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Evaluation of Maternal Thyroid Hormone Status and Atherogenic Potency in Pre Eclampsia in Kolar District- A South West of India

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Authors' contributions

This work was carried out in collaboration between all authors. Authors SRS and CDD designed the study, wrote the protocol, and wrote the first draft of the manuscript. Author Aparna managed the literature searches, analyses of the study performed the spectroscopy analysis and author NS managed the experimental process. All authors read and approved the final manuscript.

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ABSTRACT

Aim: To determine maternal thyroid hormone status and lipid profile in preeclampsia.
Study Design: A prospective case control study consist of two groups such as group 1 normotensive non-preeclamptic group and group 2 as cases with clinically diagnosed preeclampsia
Place and Duration of Study: Department of Obstetrics and Gynaecology, RL Jalappa Hospital and Research Centre kolar, between January 2012 and June 2013.
Methodology: A total number of 100 pregnant patients were enrolled in the present study. Amongst, normotensive and preeclamptic pregnant women Group 1 (n=50) as controls (n=50). Group-2 (n=50) were preeclampsia cases. Five ml of blood samples were collected from each normal pregnant and preeclampsia patients. Thyroid hormone levels and lipid parameters were estimated using spectrophotometric method. Statistical analysis carried out by using Mean ± SD, and 't' test.

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Results: The Mean ± SD values of T3 ng/ml (1.56±0.38), T4 (1.37±0.36) mcg/dl, TSH (2.45±1.23) mcIU/ml in normal pregnants and T3 ng/ml (1.37±0.36), T4 (9.87±2.83) mcg/dl, TSH (6.15±5.51) mcIU/ml in preeclampsia cases were presented. Similarly Mean ± SD values of total cholesterol (181.62±44.33) mg/dl, HDL cholesterol (49.44±11.54) mg/dl, Triglycerides (198.10±49.84) mg/dl, LDL cholesterol (104.90±29.58) mg/dl, and Total cholesterol/HDL cholesterol ratio (3.67) were from control group and total cholesterol (222.60±70.07) mg/dl, HDL cholesterol (45.92±11.81), Triglycerides (278.66±93.46) mg/dl, LDL cholesterol (116.52±49.26) mg/dl, and cholesterol and HDL cholesterol ratio (4.84) in preeclampsia were presented respectively.
Conclusion: Pre eclampsia patients have higher levels of TSH and lower levels of T3 and T4 in comparison to normotensive pregnant women. This changes in the thyroid hormones did not correlate with the severity of preeclampsia between mild and severe pre eclampsia groups. Dyslipidemia was observed in pre eclampsia group than in the normotensive group indicates the possible atherogenic potential. This association may be useful in understanding the pathologic processes of preeclampsia.

Keywords: Preeclampsia; thyroid hormones; dyslipidemia; cholesterol/HDL cholesterol ratio.

1. INTRODUCTION

Preeclampsia is pregnancy associated, newly onset hypertensive disorder with proteinuria observed during ≥ 20th week of gestation period, that continue to be one of the major causes of maternal and fetal morbidity and mortality with a prevalence rate of 5-7% of worldwide [1]. As per the World Health Report - 2005 Hypertensive disorders of pregnancy including pre-eclampsia and eclampsia are the cause of 12% of maternal deaths. However, in developing countries nearly 17% of direct obstetric deaths are due to a result of hypertension. In India, the rate of incidences found nearly 8-10%. This clinical condition is a multisystem disorder that affects different organs and systems, involves interaction of utero-placental blood flow, vascular resistance, endothelial integrity and coagulation system [2].

Preeclampsia commonly occurs in first pregnancies than subsequent pregnancies. Although, Potential causes and exact mechanisms of preeclampsia remains unknown, however maternal immune system, genetic factors and placenta have been implicated. Reversiable type of dearrangment in thyroid function is observed in Pregnancy that demands sufficient provision of thyroid hormones essentially for normal fetal brain development [3]. Enhanced transplacental uptake of iodine and increased maternal renal clearance during pregnancy relatively onsets iodine deficiency which is compensated by increasing iodine uptake and synthesis of thyroid hormones [4] has become the basis of hypothyroidism in preeclampsia.

Hypothyroidism and dyslipidemia affects developing fetus and thus associated with increased fetal risk. Thus routine TSH screening should be offered as a way to improve pregnancy outcome and maternal wellbeing [5]. Women with preeclampsia also have an increased risk of dyslipidemia, cardiovascular and renal disease [6]. Altered lipid biochemical parameters favors atherogenic condition [7] and Oxidized LDL-cholesterol particles might be involved in vascular endothelial damage in preeclampsia [8]. The current study is taken up to evaluate, thyroid hormone levels and lipid profile in normotensive pregnant women and in women with preeclampsia and to assess the relationship between the alteration of thyroid harmones and lipid profile in women with Preeclampsia in the study area.

2. MATERIALS AND METHODS

2.1 Source of Data

2.1.1 Patients

A total number of 100 subjects were enrolled in the present study. Amongst, Group1 (n=50) normotensive pregnant women as controls. Group-2 (n=50) were preeclampsia cases. These patients were clinically diagnosed by OBG dept. of RL Jalappa Hospital and Research Centre between January 2012 to June 2013 and were participating in the study. After obtaining approval by the Institutional ethics committee and also informed patient consent the study was carried out. A standard Sri Devaraj urs University Proforma was used to collect the data. Five ml of blood samples were collected in to a plain vaccutainer and stored at -80ºC until analysis. Thyroid hormone levels and lipid parameters were determined using Chemiluminescense and spectrophotometric method respectively.

Pregnants beyond 20 weeks of gestation were clinically diagnosed with preeclampsia as per National High Blood Pressure Education Programe working group (NHBPEP) Classification with blood pressure ≥ 140/90 mm of Hg and with proteinuria were included in the study group as cases. Age, gestation, and Parity matched normotensive, Non preeclamptic pregnants were also included in the study as controls.

Patients with pre-existing thyroid disease, history of renal disease and history of any metabolic disorder before or during the pregnancy, history of chronic hypertension and history of medication known to affect the thyroid function are excluded from the study.

2.2 Methods

Preeclampsia diagnosed as blood pressure of ≥ 140/90 mm of Hg noted for the first time during pregnancy on ≥ 2 occasions at least 6 hours apart, after 20 weeks of gestation with proteinuria of ≥ 300 mg/24 hours or ≥ 1+ by a dipstick method in a random urine sample (NHBPEP and ACOG criteria)

2.3 Thyroid Profile

T3, T4 and TSH were analyzed by Chemi-luminescence assay (CLIA) using Vitros immunodiagnostic kits employing the Vitros 250 analyser (Johnson and Johnson) The Revised Endocrine Society Clinical Practice Guidelines of 2012 were followed for cut-off values for TSH, T3 and T4 (based on pregnancy-specific and trimester-specific) reference ranges. The normal values for T3: 1.2-1.6 ng/ml, T4: 6.3-9.7 mcg/dl, TSH: 0.38 to 4.04mcIU/ml. Women with serum T3, T4 and TSH values within the normal range were considered to be euthyroid. Those with an abnormally low TSH but normal T4 levels were classified as having subclinical hyperthyroidism. Conversely, women with abnormally high TSH but normal T4 levels were classified as having subclinical hypothyroidism and also with abnormally high TSH and low levels of T4 and T3 were classified as having overt hypothyroidism.

2.4 Lipid Profile

Serum Lipid parameters estimation was done by dry chemistry using Vitros 250 analyser. (Johnson & Johnson). LDL cholesterol (LDL-C) was calculated by using Frederickson-Friedwald's mathametical formula [9].

2.5 Statistical Analysis

The results obtained were analyzed by using statistical tools such as Mean, SD and results on categorical variables are presented as Numbers and Percentage (%). 't' test was used to find the significance of study parameters between two groups. The level of significance between the groups were presented with P value: $0.05<P<0.10$, moderately significance with P value: $0.01<P \leq 0.05$, and strongly significant with P value $P \leq 0.01$.

3. RESULTS

The results obtained from the study on age group, gravida type, gestational age group distribution, blood pressure were presented in the tabular format in Table, showing details of age group, gravida, gestational age, and blood pressure between normotensive and preeclampsia group.

Accordingly, amongst the patients who visited the hospital, majority of the age group falls in the range of 18 to 25 years. The Data analysis indicated from the study group, particularly in Normotensive group, 52% were primigravida and 48% were multigravida where as in the Preeclampsia group, 70% were primigravida and 30% were multigravida observed as shown. Similarly, regarding gestational age group distribution, 80% of the normotensive patients were in the gestational age group of 38to 40 weeks while 64% of the preeclampsia patients were in this group. The mean Systolic Blood pressure in normotensive group was 115.20±7.62 and in preeclampsia group was 156.20±16.02 as mean diastolic blood pressure.

Syndrome of hypertension, with proteinuria and/ or edema. In majority of the patients, the clinical presentation is mild, only with a slight increase in blood pressure or proteins in the urine. Severe maternal and fetal complications such as the HELLP syndrome, eclampsia, preterm delivery, abruptio placenta, intrauterine fetal death or fetal growth restriction are seen in a minority of patients.

Table 1. Details of age group, gravida, gestational age, and blood pressure between normotensive and preeclampsia group.

Particulars		Normotensive (N=50)		Preeclampsia (N=50)	
	Age group	**Numbers**	**Percentage**	**Numbers**	**Percentage**
Age in years	18-20	12	24	16	32
	21-25	23	56	20	40
	26-30	08	16.0	09	18
	>30	02	4.0	05	10
	Weeks	**Numbers**	**Percentage**	**Numbers**	**Percentage**
Gestation age in weeks	28-33	04	08	04	08
	34-37	04	08	11	22
	38-40	40	80	32	64
	>40	02	04	03	06
	Parity type	**Numbers**	**Percentage**	**Numbers**	**Percentage**
Parity distribution	Primi gravida	26	52	35	70
	Multigravida	24	48	15	30
	Types	**Mean, SD value**		**Mean, SD value**	
Blood pressure in mm Hg	Systolic BP	115.20±7.62		156.20±16.02	
	Diastolic BP	73.80±4.90		103±11.47	

Maternal age is one of the essential risk factors in women with Preeclampsia. The risk of pre-eclampsia is higher when the age of pregnant women is less than 25 years [10]. In the present study, the majority of the patients selected in both the groups were in the age group of 21-25years, which comprising 56% in the control group and 40% in the preeclampsia group. However, this study shown blood pressure variation in the normotensive group was 73.80±4.90 and in Preeclampsia Group was + 103.00±11.47 As per the results of thyroid profile parameters, the mean TSH value (2.45±1.23) is significantly higher and the mean T3 and T4 values are significantly lower in the preeclampsia group as compared to normotensive group. (p value <0.001) which is shown in table, Comparison of Thyroid hormone levels between control and preeclampsia groups.

As per the results of lipid profile parameters, the mean Total cholesterol and Triglyceride levels are significantly elevated in the study group as compared to the control group. (p<0.001) whereas the mean HDL and LDL values are comparable in the two groups. Total cholesterol and HDL cholesterol ratio clearly indicating the atherogenic potential in the preeclampsia groups table, Comparison of Lipid profile control and preeclampsia groups.

Table 2. Comparison of thyroid hormone levels between control and preeclampsia groups

Thyroid	Normotensive group (Mean±SD)	Pre-eclampsia group (Mean±SD)	p value
T3 (ng/ml)	1.56±0.38	1.37±0.36	0.011*
T4 (mcg/dl)	11.61±3.64	9.87±2.83	0.009**
TSH (mcIU/ml)	2.45±1.23	6.15±5.51	<0.001**

Table 3. Comparison of Lipid profile control and preeclampsia groups

Lipid parameters	Normotensive group (Mean±SD)	Pre-eclampsia group (Mean±SD)	p value
Total cholesterol (mg/dl)	181.62±44.33	222.60±70.07	0.001**
Triglycerides (mg/dl)	198.10±49.84	278.66±93.46	<0.001**
HDL- cholesterol (mg/dl)	49.44±11.54	45.92±11.81	0.135
LDL-cholesterol (mg/dl)	104.90±29.58	116.52±49.26	0.161
Total cholesterol/HDL ratio	3.67	4.84	

4. DISCUSSION

Statistical significance observed with respect to age distribution among preeclampsia patients and normotensive pregnants was 23.70±3.37 and the mean age among the preeclampsia group was 24.08±4.69. This observation holds good in a study conducted by Procopciuc et al. [10] and Basbug et al. [11] where there was no statistically significant difference in the age of the patients reported.

Different case-control studies proposed that women with Preeclampsia are two times expected to be Primiparous as women without PIH [12,13-17] similarly, a Canadian study reported that women with hypertensive disorders were more expected to be nulliparous in the range of 42.2% - 78.2% when matched with normotensive (41.9%) pregnant women [18]. Duckitt and Harrington (2005) found that nulliparous women are at increased risk of preeclampsia, and It is believed that this high risk is related to the maternal first exposure to chorionic villi, specifically the trophoblast, which is of fetal origin [18]. In the similar way, our study indicated about 70% were primigravida among the preeclampsia group where as 52% were Primigravida among the controls.

As per the observation of the study, the majority of the patients were in the gestational age group of 38-40 weeks who belong to 80% in the normotensive group and 64% in the preeclampsia group. This was comparable to the study carried out by Basbug et al. and Ashoor et al. [19,20] where they found no statistical significance between the studied groups.

In the current study, the mean TSH value is significantly higher and the mean T3 and T4 values are significantly lower in the preeclampsia group compared to normotensive group. (p value <0.001). However the mean T3, T4 and TSH levels were similar in the mild and severe preeclampsia groups. These findings supported the reports that preeclamptic women had a higher incidence of hypothyroidism compared to normotensive pregnant women [21-26].

The decrease in the thyroid hormones with a concomitant increase in the TSH levels has been found to correlate with the severity of preeclampsia. It has also been observed that preeclamptic women with higher TSH and lower thyroid hormones are likely to have a Small for Gestational age infants [21,23]. These results supported by a study conducted by Pasupati et al. [21] where they concluded that higher levels of mean TSH values in preeclampsia in comparison with the control group.

In the study of Procopciuc et al. [10] preeclamptic patients were genotyped for TSH receptors and serum TSH levels and they found that TSH levels were significantly higher in preeclamptic women than in the normal pregnant women and concluded that high TSH represent a risk factor for preeclampsia and could be correlated with its severity. Bankowska et al. reported that thyroid dysfunction was seen in 78.2% of pregnant women with preeclampsia. They concluded that the thyroid function tests should be performed on all pregnant women with preeclampsia [26].

In the present study, the mean total cholesterol and Triglyceride levels are significantly elevated in the preeclampsia group as compared to the normotensive group. (P value <0.001) whereas the mean HDL and LDL values were found to be statistically non - significant. This observation differs from the study reported by Phalak et al. where he showed that there was a significant rise in Serum Triglycerides, Total cholesterol and LDL-C levels and a significant decrease in HDL-C levels in cases as compared to controls [27-29].

Earlier studies reported that the striking changes in the lipid profile in normal pregnancy are Serum hypertriglyceridemia, which may be as high as two to three folds in the third trimester over the levels in non-pregnant women [30]. In our study also this observation holds true and the rise in serum triglycerides was statistically significant (P<0.001) in pregnancy induced hypertensive patients when compared to women with normal pregnancy. The change in LDL-C cholesterol was not significant in the two groups. Our study results are similar to the study carried out by Lima et al where the preeclamptic patients had significantly higher concentrations of triglycerides than healthy women. It was also suggested that triglyceride assessment between 28 and 32 weeks could be predictive of preeclampsia [30-33].

Several other investigators have reported that hypertriglyceridemia could be involved in the pathogenesis of hypertensive disorders during pregnancy. They also found a significant and positive association between proteinuria and triglyceride levels. These findings suggest that

these lipids may be involved in the endothelial damage observed in preeclampsia patients [34-37].

5. CONCLUSION

The conclusion of the present study is that preeclampsia patients have significantly higher levels of TSH and low levels of T3 and T4 in comparison to normotensive pregnant women. However, the changes in the thyroid hormones did not correlate with the severity of preeclampsia since there was no statistical significance observed between mild and severe preeclampsia groups. Dyslipidemia is more pronounced and found statistically significant in preeclampsia group than in the normotensive group. The lipid parameters between these groups could indicate possible atherogenic potential. This association may be useful in understanding the pathologic processes of preeclampsia. Thus, estimation of lipid profile may have a predictive role in the assessment of the extent of endothelial damage in preeclampsia and may help by preventing or foreseeing the complications of pre-eclampsia.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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