# Evaluation of Serum Lipids and Thyroid Hormone Changes in Non-Pregnant, Pregnant, and Preeclampsia Women

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***Abstract.*** Pregnancy-induced hypertension (PIH) continues to be a major obstetric problem in present-day healthcare practice. To supply adequate nutrition to the growing fetus, maternal physiological adjustments of different organ systems occur in pregnancy. The adjustments include circulatory, metabolic, and hormonal changes. **Objective of Study:** The object of this study was to investigate lipids and thyroid hormone ($TT_3$, $TT_4$, $FT_3$, $FT_4$ and TSH) status among women who were healthy and non-pregnant (HNP n = 30) compared with health pregnant women (HP n = 30), and pregnant women with preeclampsia (PIH n = 30). **Results:** The mean serum $TT_4$ and $TT_3$ in normally pregnant woman were significantly higher compared to the levels in non-pregnant women. However, the mean $FT_4$ and $FT_3$ were similar in both normally pregnant and non-pregnant women. In women with preeclampsia, the mean serum $TT_4$ and $TT_3$ were significantly higher than in non-pregnant women. But compared to normally pregnant women, women with preeclampsia had a non-significantly higher $TT_4$ level and a significantly lower $TT_3$. Compared to non-pregnant women, TSH levels were significantly higher in both preeclamptic and normally pregnant women ($p < 0.001$). In women with preeclampsia, the mean serum $FT_4$ was not significantly higher than in normally pregnant women, but was significantly higher than in non-pregnant women. The mean serum $FT_3$ was similar in both non-pregnant and normally pregnant women, but was significantly lower in preeclampsia than in normally pregnant women. **Conclusions:** These findings indicate that there is a state of hypothyroxinemia in normal pregnancy and in preeclampsia, and that biochemical hypothyroidism (raised TSH) occurs. Identifying changes in thyroid hormone status in preeclampsia might be of help in preventing the occurrence of preeclampsia.

***Keywords.*** Lipids • Preeclampsia • Pregnancy • Pregnancy-induced hypertension • $T_3$ • $T_4$ • TSH

## *Introduction*

Pregnancy-induced hypertension continues to be a major obstetric problem in present-day healthcare practice. It presents a great medical dilemma because it affects not only maternal health but also puts foetal development at risk. Worldwide, the hypertensive disorders of pregnancy are common and are responsible for 12% of maternal mortality during pregnancy and the puerperium. Preeclampsia is the leading cause of maternal mortality in developed countries and is associated with a five-fold increase in perinatal mortality. The major cause of foetal compromise in preeclampsia is reduced uteroplacental perfusion.[1,2]

Pregnancy is a physiological process. To supply adequate nutrition to the growing fetus, maternal physiological adjustments of different organ

systems occur in pregnancy. The adjustments are circulatory, metabolic, and hormonal.[5] Pregnancy is usually associated with mild hyperthyroxinemia, but preeclamptic women have a high incidence of hypothyroidism that might correlate with the severity of preeclampsia.[3,4] On the other hand, preeclampsia has also been observed in 16.7% of cases of subclinical hypothyroidism and 43.7% of cases of overt hypothyroidism during pregnancy.[5]

liver, kidneys, and brain. Due to autointoxication, functional disorders in these organ systems are evident.[8] As liver, kidneys, and muscles are the main organs of peripheral deiodination of $T_4$ to $T_3$, the serum concentration of $T_4$ and $T_3$ may different in preeclampsia than in normal pregnancy.[5] In India, where preeclampsia/eclampsia is among major health problems, little research of the conditions has yet been done. The present study examines the lipids and thyroid hormonal levels in healthy pregnant women, those with preeclampsia, and healthy non-pregnant (control) subjects.

**Table 1.** Shows the demographic characteristics of study population in non-pregnant, pregnant and preeclepsia subjects.

| Parameter | Non-pregnant Women | Healthy Pregnant Women | Preeclampsia Women |
|---|---|---|---|
| Total number of subjects (n) | 30[100%] | 30{100%] | 30 [100%] |
| Mean age (mean ± SD; years) | 25 ± 5 | 28 ± 9 | 27 ± 8 |
| Weight | 55 ± 8 | 65 ± 5 | 67 ± 7 |
| Body mass index (Kg/m2) | 23 ± 3.0 | 27 ± 4.6** | 29 ± 5.3¤¤¤ |
| Hypertension | - | - | 30 [100 %] |
| Average Systolic blood pressure (mm of Hg) | 120 ± 2 | 119 ± 2$^{NS}$ | 167 ± 20¤¤¤‡ |
| Average Diastolic blood pressure (mm of Hg) | 80 ± 1 | 80 ± 2$^{NS}$ | 117 ± 12¤¤¤‡ |
| Average period of gestation | - | 36 weeks | 35 weeks |

Values are given as mean ± S.D from 30 subjects in each group.
¤ Preeclampsia women compared with non-pregnant women (¤¤¤$p < 0.001$)
* Normal pregnant women compared with non-pregnant women (**$p < 0.01$, $^{NS}$-Not significant)
‡ Preeclampsia women compared with normal pregnant women (‡$p < 0.001$)

Dyslipidemia is common in preeclampsia, and, via oxidation of susceptible lipids, may contribute to endothelial activation. We previously reported that triglyceride and free fatty acids were elevated as early as in the first and second trimesters in women who subsequently developed preeclampsia. Hyperlipidemia in preeclampsia is associated with a predominance of both atherogenic small low-density lipoproteins (LDL) and vascular cell adhesion molecutes.[6,7]

In preeclampsia, the most affected organs are

## Materials and Methods

**Study Population.** The study population we investigated consisted of 90 women divided into three groups. Ages ranged from 19-to-37 years. The three groups consisted of 30 healthy non-pregnant women, 30 normally healthy pregnant women, and 30 pregnant women with preeclamp-

sia.

The prospective study was carried out at the Raajam Hospital, Karruppur, Salem, Tamil Nadu, India, between January 2008 to January 2009. The study was approved by the Human Bioethics Committee for Clinical Research of the Raajam Hospital. Informed verbal consent was obtained from all subjects.

The objectives of the study were explained and a written concept was taken from each subject. Detailed case histories were obtained and bedside urine examination for sugar was done. Women who gave a present or past history of thyroid disease, diabetes mellitus, or glycosuria were excluded from the study.

Classification of the values into raised, low, or normal thyroid hormone levels were based on the following criteria: Subjects classified as having raised levels of thyroid hormone had $FT_4$ values > 1.6 ng/L, TSH levels < 0.4 miu/mL, or both. Subjects classified as having low $FT_4$ values had < 0.68 ng/mL, TSH values > 5.0 miu/mL, or both. Subjects grouped as normal had $FT_4$ and TSH values within the range of > 0.68–1.6 ng/mL and 0.4–5.0 miu/mL, respectively.

**Sample collection.** Single samples of 10-ml of ante-cubical venous blood was obtained with 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.

**Biochemical Investigation.** The levels of serum thyroid stimulating hormone (TSH), total triiodothyroxine ($T_3$), free thyroxine ($FT_4$), and free triiodothyronine ($FT_3$) were measured by a Microparticle Enzyme Immunoassay (MEIA) on the AXSYM System (Abbott Laboratories, Abbott Park, USA). Serum total thyroxine ($TT_4$) was measured by the Fluorescence Polarization Immunoassay (FPIA) method on AXSYM System using standard laboratory methodologies. Serum lipids were determined using a fully automated clinical chemistry analyzer (Hitachi 912, Boehringer Mannheim, Germany).

**Statistical Analysis.** All data were expressed as mean ± S.D of number of experiments. The statistical significance was evaluated by Student's *t*-test using SPSS version 10.0 (SPSS, Cary, NC, USA).

**Table 2.** Lipids level changes in non-pregnant, pregnant, nd preeclempsia subjects.

| Parameter | Non-pregnant Women | Normal Pregnant Women | Preeclampsia Women |
|---|---|---|---|
| Total cholesterol (mg/ dl) | 154 ± 12.7 | 168 ± 10.5$^{NS}$ | 221 ± 18.8¤¤¤‡ |
| Triglyceride (mg/dl) | 92 ± 11.5 | 132 ± 18** | 252 ± 22¤¤¤‡ |
| HDL-cholesterol (mg /dl) | 47 ± 4 | 44 ± 5$^{NS}$ | 34 ± 7¤¤‡ |
| LDL-cholesterol (mg /dl) | 78 ± 8 | 85 ± 10$^{NS}$ | 138 ± 13¤¤¤‡ |
| VLDL-cholesterol (mg /dl) | 25 ± 5 | 39 ± 6* | 50 ± 5¤¤‡ |

Values are given as mean ± S.D from 30 subjects in each group.
¤Preeclampsia women compared with non-pregnant women (¤¤$p$ <0.01, ¤¤¤$p$ < 0.001)
*Normal pregnant women compared with non-pregnant women (*$p$ < 0.05, **$p$ < 0.01, $^{NS}$-Not significant)

## *Results*

Table 1 shows the demographic characteristics of the study population in non-pregnant, pregnant, and preeclampsia subjects. All the studied groups had a similar mean age and mean pregnancy period. Indices of obesity (weight and BMI) were significantly increased in the pregnancy groups compared to the control group of non-pregnant women. Mean blood pressure (both systolic and

diastolic) and urine protein were significantly raised in preeclamptic patients compare with pregnant and non-pregnant subjects.

Table 2 shows the lipid level changes in non-pregnant, pregnant, and preeclempsia subjects. The lipid profile (total cholesterol, triglyceride, VLDL, and LDL-C) levels were significantly higher in the preeclamptic patients compare to healthy pregnant and non-pregnant subjects. The mean plasma HDL-C concentration, however, was much lower in preeclamtic subjects than in the other groups of women. The mean lipid levels, therefore, were statistically significantly different in preeclampsia women than in normal pregnant women ($p < 0.001$). But the mean TSH level for preeclampsia woman was even higher than in either other the other two groups, and the mean preeclampsia level was significantly higher than that in normal pregnant women ($p < 0.001$).

The mean serum $FT_4$ level was significantly higher in preeclampsia compared to non-pregnant women. However, $FT_4$ levels did not significantly differ between women with normal pregnancies and those with preeclampsia. The mean serum $FT_3$ was significantly higher in women with normal pregnancies than in non-pregnant women. Subjects with preeclampsia had significantly higher $FT_3$ than non-pregnant women but a significantly lower mean level than women with normal pregnancies.

**Table 3.** Showing mean ± SE of $TT_3$, $TT_4$, $FT_3$, $FT_4$ and TSH in non-pregnant,pregnant and preeclempsia subjects.

| Parameter | Non-pregnant Women | Normal Pregnant Women | Preeclampsia Women |
|---|---|---|---|
| $TT_3$ (ng/ml) | 0.87 ± 0.19 | 2.17 ± 0.57* | $1.85 \pm 0.49^{‡¤}$ |
| $TT_4$ (µg/dl) | 7.01 ± 2.32 | 12.62 ± 5.16* | $12.75 \pm 5.08^{‡NS}$ |
| $FT_3$ (pg/ml) | 2.65 ± 0.79 | 3.57 ± 1.21* | $2.72 \pm 1.15^{‡¤¤}$ |
| $FT_4$ (ng/ml) | 1.15 ± 0.52 | 2.38 ± 0.99* | $2.42 \pm 0.75^{‡NS}$ |
| TSH (mIU/ml) | 2.15 ± 1.23 | 3.89 ± 2.32* | $5.24 \pm 2.58^{‡¤¤¤}$ |

Values are given as mean ± S.D from 30 subjects in each group.
*Normal pregnant women compared with non-pregnant women (*$p < 0.001$)
‡Preeclampsia women compared with Non-pregnant women (‡$p < 0.001$)
¤Preeclampsia women compared with Normal pregnant women
(¤$p < 0.05$, ¤¤$p < 0.01$, ¤¤¤$p < 0.001$, NS-Not Significant)

women.

Table 3 illustrates the serum thyroid status ($TT_3$, $TT_4$, $FT_3$, $FT_4$ and TSH) of non-pregnant, pregnant, and preeclempsia subjects. The mean serum $TT_4$ and $TT_3$ in normal pregnancy were significantly higher compared to that of non-pregnant women. Mean $FT_4$ and $FT_3$ levels were similar in both normal pregnancy and non-pregnant women. In preeclampsia, the mean serum $TT_4$ and $TT_3$ levels were significantly higher than in non-pregnant women. But compared to the level of women with normal pregnancies, $TT_4$ was clearly higher but not significant when $TT_3$ was significantly lower.

Mean TSH levels were significantly higher in normal pregnant women than in non-pregnant wo-

## *Discussion*

Our finding in this study of increased mean BMI in both groups of pregnant women could partly explain the significant increase in triglycerides and LDL; increases in weight and BMI are associated with an increase in body fat percentage levels.

It is known that preeclampsia is associated with hypertriglyceridemia. The above-mentioned interactions along with increased endothelial triglyceride accumulation may result in endothelial cell dysfunction during gestation. Increased triglycerides found in the pregnancy-induced hyperten-

sion (which we call preeclampsia) is likely to be deposited in predisposed vessels, such as the uterine spiral arteries. If so, this may contribute to endothelial dysfunction, both directly and indirectly, through the generation of small, dense LDL. Moreover, this hypertriglyceridemia may be associated with hypercoagulability.[9,10]

A significant fall in LDL-C concentration in the control group in this present study may be attributed to hyperoestrogenaemia. On the other hand, LDL-C levels increased significantly in the pregnancy-induced hypertension subjects. Moreover, other studies have also demonstrated a predominance of the atherogenic small LDL and that vascular cell adhesion molecules are increased in association with hyperlipidemia in preeclampsia. The endothelial dysfunction in preeclampsia could originate from oxidative stress as well as dyslipidaemia. Many different enzymatic processes can generate free radicals. They are extremely reactive and interact with polyunsaturated fatty acids to produce lipid peroxides with a much longer half-life.[11,12]

In the present study, we evaluated thyroid status in normal pregnancy and preeclampsia without detectable thyroid abnormalities. Elevation in serum thyroid hormone levels in pregnancy indicates an important modification of thyroid activity in pregnancy.[8]

In this study, serum $TT_4$ and $TT_3$ were significantly higher in pregnant woman compared to non-pregnant control, whereas free forms of the hormones ($FT_4$ and $FT_3$) were similar in both groups. The increase in serum binding forms of thyroid hormone may be due to the marked increase in the circulating level of the major $T_4$ binding protein, thyroid-blinding globulin. This globulin is induced by high estrogen levels in pregnancy. In addition, in pregnancy, the stimulatory effect of serum hCG of placental origin, increased metabolic demand, and mental stress may play increase overall thyroid activity and elevate thyroid hormone levels.

During pregnancy, increased estrogen levels cause increased production of proteins by the liver. As a result, hypatocytes increases their production of thyroid-binding globulin, the protein that tranaports $T_4$ in the circulation. High estrogen, on the other hand, due to oligosaccharide modification, reduces peripheral degradation of thyroid-binding globulin. As a result, the content of thyroid-binding globulin in the serum is increased. As the binding capacity of the plasma is increased due to the elevated serum level of thyroid-binding globulin, more hormones bind to the globulin. As a result, the total plasma content of thyroid hormones is increased. Despite this, free thyroid hormone levels remain unchanged and hyperthyroidism does not occur.

Different studies are controversial regarding free hormone levels during pregnancy. Different investigators have found that free hormone levels remain unchanged, decrease, or even increase in pregnant women compared to non-pregnant controls. The present study shows no significant change in free thyroid hormone levels between non-pregnant and pregnant women; the study, then, contributes to the ongoing controversy.[13]

In this study, we also compared thyroid hormone levels in preeclampsia to those in normal pregnancy. In preeclampsia, the mean serum total and free $T_4$ levels were slightly higher than in women with normal pregnancies but the levels of the two groups did not reach statistical significance. However, compared to women with normal pregnancies, women with preeclampsia did have statistically significantly lower total and free $T_3$ levels. We believe that reduced extrathyroidal conversion of $T_4$ to $T_3$ was the cause of the non-significant higher $T_4$ levels and significant lower $T_3$ levels in preeclampsia.

Preeclampsia is pregnancy-induced autointoxication with multisystem disorders; the most affected organs are brain, liver, and kidneys. Functional disorders in these organ systems are evident in preeclampsia.[14]

However, the liver and kidneys are the most important organs in peripheral deiodination (conversion of $T_4$ to $T_3$) and in the maintenance of normal blood levels of $T_4$ and $T_3$. This is why involvement of liver and kidneys in preeclampsia is likely to change serum $T_4$ and $T_3$ levels.

In some other studies, investigators have observed that preeclamptic women may affected by a variety of conditions. These include systemic illnesses, protein-energy malnutrition, starvation, anorexia nervosa, Cushing's syndrome, and excessive steroid therapy. When the women have developed such systemic disorders, the extrathyroidal deiodination of $T_4$ to $T_3$ has been reduced.[15] Due to wide range of normal limits, however, the differences in $T_4$ and $T_3$ usually neither exceed normal limits nor produce significant metabolic changes.

**Conclusion.** The main finding of the current study is a statistically significantly higher number of cases pregnant women with preeclampsia who had abnormally high TSH levels. Thyroid gland diseases are predisposing factors for the development of preeclampsia. If the titers of TSH are

above 5 mIU/ml, then the risk of developing preeclampsia is 4.8 times higher. This high-risk potential marker of preeclampsia needs further investigation because of the small number of subjects in this study. A multicenter study may reveal the association and mechanism of thyroid abnormalities in preeclamptic women in different geographical regions. Such a study, by enabling us to identify thyroid abnormalities and take appropriate therapeutic action to correct them, might lower the occurrence and severity of morbidity and mortality associated with preeclampsia.

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