

## MATERNAL PLASMA LIPID CONCENTRATIONS IN FIRST TRIMESTER OF PREGNANCY AND RISK OF SEVERE PREECLAPMSIA

Akhavan Setareh<sup>1</sup>, Modarres Gilani Mitra<sup>2</sup>, Borna Sedigheh<sup>3</sup>,  
Shahghaibi Shoaleh<sup>4</sup>, Yousefinejad Vahid<sup>5</sup>, Shahsavari Siroos<sup>6</sup>

### ABSTRACT

**Objective:** The role of abnormal lipid profile as a risk factor in pathology of pre-eclampsia is controversial. We investigated the relationship between early pregnancy plasma lipid concentrations and risk of severe pre-eclampsia.

**Methodology:** It was a prospective cohort study, in which one thousand maternal blood samples were collected at first trimester of pregnancy. We selected 63 women who developed severe preeclampsia from the cohort and 280 normotensive as control group matched with pre-eclamptic group. Plasma lipid concentrations were measured enzymatically. Data was analyzed with student t-test, and Relative risk with 95% confidence interval was calculated.

**Results:** The risk of severe preeclampsia among women with serum triglyceride level >175 mg/dl was 13.14 fold the ones with serum triglyceride level <100 (95% CI 1.84-265.4).

**Conclusion:** This study has showed that early pregnancy dyslipidemia is associated with an increased risk of severe pre-eclampsia.

**KEYWORDS:** Lipids, Pregnancy, Severe Pre-eclampsia.

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1. Akhavan Setareh, MD, Assistant Professor of Obstetric and Gynecology,
  2. Modarres Gilani Mitram, MD,
  3. Borna Sedigheh MD,
  - 2,3: Associate Professor of Obstetric and Gynecology, Tehran University of Medical Sciences, Imam Khomeini Hospital, Tehran.
  4. Shahghaibi Shoaleh, MD, Assistant Professor of Obstetric and Gynecology,
  5. Yousefinejad Vahid MD, General Practitioner, Researcher,
  6. Shahsavari Siroos, MSc, Instructor,
- 1,3,4-6: Kurdistan University of Medical Sciences, Behsat Hospital, Sanandaj, Iran.

### Correspondence

Dr. Akhavan Setareh,  
E-mail: S\_akhavan2007@yahoo.com

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## INTRODUCTION

Preeclampsia is one of the most important pregnancy's disorders, diagnosed with hypertension and proteinuria and is the leading cause of fetal and maternal morbidity and mortalities.<sup>1,2</sup>

Natural rising of plasma lipids is being seen in normal pregnancy, but this event is not atherogenic in normal pregnancy, and it is believed this process is under hormonal control. But in complicated pregnancy there is a possible defect in mechanism of adjusting physiologic hyperlipidemia.<sup>2</sup> There have been various studies carried out to evaluate the relationship between hyperlipidemia and incidence of preeclampsia that majority of them were based on case control study,<sup>3,4-9</sup> and some of them

were prospective.<sup>1,10-15</sup> There were a few studies done for evaluation of relationship between plasma lipid concentrations and severity of preeclampsia.<sup>9,16</sup>

We investigated the relationship between early pregnancy plasma lipid concentrations and risk of severe preeclampsia.

## METHODOLOGY

This was a prospective cohort study. Subjects were recruited from pregnant women before sixteenth week of pregnancy referred to the treatment and health care centers for prenatal care in Sanandaj city after approval of Kurdistan University of Medical Sciences ethics committee. The demographic characteristics and midwifery information were collected by questionnaire. The written informed consent was obtained from all women who participated in the study and then Fasting venous blood sample was taken from subjects. Plasma was separated from blood and stored at -80°C until the time of assay.

Individuals with background of midwifery's complications containing: abortion, preterm delivery, pre-eclampsia, intra uterine fetal death (IUFD), and also patients involving systematic disorders such as chronic hypertension, diabetes history, and other chronic diseases were excluded. Blood pressure was recorded in first trimester before the sixteenth week of pregnancy, and care was continued. Severe pre eclampsia was defined by criteria of BP >160/110 mm Hg after 20 weeks' gestation, proteinuria 2.0 g/24 hours or >2+ dipstick, serum creatinine >1.2 mg/dl unless known to be previously elevated, platelets < 100,000/mm<sup>3</sup>, microangiopathic hemolysis (increased LDH), elevated ALT or AST, persistent headache or other cerebral or visual disturbance, and persistent epigastric pain.<sup>2</sup>

Sixty three women developed severe preeclampsia from the cohort and 280 normotensive as control group matched for age, parity, and cigarette consuming with preeclamptic group. After liquefying frozen plasma's samples, standard enzymatically assays of plasma lipids were performed on both groups.

Enzymatic colorimetric test was used to define serum triglyceride, total cholesterol, and Low-density Lipoprotein (LDL) cholesterol (GPO-PAP, CHOD-PAP, and LDL-C method respectively; Parsazmun Co kits, Iran/ Auto analyzer RA100, USA). High-density lipoprotein (HDL) cholesterol was determined by detergent-based isolation and enzyme-linked colorimetric detection (CHOD-PAP; Parsazmun Co kits, Iran/ Auto analyzer RA100, USA).

In follow up blood pressure of both severe pre-eclampsia and control group were recorded again in 38th week of pregnancy and pr delivery. Data were analyzed by using descriptive tables, student t-test and calculating Relative risk with 95% confidence interval by SPSS statistical software.

## RESULTS

Characteristic of study subjects are presented in Table-I. There was a significant difference in all the plasma lipid concentrations between two groups (Table-II). Severe preeclampsia group had more LDL concentration, triglyceride, LDL/HDL ratio in comparison to control group (P=0.000).

The HDL concentration among severe pre eclampsia group were less than control group (P=0.000). But the mean of total cholesterol concentration among severe pre eclampsia group were less than control group (P=0.002). There was 13.14 fold increases seen in risk of severe preeclampsia among subjects with triglyceride level >175mg/dl in comparison to ones with triglyceride level <100 mg/dl (95% CI 1.84-265.4). The calculated relative risks of the association between severe preeclampsia risk and maternal plasma lipid concentrations are presented in Table-III.

There was also 3.28 fold increases seen in risk of severe preeclampsia among women with LDL>108 mg/dl in comparison to individuals have LDL<83.3 mg/dl (95% CI 1.93-153.8).

## DISCUSSION

Our results are in line with to majority of previous studies in this field which have reported significant relationship between hyper-

Table-I: Characteristic of study subjects according to preeclampsia status.

	Severe Preeclampsia Patients (n=63) N(%)	Normotensive Subjects (n=280) n(%)
Parity *		
First	18(28.)	75(26.8)
Second	33(52.4)	147(52.5)
Third	12(19)	58(20.7)
Smoked during pregnancy *		
Yes	0	0
BMI at blood sample collection *		
<20	3(4.8)	9(3.2)
20.0-24.9	16(25.)	88(31.)
25.0-29.9	41(65.)	149(53.2)
>30	3(4.8)	34(12.1)
		<i>Mean ± SD</i>
	<i>Patient</i>	<i>Control Subject</i>
Gestational age at blood sample collection (wk)	13.95±0.77	14.01±0.75
Age	26.3±5.8	27.5±4.6
Systolic blood pressure (mmHg in first trimester)	109.9±8.9	107.9±12.3
Diastolic blood pressure (mmHg in first trimester)	70.00±7.4	67.6±9.2
Systolic blood pressure (mmHg in third trimester)	179.8±14.7	114.5±13.3**
Diastolic blood pressure (mmHg in third trimester)	118.5±18.2	73.3±11.2**
Systolic blood pressure (mmHg predelivery)	144.4±11.5	107.9±11.1**
Diastolic blood pressure (mmHg predelivery)	93.0±7.1	67.4±7.3**

\*P&gt;0.05 \*\*P&lt;0.05

lipidemia, and preeclampsia, specially for triglyceride.<sup>1,3,4,8-13,16</sup> but is contrary to limited previous studies which have not mentioned any differences in lipid concentrations in both groups.<sup>5,7</sup>

The limited studies which have evaluated the relationship between plasma lipid concentrations and severity of preeclampsia.<sup>9,16</sup> The triglyceride levels at 20 and 34 weeks gestation were significantly higher than controls in women with mild and severe preeclampsia.<sup>16</sup> These findings are in agreement with our results.

The association between hypertriglyceridemia and severity of preeclampsia at 28-37 weeks gestation was evaluated in a study in the United States. In that study patients with mild preeclampsia had significant increase in plasma triglyceride levels while patients with severe preeclampsia had comparable triglyceride levels to controls.<sup>9</sup> That is not comparable with our results. The time variation of

taking blood samples to assess plasma lipids that was in third trimester in Mikhail and et al study<sup>9</sup> and first trimester in our study, would be noticeable in interpretation of two studies' results.

In another study performed in Spain, at 20 and 34 weeks' gestation, triglyceride levels were significantly higher than controls in women with severe gestational hypertension, mild and severe preeclampsia<sup>16</sup> and the significant elevation in triglycerides was already present at 10 weeks in mild and severe preeclampsia, this result is in agreement with our findings.

There was 4.15 fold increase in preeclampsia among subjects with triglyceride above 133 mg/dl comparing ones having triglyceride under 93 mg/dl in the performed cohort study in the United States (95% CI 1.50-11.49).<sup>10</sup> In our study, severe preeclampsia risk was 13.14 fold of increase among individuals having triglyceride above 175 mg/dl comparing ones under 100 mg/dl (95% CI 1.84-265.4).

Table-II: Maternal plasma lipid concentration according to preeclampsia status.

Lipid Concentration (mg/dl)	Severe Preeclampsia Patients(n=63)		Normotensive Subjects(n=280)		Pvalue*
	Mean	SD	Mean	SD	
Total cholesterol	175.4	12.9	182.0	22.0	0.002
LDL cholesterol	118.7	10.7	109.9	19.4	0.000
HDL cholesterol	39.9	2.9	48.8	11.5	0.000
LDL/HDL ratio	2.9	0.36	2.3	0.55	0.000
Triglycerides	186.7	13.5	163.5	42.8	0.000

\* From Student t test

In our study the mean of total serum's cholesterol in severe pre-eclampsia group comparing normal group was lower slightly, but it is significant, and risk of pre-eclampsia among individuals having total cholesterol above 205 mg/dl, was 0.2 as compared to those having cholesterol less than 172 mg/dl (95% CI 0.03-0.94). This result is similar to the findings by

with Turner and colleague's study that reported less cholesterol concentration among pre-eclampsia group,<sup>6</sup> Studies performed in France and Spain did not have a meaningful difference in cholesterol concentration in both groups,<sup>7,16</sup> but the total cholesterol serum concentrations have been cited more in pre-eclampsia group in other studies.<sup>3,4,10,11</sup>

Table-III: Relative risk (RR) and 95% confidence interval (CI) of the association between severe preeclampsia risk and maternal plasma lipid concentration.

Lipid Concentration (mg/dl)	Severe Preeclampsia Patients(n=63)		Normotensive Subjects(n=280)		Relative Risk (95% CI)
	n	%	n	%	
Total cholesterol					
<172	24	38.1	89	31.8	Referent
172-205	37	58.7	154	55.0	0.89 (0.48-1.65)
>205	2	3.2	37	13.2	0.2 (0.03-0.94)
				P for trend	0.07
LDL cholesterol					
<83.3	1	1.6	20	7.1	Referent
83.3-108	6	9.5	111	39.6	1.08 (0.12-25.1)
>108	56	88.9	149	53.3	3.28 (1.03-153.8)
				P for trend	0.000
HDL cholesterol					
>50	1	1.6	115	41	Referent
40-50	37	58.7	129	46.1	32.98 (4.75-656)
<40	25	39.7	36	12.9	79.86 (10.86-1638)
				P for trend	0.000
LDL/HDL ratio					
<1.7	1	1.6	32	11.4	Referent
1.7-2.7	12	19.0	187	66.8	2.05 (0.26-43.7)
>2.7	50	79.4	61	21.8	26.23 (3.62-533.81)
				P for trend	0.000
Triglycerides					
<100	1	1.6	31	11.1	Referent
100-175	9	14.3	124	44.3	2.25 (0.27-49.17)
>175	53	84.1	125	44.6	13.14 (1.84-265.4)
				P for trend	0.000

Comparing our results and those of other studies, it seems the role of hypertriglyceridemia and high LDL cholesterol level in pathogenesis of preeclampsia is seen in majority of studies. However, there is controversy as regards total cholesterol concentrations in several studies. As such it is essential to perform more studies in different populations in view of the present limited studies and some controversial findings about the relationship between severity of preeclampsia and plasma lipid concentrations.

### CONCLUSION

Our results have shown early changes in plasma lipid concentrations, which suggest their role in causation and severity of the disease. As such it is considered as a significant etiologic and pathophysiologic factor in this prevalent complication of pregnancy. Plasma lipid profile assay in first trimester of pregnancy is noticeable to predict incidence and severity of preeclampsia.

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