trimester, it decrease to control in 3rd trimester may be due to weak thyrotropic effect of hCG

which remains maximum concentration in the 1st trimester and declined markedly in 2nd and 3rd trimester. Little works have been done in this regards in Bangladesh. The present study has been designed to compare the total and free thyroxine and tri-iodothyronine in normal pregnancy 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. and Gynae, Rajshahi Medical College Hospital. The study was started January 2010 and ended on December 2010. The total duration was 12 months. The ages of the subjects range 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.

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A total of 84 subjects were selected as study subject in the study. The study subjects were divided into 4 groups. The group I includes 10 apparently healthy non pregnant women without having hormonal contraceptives at least for 6 months. The group II includes 22 women in their normal 1st trimester of pregnancy. The group III includes 20 women in their normal 2nd trimester of pregnancy. The group IV includes 32 women in their normal 3rd trimester of pregnancy. The objectives of the study were explained and a written concept was taken from each subject.

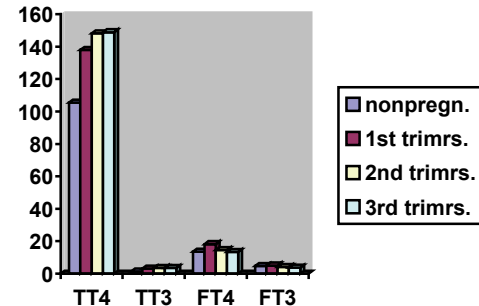
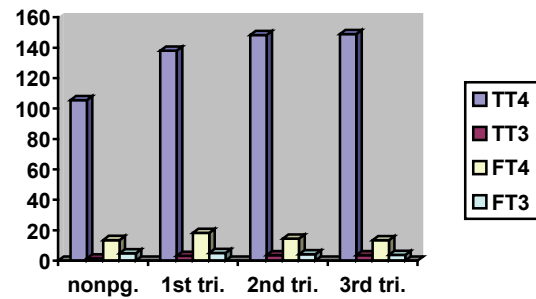
Detailed case history was obtained and bed-side examination of blood for random blood sugar (RBS) and urine for urine sugar were done carefully. Single sample of 10ml ante cubital venous blood was obtained with all aseptic measure. After let it be clotted, it was centrifuged for 30 minutes and the supernatant (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 ± SE (standard error of mean). The bio-chemical parameters of thyroid function per trimester of gestation are given in Table 1

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

Parameters	Group I n =10 non pregnant	Group II n =20 1st trimester	Group III n =22 2nd trimester	Group IV n =34 3RD trimester
TT4 (nmol/L) mean ± SE	105.5 ± 8.7	138 ± 3.0	148.2 ± 3.2	148.9 ± 3.6
TT3 (nmol/L) mean ± SE	1.4 ± 0.1	3.15 ± 0.03	3.5 ± 0.35	3.6 ± 0.2
FT4 (pmol/L) mean ± SE	13.5 ± 1.6	18.2 ± 0.3	14.5 ± 0.1	13.4 ± 0.1
FT3 (pmol/L) mean ± SE	4.8 ± 0.4	5.0 ± 0.2	4.2 ± 0.3	3.8 ± 0.4



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

**Serum total thyroxine (TT4)**

The mean serum TT4 was significantly higher in all three trimester of normal pregnancy than that of non pregnant women. The values at mid-pregnancy and at late pregnancy though are not significantly different from each other but are higher than that of non pregnant subjects ( $P \leq 0.05$ ). Serum T4 level increased sharply early pregnancy and thereafter only slowly.

**Table 2 :** Showing statistical comparison between non pregnant and 1st trimester of pregnancy.

Parameters	Group I n =10 non pregnant	Group II n =20 1st trimester	Significance
TT4 (nmol/L) mean ± SE	105.5 ± 8.7	138 ± 3.0	Significant ( $P \geq 0.05$ )
TT3 (nmol/L) mean ± SE	1.4 ± 0.1	3.15 ± 0.03	Significant ( $P \geq 0.05$ )
FT4 (pmol/L) mean ± SE	13.5 ± 1.6	18.2 ± 0.3	Non-significant ( $P \leq 0.05$ )
FT3 (pmol/L) mean ± SE	4.8 ± 0.4	5.0 ± 0.2	Non-significant ( $P \leq 0.05$ )

### Serum total tri-iodothyronine (TT3)

The mean serum TT3 in this study is significantly higher in normal pregnancy than that of non pregnant women. In contrast to TT4, the rise of TT3 is pronounced in 1st trimester and it becomes slow and steady in 2nd and 3rd trimester. The mean serum T3 concentrations at 2nd and 3rd trimester are not significantly different from each other.

**Table 3 :** Showing statistical comparison between non pregnant and 2nd trimester of pregnancy.

Parameters	Group I n =10 non pregnant	Group III n =22 2nd trimester	Significance
TT4 (nmol/L) mean ± SE	105.5 ± 8.7	148.2 ± 3.2	Significant (P ≥ 0.05)
TT3 (nmol/L) mean ± SE	1.4 ± 0.1	3.5 ± 0.35	Significant (P ≥ 0.05)
FT4 (pmol/L) mean ± SE	13.5 ± 1.6	14.5 ± 0.1	Non-significant (P < 0.05)
FT3 (pmol/L) mean ± SE	4.8 ± 0.4	4.2 ± 0.3	Non-significant (P < 0.05)

### 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 different among the different trimesters as well as from those of non pregnant subjects.

**Table 4 :** Showing statistical comparison between non pregnant and 3rd trimester of pregnancy.

Parameters	Group I n =10 non pregnant	Group IV n =34 3rd trimester	Significance
TT4 (nmol/L) mean ± SE	105.5 ± 8.7	148.9 ± 3.6	Significant (P ≥ 0.05)
TT3 (nmol/L) mean ± SE	1.4 ± 0.1	3.6 ± 0.2	Significant (P ≥ 0.05)
FT4 (pmol/L) mean ± SE	13.5 ± 1.6	13.4 ± 0.1	Non-significant (P < 0.05)
FT3 (pmol/L) mean ± SE	4.8 ± 0.4	3.8 ± 0.4	Non-significant (P < 0.05)

### Serum free tri-iodothyronine (FT3)

The differences in mean serum FT3 between normal pregnancy and non pregnant women are not significantly different.

### Discussion

The present study represents an evaluation of thyroid hormone levels in different trimesters of normal pregnancy without detectable thyroid abnormalities. Elevation in serum thyroid hormone levels in pregnancy indicates important modification in thyroid activity in pregnancy. We have focused our attention on both total and free T4 and T3 in 1st 2nd and 3rd trimester of normal pregnancy comparing them with non pregnant control subjects. During the 1st trimester of pregnancy, both TT3 and TT4 are increased significantly and the elevation remains significant in the successive 2nd and 3rd trimesters than the control subjects. The values at 1st, 2nd and 3rd trimester are not significantly differing from each other. The serum FT4 and FT3 though elevated but are not significant throughout the pregnancy than the control. In contrast to TT4, the rise of TT3 is more pronounced in 1st trimester and slow and steady in 2nd and 3rd trimester. The results of this study confirm the findings of previous investigators that in normal pregnancy, while the serum concentrations of total thyroxine and tri-iodothyronine are elevated, the absolute serum concentrations of free thyroxine and tri-iodothyronine 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<sup>6</sup>. In addition, stimulatory effects of human chorionic tropic 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<sup>6</sup>. High estrogen level on the other hand reduces peripheral degradation due to oligosaccharide modification<sup>7</sup>. 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.

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 on going controversy. In some other studies, the investigators observed that in variety of systematic illness, protein-energy malnutrition (PEM), starvation, anorexia nervosa, Cushing's syndrome, excessive steroid therapy etc. when systemic disorder developed, the extra thyroidal deiodination of T4 to T3 had been reduced<sup>5,8</sup>. Due to wide range of normal limits, these differences usually neither exceed normal limit nor produce significant change on metabolism.

Though the exact mechanism of change 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, hCG and estrogen level.
2. Estimation of plasma proteins including TBG.
3. Increase in number of sample size.

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