

# Comparison of Lipid Profile Parameters between Normal and Pre-eclamptic Pregnancies

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## ABSTRACT

**Introduction:** Pregnancy-induced hypertension (PIH) is one of a major cause of the fetal and maternal morbidity and mortality. Serum lipid profile plays important role in the regulation of normal blood pressure during pregnancy.

**The aim:** To evaluate the alteration of serum lipid profile during normotensive and hypertensive pregnancy.

**Study Design:** This case-control study was conducted among the pregnant women visiting AL-Batool Maternity Teaching Hospital and AL-Khansa Hospital. Total 150 participants were evaluated out of which 75 were normotensive pregnantwomen (26-37 years) taken as a normal control group and 75 were enrolled as hypertensive (25-38 years) study group. Average blood pressure for normotensive pregnant women at admission was 108/73 whereas, for hypertensive pregnant women it was 157/103  $\pm$  4/2. The levels of different serum lipids were measured using respective analytical kits.

**Result:** Pre-eclampsia was directly associated with increased levels of serum TGs (3.70  $\pm$  0.4 vs. 2.86  $\pm$  0.30), TC (6.14  $\pm$  0.39 vs. 5.96  $\pm$  0.56), LDL (3.49  $\pm$  0.43 vs. 2.96  $\pm$  0.26) and VLDL (1.43  $\pm$  0.24 vs. 1.12  $\pm$  0.18), and fall in HDL (1.19  $\pm$  0.15 vs. 1.57  $\pm$  0.20) as compared to that of normotensive pregnant women. The increased levels of TGs, TC, and LDL in hypertensive pregnant women were also correlated with significantly increased values of TC/HDL in hypertensive pregnant women.

**Conclusion:** The findings of the present study are consistent with previous studies, suggesting increased level of serum TC, TGs, LDL and VLDL as an importantfactor in pathological process of pre-eclampsia,this association may help in developing the strategies for prevention and treatment of PIH.Any pregnant female with higher serum triglyceride concentrations may be further investigated for pre-eclampsia.

**Keywords:** Normal pregnancy; Pregnancy induced hypertension; Pre-eclampsia; Triglycerides; Total cholesterol, LDL-cholesterol; VLDL-cholesterol; HDL-cholesterol.

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## INTRODUCTION

Pregnancy induced hypertension (PIH) is one of the major health problems in pregnant women. It is one of the leading causes of perinatal morbidity and mortality<sup>[21]</sup>.

PIH, is defined as a rise in blood pressure above 140/90 mm of Hg or rise in systolic blood pressure of more than 30mm of Hg or diastolic blood pressure of more than 15mm of Hg after 20 weeks of gestation accompanied by proteinuria  $\geq$  300mg / 24 hrs. or greater or equal to 1+ or 100mg /dl by dipstick response<sup>[12,19]</sup>.

Pre-eclampsia is mainly a disease of primgravidae, it only occurs in multigravidawomen under certain conditions like pregnancy complicated by hydatid form mole, multiple pregnancies, and gestational diabetes<sup>[7]</sup>.

The etiology and pathogenesis of pre-eclampsia remain to be elucidated. The ischemic placenta produces a number of toxic substances into maternal circulation which result in generalized maternal endothelial dysfunction which is considered as a widely accepted theory for the etiology and the pathogenesis of disease<sup>[4,19]</sup>.

Several other factors including genetic, immune, vascular and oxidative stress, due to significant increase in the generation of lipid peroxides, free radicals and reactive oxygen species are implicated in the pathogenesis of pre-eclampsia<sup>[3]</sup>.

While other studies in the field of cardiovascular research have shown that serum lipids have a direct effect on endothelial function and in this way, abnormal serum lipid profiles are also associated with endothelial dysfunction, the increased triglycerides is likely to be deposited in predisposed vessels, such as uterine spiral arteries<sup>[6]</sup>, this accumulation decrease the release of prostacyclin, resulting in oxidative stress via endothelial dysfunction, a key mechanism in the proposed pathophysiology of pre-eclampsia<sup>[3]</sup>.

Lipid profile abnormalities also, lead to reduction in the PGI<sub>2</sub>:TXA<sub>2</sub> proportion which is additionally expected to be an essential method for pathogenesis in PIH<sup>[2]</sup>.

The oxidized low density lipoprotein (ox LDL) result from one of the biologically relevant modifications in LDL in the form of oxidation. Dyslipidemia has been found to be one of the strongest predictors of levels of ox LDL in middle-aged adults, and the effect seems to be amplified in pregnant women with pre-eclampsia, where the dyslipidemia is even more pronounced<sup>[22]</sup>.

Characteristic pathological lesions of pre-eclampsia in utero-placental bed are like necrotizing arteriopathy, accumulation of foam cells or lipid laden macrophages in decidua and fibroblast proliferation, similar to lesion found atherosclerosis<sup>[11]</sup>. The risk of developing pre-eclampsia appears to be greater in woman, who have family history of essential hypertension or metabolic disorder<sup>[2,20]</sup>.

Complications of pre-eclampsia are consistently listed among the three most common causes of maternal death in virtually all developed countries<sup>[5]</sup>. Maternal morbidity is directly related to the severity and duration of hypertension<sup>[1]</sup>; While perinatal mortality increases progressively with each 5 mm Hg increase in mean arterial pressure<sup>[10]</sup>. PIH may cause several critical problems in pregnancy such as premature delivery, intrauterine growth restriction, fetal death<sup>[6]</sup>.

**Aim:** the aim of this study was to compare the altered lipid profile in hypertensive pregnant women with that of normotensive pregnant women. Moreover, the ratio of TC/HDL was calculated.

## MATERIALS AND METHODS

It was a case control study done in AL-Batool Maternity Teaching Hospital and AL-khansa Hospital. A total 150 participants were enrolled in this study, blood pressure (BP) was measured and on the basis of BP, all the participants were divided into two groups:

**Group 1-** Control Group: include 75, aged (26-37) years, pregnant women with normal blood pressure (106/61+ 2/1.6 mmHg) at third trimester of pregnancy, without any evidence of pre-eclampsia signs, renal disorders, hematological abnormalities.

**Group 2-** Study Group: 75 pregnant women, aged (25-38) years with pre-eclampsia. symptoms and signs, the mean of their blood pressure at admission was 157/103 + 4/2 mmHg, and urinary protein (by dipstick) averaged from (+2 to +3).

The pre-eclamptic patients were diagnosed by the presence of persistent hypertension (140/90 mmHg or more), gross proteinuria (tested by heat test of urine) with or without oedema.

The hypertension was diagnosed by the presence of persistent hypertension (more than 140/90 mm of Hg) measured on two occasions at least 6 hours apart.

**Inclusion criteria:** All pregnant women who come to our hospital with gestational age of 32-40 weeks as determined by last menstrual period or ultrasound scan, irrespective of parity and gravida were pregnant women, in the third trimester.

**Exclusion criteria:** Pregnant women with known renal disease, diabetes, hepatic dysfunction, dyslipidemia and pre-existing hypertension before pregnancy were excluded from this study in both control and study groups. The demographic and the clinical characteristics of the study groups are summarized in (Table 1).

**Table 1: The demographic and the clinical characteristics of the study groups.**

Characteristics		Normotensive pregnant (n=75)	Pre-eclamptic pregnant (n=75)
Maternal age, years		27.9 ± 5.62	33.4 ± 5.54
Weight Kg		74.5 ± 3.2	82.5 ± 6.19
Gravida	Primi	46	53
	Multi	29	22
Gestational age, weeks		37.3 + 0.7	34.9 + 0.6
Systolic B.P, mmHg		106 + 1.6	157 + 4
Diastolic B.P, mmHg		61 + 1.6	103 + 2
Urin Protein by dipstick		0	+ 2 → + 3
Past medical history of PIH	Present	0	16
	Absent	75	59
Family history of PIH	Present	0	58
	Absent	75	17

### Sample collection and preparation

Fasting Peripheral blood samples were collected from all participants(10 ml) and dispensed into plain tubes. The specimens were centrifuged for 5 min at 3000 rpm to separate the serum which were then collected in plain tubes labeled and stored at -80°C. The stored samples were analyzed within two weeks of collection was used for estimation of serum lipid profile.

### Biochemical analysis of serum lipid profiles

The serum levels of TC was estimated by cholesterol oxidase-Peroxidase colorimetric endpoint method (CHOD-PAP enzymatic method) using BIOLABO kit(Maizy, France, Batch no.091704B), the intensity of coloured quinonimine complex was measured at 505 nm by spectrophotometer (Cecil, Ce 303, England).

Estimation of serum HDL-C by direct method using, BIOLABO kit (Maizy, France, batch no.02160)

Estimation of serum TGs by Glycerol phosphate oxidase–Peroxidase colorimetric endpoint method (enzymatic method) using BIOLABO kit (Maizy-France), the purple coloured complex read at 546 nm by spectrophotometer (Cecil, Ce 303, England).

VLDL-C level in serum is derived by dividing serum TGs by 5.

Serum LDL-C was calculated by Frederickson – Friedwald’s Formula (Friedwald et al., 1972) according to which LDL-C = Total Cholesterol – (HDL-C + VLDL-C). (VLDL-C) was calculated as 1/5th of Triglycerides.

### Statistical analysis

Values for both normotensive and hypertensive pregnant women were expressed as mean ± SD. Level of significance between hypertensive pregnant women and normotensive pregnant women were performed using the Student t-test. P value < 0.001 was considered statistically significant.

## RESULTS

The collected clinical data from normotensive and hypertensive pregnant women to characterize the lipid profile within study groups (Table 2).

**Table2: Comparison of lipid parameters between normotensive and hypertensive pregnant women.**

Parameters	Normotensive pregnant (n=75)	Pre-eclampsia(n=75)	P value
Triglyceride(mmol/L)	2.86 ± 0.30	3.70 ± 0.40	<0.001
Cholesterol (mmol/L)	5.96 ± 0.56	6.14 ± 0.39	>0.05
HDL-C (mmol/L)	1.57 ± 0.20	1.19 ± 0.15	<0.001
VLDL-C (mmol/L)	1.12 ± 0.12	1.43 ± 0.24	<0.001
LDL-C (mmol/L)	2.96 ± 0.26	3.49 ± 0.43	<0.001
Atherogenic index	3.79±0.44	5.15 ± 0.65	<0.001

In hypertensive pregnant women, the serum levels of TGs, LDL and VLDL were significantly high ( $P < 0.001$ ). No significant difference in mean total cholesterol concentration in the pre-eclamptic group when compared with that in normal pregnant group was found, whereas, the serum level of HDL was significantly low ( $P < 0.001$ ) when directly compared with that of normotensive pregnant women. The ratio of TC/HDL was calculated, The values of this ratio (TC/HDL) for hypertensive pregnant women were significantly higher as compared to that in normotensive pregnant women.

**Abbreviations:** BP: Blood pressure; Pregnancy Induced hypertension: PIH; TC: Total cholesterol; TGs: Triglycerides; HDL: High density lipoproteins; LDL: Low density lipoproteins; VLDL: Very low density lipoproteins.

## DISCUSSION

Pre-eclampsia is a complex pathophysiological process associated with abnormal placentation and impaired placental perfusion. However, other conditions characterized by poor placentation, such as intrauterine growth retardation, do not necessarily result in pre-eclampsia. This has led to the growing concept that maternal predisposing factors must combine with the placental disorder to result in pre-eclamptic maternal syndrome<sup>[13]</sup>. It is common that during healthy pregnancy, progressive rise in blood insulin and gestation hormones (progesterone, 17 $\beta$ -estradiol, human placental lactogen) is accompanied by elevations in blood lipids and weight gain<sup>[8]</sup>.

In the present study, serum levels of TGs, LDL and VLDL were significantly increased whereas, the level of HDL was significantly decreased in hypertensive pregnant women as compared to controls (Table 2). It is common that during healthy pregnancy, the progressive rise in blood insulin and gestation hormones (progesterone, 17 $\beta$ -estradiol, human placental lactogen) is accompanied by elevations in blood lipids (TG and cholesterol) and weight gain<sup>[8]</sup>.

The principal modulator of hypertriglyceridemia is hyperestrogenemia in pregnancy that induces hepatic lipase which is responsible for the increased synthesis of the triglycerides at the hepatic level<sup>[12]</sup>. Lipolysis is increased as a result of insulin resistance, leading to increased flux of fatty acids to the liver promoting the synthesis of VLDL and increased TG concentrations<sup>[17]</sup>. Because of a decrease in the activity of lipoprotein lipase during pregnancy, VLDL remain in the plasma for longer and leads to the accumulation of LDL. Women with pre-eclampsia display additional alterations in lipids reflecting disordered lipid and lipoprotein metabolism<sup>[6]</sup>.

The increased serum triglyceride found in pre-eclampsia is likely to be deposited in pre-disposed vessels such as the uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small dense LDL<sup>[3,10]</sup>.

Moreover this hypertriglyceridemia may be associated with hyper-coagulability and the development of atherotic changes in spiral arteries hypercoagulability<sup>[14]</sup>.

In this study the increase in serum TG, VLDL was statistically significant ( $p < 0.001$ ) in pre-eclamptic patients in contrast to normotensive pregnant women. The findings of TGs, LDL and VLDL in this study are consistent with already published reports in which increased levels of these lipid profile were observed in hypertensive pregnant women, Attah et al,<sup>[3]</sup>; Anila et al,<sup>[2]</sup> and. While the increase in the mean value of TC concentrations in the pre-eclampsia was regarded non-significant ( $P > 0.05$ ) as compared with normotensive pregnant women. Similar types of findings were also observed in previous studies of Monica et al,<sup>[16]</sup> and De J et al,<sup>[9]</sup>. However, another study done by Mohini et al,<sup>[15]</sup> has found significant rise in serum total cholesterol (TC) in pre-eclamptic patients.

HDL is good cholesterol for the health as it regulates the BP towards normal levels. In hypertensive pregnant women, the serum levels of HDL-C were significantly decreased in the 3rd trimester of pregnancy in comparison to normotensive pregnant women. The low level of HDL is due to insulin resistance<sup>[12]</sup>. A low level of HDL-C hinders reverse cholesterol transport, which may be a reason for the atherosclerosis like features in pre-eclampsia<sup>[13]</sup>. Similarly, study conducted by Mohini et al,<sup>[15]</sup>; Anila et al,<sup>[2]</sup> and Rabia et al,<sup>[18]</sup> concluded significant fall in the level of HDL-C in pre-eclamptic women. The ratio of lipid profile TC/HDL increases significantly in pre-eclamptic women. From the results of this study, it can be found that serum levels of TC, TGs, HDL, LDL and VLDL are more profound in the 3rd trimester of pregnancy in hypertensive pregnant women as compared to that normotensive pregnant women.

## CONCLUSION

The findings of the present study suggest that the woman who developed pre-eclampsia had altered lipid profile due to abnormal lipid metabolism. Increased Triglyceride levels and its delayed clearance appeared to be of immense value in understanding the pathological process of pre-eclampsia.

This association may help to investigate the underlying pathological process of hypertension in pregnancy. It is therefore imperative that serum lipid profiles should be continuously monitored throughout the whole pregnancy period as it would be helpful in the early detection and/or developing the strategies to prevent any obstetric-associated complication during PIH and/or at the time of delivery.

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