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Serum triglyceride level in early pregnancy as a predictive marker for risk of pre eclampsia; A prospective clinical controlled study

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Abstract
Pregnancy is a hyperlipidemic state as atherosclerosis, due to hormonal changes. To study aimed to investigate the relationship between early pregnancy serum triglyceride concentration and the risk of pre-eclampsia. 270 cases were selected from pregnant women 13- 20 weeks of gestational age who attended outpatient antenatal clinic. All routine investigations with a special investigation of serum lipid profile including triglyceride level were done. The mean triglyceride level was found to be 153.95 ± 23.52 mg/dl in the control group and 205.25 ± 42.48 mg/dl in the study group. It was 198.99 ± 36.12 mg/dl in mild PET group and 220.35 ± 53.13 mg/dl in severe PET group. The mean triglyceride levels in the control group were found to be significantly lower as compared to that in the study group ($p<0.001$) In the present study we have observed that maternal dyslipidemia in the early second trimester is associated with an increased risk of developing pre eclampsia.

Keywords: triglyceride level, pregnancy, dyslipidemia, pre eclampsia

Introduction
Pre eclampsia is a pregnancy specific syndrome that can affect every organ system. Pre eclampsia is characterized by the development of hypertension and proteinuria after 20 weeks of pregnancy. The prevalence of preeclampsia ranges from 1.8% to 16.7% in developing countries [1]. Etiopathogenesis of preeclampsia remains unclear however endovascular cytotrophoblast invasion in the spiral arteries, an exaggerated inflammatory response, and inappropriate endothelial cell activation have been proposed in the pathogenesis of pre-eclampsia [2, 3, 4]. Pregnancy is a hyperlipidemic state as atherosclerosis, due to hormonal changes [5, 6]. Triglyceride is formed by the esterification of glycerol with fatty acids, which have a hydrocarbon group attached to a carboxyl group. Triglycerides in adipose tissue provide our principal energy store.

Aims and Objectives
1. To investigate the relationship between early pregnancy serum triglyceride concentration and the risk of pre -eclampsia.
2. Comparison of serum triglyceride levels between women who remained normotensive and those who develop pre-eclampsia.

Material and Methods
This was a prospective cohort study to analyze the relationship between early pregnancy plasma lipid concentration and the risk of developing pre eclampsia. We tried to compare the lipid profile between women who remained normotensive and those who developed pre-eclampsia. This study was conducted in the department of obstetrics and gynecology, Queen Mary's Hospital, CSM medical university, Lucknow for a period of one year in collaboration with the department of pathology.

Selection of cases
270 cases were selected from pregnant women 13- 20 weeks of gestational age who attended outpatient antenatal clinic. Informed consent of patients was taken. Detailed obstetrical, menstrual and medical history was taken followed by a general, systemic and obstetrical

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examination. All routine investigations with a special investigation of serum lipid profile including triglyceride level were done.

All the subjects were normotensive at the time of enrolment. All the subjects were followed up for the development of pre eclampsia on the basis of systolic /diastolic blood pressure and urine albumin by the dipstick method.

Study population: These subjects were divided into two groups.
1. Control group: Those women who remained normotensive.
2. Study group: Those women who developed pre- eclampsia. Pre eclamptic toxemia (PET) were further divided into two groups
- Mild PET: BP≥140/90 mmHg and urine albumin +1 (By dipstick method)
- Sever PET: BP≥160/110mmHg and urine albumin ≥ +2 (By dipstick)

Out of 270 subjects, 58 subjects developed pre eclampsia (study group) and 212 subjects remained normotensive (control group). In the present study, 41 subjects developed mild PET and 17 subjects had severe PET.

Inclusion criteria: pregnant women included in this study
- 13 -20 wk. gestational age
- Age 20 -35yr
- Singleton pregnancy
- BMI <25

Exclusion criteria
Women with any of the following were not included:
- Diabetes mellitus, chronic hypertension or any other cardiovascular disease
- Smoker
- History of thromboembolism, Renal disease, Liver disease
- Multiple gestations
- BMI >25
- Age >35yr

Analysis of triglycerides
Enzymatic colorimetric method (Glycerol phosphate oxidase method) was used by using *AutoZyme NEW Triglycerides kit*

Results
Gestational age at which PET occurred
In maximum patients (n=40; 69%) PET developed between the gestational age 29-34 weeks. In only 3 (5.2%) cases PET developed after 34 weeks of gestational age. (Table 1)

Table 1: Gestational age at which PET occurred (Fig 1)

S. No.	Gestational Age (wks)	No. of Patients	Percentage
1.	20-28	15	25.9
2.	29-34	40	69.0
3.	>34	3	5.2

Table 2a: Level of Mean Triglyceride (mg/dl) in Control and Study Groups

Group	No. of cases	Range	Mean	SD
Control	212	88.2-206.7	153.95	23.52
Study	58	124-340	205.25	42.48

t=12.094; *p*<0.001

Table 2b: Level of Mean Triglyceride (mg/dl) levels in different groups

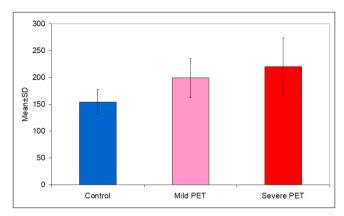| Group	No. of cases	Range	Mean	SD
Control	212	88.2-206.7	153.95	23.52
Mild PET	41	126.3-282.2	198.99	36.12
Severe PET	17	124-340	220.35	53.13

F=78.138; *p*<0.001

Fig 1: Level of Mean Triglyceride (mg/dl) levels in different groups

Table 2C: Comparison of Mean Triglyceride levels in different groups

S. No.	Comparison	"t"	"p"
1.	Control vs Mild PET	10.175	<0.001
2.	Control vs Severe PET	9.863	<0.001
3.	Mild PET vs Severe PET	1.776	0.081

The mean triglyceride level was found to be 153.95±23.52 mg/dl in the control group and 205.25±42.48 mg/dl in the study group. (Table 2a) It was 198.99±36.12 mg/dl in mild PET group and 220.35±53.13 mg/dl in severe PET group. (Table 2b) Analysis of variance (ANOVA) revealed a statistically significant difference among groups (F=78.138; *p*<0.001). The mean triglyceride levels in the control group were found to be significantly lower as compared to that in the study group (*p*<0.001). It was seen that both the study groups had significantly higher mean value as compared to the control group (*p*<0.001). However, no statistically significant difference was seen between the two study groups (p=0.081). (Table 2c)

Discussion
Pregnancy is associated with hyperestrogenemia that is principal modulator of hyperlipidemia. 3 Estrogen induces hepatic biosynthesis of endogenous triglycerides which is carried by VLDL. This process may be modulated by hyperinsulinism found in pregnancy. So Pregnancy is known as a hyperlipidemic state [4-6].

The present study was planned with the aim to asses serum lipid profile in early pregnancy and its relation with development of pre eclampsia. Several studies have been done by various authors to assess the serum lipid profile in early pregnancy and find out its relation with development of pre eclampsia [7-13].

The observation of various studies quoted above has shown that maternal dyslipidemia in early second-trimester pregnancy associated with increased risk for development of pre eclampsia. In our study incidence of the pre eclampsia was 21.5 %.

All the subjects were included in this study aged 18-34 years Most of the patients in all groups were aged between 25-35 yrs.

The mean age of control group was 25±3.21yrs, in mild PET was 27.90± 3.25 yrs and in severe PET was 27.53±3.68 yrs. Proportion of higher age group is significantly higher in study group as compared to control group (p=0.024) (Table-1).

In our study mean levels of Triglyceride was153.95±23.52 mg/dl found in control group and 205.25±42.48 mg/dl was in study group. That was a statistically significant difference between groups (F=78.138, p=0.001).In mild PET mean value of Triglyceride was 198.99±36.12mg/dl and in severe PET it was 220.35± 53.13mg/dl. It was seen that both the study group had significantly higher mean value as compared to the control group (p=0.001) However, no statistically significant difference was seen between two study groups. (Table 2a, 2b, 2c, Fig. 1)

Vidyabati RK *et al*. [7] found in their study that Mean level of triglyceride was visibly higher 213.94±51.07mg/dl in PET group as compared to normotensive group 197.78±59.20mg/dl. However, there was no statistically significant difference seen between two study groups (p=0.059).

M. Baker *et al*. [8] showed that mean value of Triglyceride in control group was 164± 56.2mg/dl and in mild PET group was 200±79.5 mg/dl. Triglyceride level was 18% higher (p=0.02) in women with mild pre eclampsia compared with control subjects but in severe pre eclampsia mean value of Triglyceride 146±53.5mg/dl was lower than control and mild PET(p=0.25).

Danial Enquabahrie *et al*. [9] discovered in their study, 4.15 fold increase risk of development of pre eclampsia if triglyceride level was >133 mg/dl.

So in the present study, all the lipid profile levels (TC, TG, VLDL, LDL, TC/HDL, and LDL/HDL) were significantly higher in study group as compared to control group. Mean levels of lipid profile for all variable was found higher in severe PET group but TC/HDL and LDL/HDL ratio was higher in mild PET group. In a study by Takahashi WH *et al*. [10] Serum total cholesterol, low-density lipoprotein cholesterol and triglyceride levels were similar in both groups during the first and second trimesters of pregnancy (p = 0.25, p = 0.71 and p = 0.30, respectively). However, serum total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels were significantly higher during the second trimester compared to the first trimester in both groups (p < 0.001, p < 0.005 and p < 0.001, respectively). Serum high-density lipoprotein cholesterol and very low-density lipoprotein cholesterol levels were similar in both groups during the first trimester (p = 0.21 and p = 0.38, respectively); during the second trimester, However, these levels were significantly higher in the pre-eclampsia group compared to the group with no pre-eclampsia (p = 0.005 and p = 0.003, respectively).

In present study 122 (60.7%) patients of control group had vaginal delivery and 79 (39.3%) patients had caesarean section while in mild PET out of 40 patients 32 (80%) delivered by caesarean section and 8 (20%) by vaginal, in severe PET out of 16 patients 9 (56.3%) delivered by caesarean section and 7(43.7%) by vaginal route. So significantly higher proportion of control subjects had vaginal delivery while cesarean section seems to be significantly higher in mild PET (*p*<0.001)

Conclusions
The incidence of pre eclampsia was 21.5%. It was found that mean Triglyceride level was significantly higher in study group as compared to control group (205.25±42.48 vs. 153.95±23.52 mg/dl, *p*<0.001). This shows that if triglycerides levels higher in early second trimester there was increased risk of developing pre eclampsia and severity of pre eclampsia directly proportional to levels of triglycerides.

In present study we have observed that maternal dyslipidemia in early second trimester is associated with an increased risk of developing pre eclampsia, so dyslipidemia in early second trimester is a very good predictor of pre eclampsia. By detecting maternal dyslipidemia in early second trimester we can detect patients at risk of pre eclampsia. We can prevent pre eclampsia and improve feto-maternal outcome by early detection of high-risk patients.

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