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Original Article

Obstetrics and Gynaecology Section

Association between Mid-trimester Maternal Triglyceride Levels and Subsequent Development of Preeclampsia: A Prospective Cohort Study

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ABSTRACT

Introduction: Hyperlipidaemia, specifically hypertriglyceridaemia, is a well-known risk factor for metabolic syndrome and cardiovascular atherosclerosis. Serum triglyceride levels are significantly elevated in women with Hypertensive Disorders of Pregnancy (HDP), and such elevations are consistent across the first, second, and third trimesters of pregnancy. Therefore, triglyceride levels in the early mid-trimester can act as predictors for the development of preeclampsia.

Aim: To determine whether serum triglyceride levels measured during the early mid-trimester of pregnancy can serve as a predictive biomarker for the development of preeclampsia.

Materials and Methods: A hospital-based prospective cohort study was conducted in the maternity unit of the Department of Obstetrics and Gynaecology at R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India from February 2020 to July 2021. Serum triglyceride levels were measured, and participants were divided into two groups of 75 each. Group 1 had normal serum triglyceride levels, while Group 2 had high triglyceride levels. The Adult Treatment Panel (ATP) III classification of serum triglycerides was used, with values >200 mg/dL taken as the cut-off level. Patients were followed up until delivery, and the incidence of preeclampsia was recorded in both groups. The Chi-square test was employed to compare categorical variables.

Results: The mean age of the study participants in Group 1 and Group 2 was 25.8±3.86 and 26.6±4.29 years, respectively. Group 1 (normal triglyceride levels) had seven cases of preeclampsia, whereas Group 2 (hypertriglyceridaemia) had 17 cases. Overall, the study demonstrated that high serum triglyceride levels in the antenatal period were statistically significant in predicting the occurrence of preeclampsia during pregnancy (p-value=0.02).

Conclusion: Higher serum triglyceride levels were found to be associated with an increased incidence of preeclampsia.

Keywords: Atherosclerosis, Hypertriglyceridaemia, Predictor, Pregnancy

INTRODUCTION

Hypertensive disorders of pregnancy are among the most common antenatal complications. These disorders contribute significantly to maternal morbidity and mortality rates and are one part of the deadly triad, which also includes haemorrhage and infection [1]. Pregnancy is often considered a “stress test” for metabolic and cardiovascular conditions [2, 3]. Hypertensive Disorders of Pregnancy (HDP) are associated with an elevated risk of developing subsequent systemic hypertension, adversely affecting the cardiovascular system [4].

Endothelial cell dysfunction is a key feature in the pathogenesis of preeclampsia. In preeclampsia, fibrin deposits, acute atherosclerosis, and thrombosis are characteristic pathological lesions found in the placenta. The similarities between the lesions of preeclampsia and atherosclerosis have led to speculations regarding a common pathophysiological pathway. An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular disease and directly impacts endothelial cell activation. Abnormal lipid metabolism seems to play an important role in the pathogenesis of preeclampsia [5].

Hyperlipidaemia, specifically hypertriglyceridaemia, is a recognised risk factor for metabolic syndrome. Triglyceride levels are significantly elevated in women with HDP, and these elevations are consistent throughout the first, second, and third trimesters of pregnancy [6, 7]. Therefore, triglyceride levels in the early mid-trimester can act as predictors for the development of preeclampsia, enabling early detection and timely monitoring or intervention, when necessary.

MATERIALS AND METHODS

A hospital-based prospective cohort study was conducted in the maternity unit of the Department of Obstetrics and Gynaecology at R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India from February 2020 to July 2021, following Institutional Ethical Clearance (Memo no. RKC/96, dated 20.01.2020).

Inclusion criteria: Pregnant women, irrespective of gravida status, Gestational age between 13 to 20 weeks, Age under 35 years, singleton uncomplicated pregnancy, Blood pressure below 140/90 mmHg, Willingness to follow-up.

Exclusion criteria: Women with chronic diseases (chronic hypertension, diabetes mellitus, severe anaemia, New York Heart Association (NYHA) grade 3/4 heart disease [8], renal disease), Bad obstetric history, Smoking history, Age over 35 years.

Sample size calculation: Niromanesh S et al., found that among 45 pregnant women who had high triglyceride levels, eight women developed preeclampsia (17.8% vs 3.7% in the control group, p<0.004) [9]. Based on present study, a total of 150 women were considered for the study.

Study Procedure

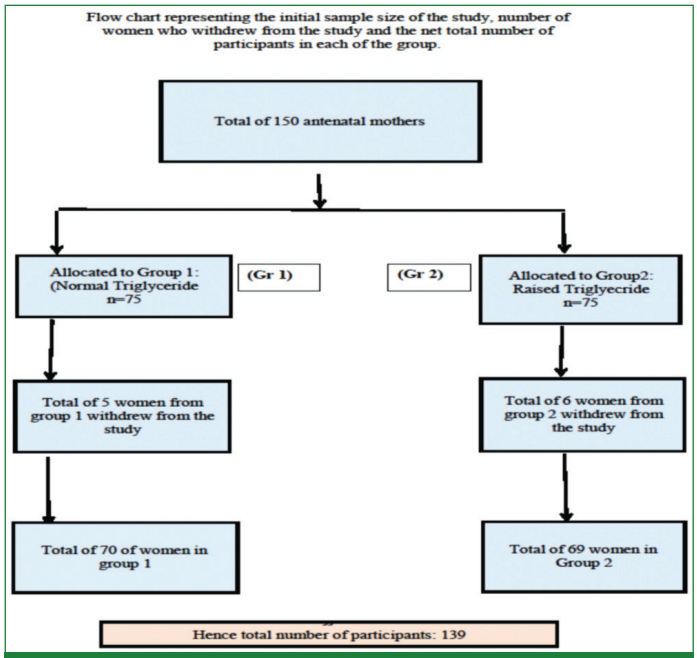
After fulfilling appropriate inclusion and exclusion criteria and obtaining informed consent, the authors enrolled pregnant mothers in their early second trimester. Serum triglyceride levels were measured, and participants were then divided into two groups of 75 each. Group 1 consisted of women with normal serum triglyceride

levels, while Group 2 comprised women with high triglyceride levels.

The flowchart depicted two groups:

Group 1 (GR I): Women with normal serum triglyceride levels, consisting of 75 participants, 5 of whom withdrew from the study.

Group 2 (GR II): Women with hypertriglyceridaemia, also numbering 75, with 6 withdrawing midway through the study [Table/Fig-1].



[Table/Fig-1]: Flowchart representing net total number of participants in each of the group.

The ATP III classification of serum triglycerides was applied, with values >200 mg/dL set as the cut-off level [10]. According to the 2016 World Health Organisation Antenatal Care Model (WHO ANC) model [11], a minimum of eight antenatal care (ANC) visits is recommended, including one visit in the first trimester (up to 12 weeks of gestation), two visits in the second trimester (at 20 and 26 weeks of gestation), and five visits in the third trimester (at 30, 34, 36, 38, and 40 weeks).

Preeclampsia was defined as new-onset hypertension (systolic pressure >140 mmHg or diastolic pressure >90 mmHg) after 20 weeks of gestation, coexisting with one or more of the following new-onset conditions:

1. Proteinuria: Urine protein-to-creatinine ratio of 30 mg/mmol or more, or albumin-to-creatinine ratio of 8 mg/mmol or more, or at-least (+2) on a dipstick test.

2. Other maternal organ dysfunctions:

- Renal insufficiency: Creatinine ≥90 micromol/L or ≥1.02 mg/dL.
- Liver involvement: Elevated transaminases {Alanine Aminotransferase (ALT) and Asparate Aminotransferase (AST) >40 IU/L)} with or without right upper quadrant or epigastric abdominal pain.
- Neurological complications: Convulsions, altered mental status, clonus, severe headache, or persistent visual scotoma.
- Haematological complications: Thrombocytopenia (count <150,000/μL), Disseminated Intravascular Coagulation (DIC), or haemolysis.
- Uteroplacental dysfunction: Foetal growth restriction, abnormal umbilical artery Doppler waveform analysis, or stillbirth.

The mode of delivery was noted, and neonatal status was assessed by the presence or absence of birth asphyxia {Appearance, Pulse, Grimace, Activity Respiration (APGAR) score of 0-3 at 1 minute or 5 minutes, defined as birth asphyxia} and whether there was Intrauterine Growth Restriction (IUGR), defined as estimated fetal weight below the 10th percentile for gestational age [12].

STATISTICAL ANALYSIS

All statistical analyses were performed using International Bussiness Machine (IBM) Statistical Packages for the Social Sciences (SPSS) Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean±Standard Deviation (SD), while categorical variables were presented as frequencies and percentages. The Chi-square test was used to compare categorical variables.

RESULTS

Out of a total of 139 participants, 69 (49.6%) were primigravida, while the rest were multigravida [Table/Fig-2]. In Group 1 (normal triglyceride levels), there were 7 (10%) preeclamptic patients, whereas Group 2 had 17 (24.6%). The p-value was 0.02, with a Chi-square statistic of 5.2119, indicating significance at p <0.05 [Table/Fig-3].

Groups	Age (Mean±SD) (in years)	Age (years)				Level of education					Gravida		Socio-economic class (modified BG Prasad scale 2021)					Gestational age of delivery			
		<20	20-24	25-29	30-35	Illiterate	Primary school	Middle school	High school	Graduate	Primi	Multi	I	II	III	IV	V	32-34 weeks	34+1-36+6 weeks	37-40 weeks	≥40 weeks
GR I	25.9±3.86	5	21	34	10	10	26	12	17	5	33	37	6	16	24	20	4	3	17	46	4
GR II	26.6±4.29	6	17	32	14	8	32	11	16	2	36	33	2	11	18	31	7	9	19	36	5

[Table/Fig-2]: Sociodemographic table (including gestational age of delivery).

Group	Preeclampsia present	Preeclampsia absent
Group 1	7 (10%)	63 (90%)
Group 2	17 (24.63%)	52 (75.37%)

[Table/Fig-3]: Number of women who developed preeclampsia in each group.

Parameters	IUGR	Birth asphyxia
Preeclampsia	8	7
Without preeclampsia	10	13

[Table/Fig-4]: Distribution of cases of IUGR and birth asphyxia (poor neonatal outcome) in women with preeclampsia and without.

Out of the 24 women who developed preeclampsia, 11 were multipara, and 9 of these had a history of preeclampsia in a previous pregnancy (82%). Among women with preeclampsia, the majority underwent caesarean section, with 19 (79.16%).

Regarding neonatal outcomes, [Table/Fig-4] shows that out of the 24 preeclamptic women, 15 experienced poor neonatal outcomes (IUGR, asphyxia, or both). [Table/Fig-5] depicts that maternal complications were more prevalent in Group 2 (patients with hypertriglyceridaemia). The most common complication was proteinuria (12 cases), followed by haematological complications

Groups	Proteinuria	Renal insufficiency	Neurological complications	Liver involvement	Haematological complications
Group 1	6	2	2	4	4
Group 2	12	5	4	7	10

[Table/Fig-5]: Number of women with complications in each group.

(10 cases), with liver involvement being the third most common complication (7 cases).

DISCUSSION

In the present study, the majority of mothers were between 25 and 29 years of age. Similarly, in a study conducted by Nidhi D et al., the largest number of participants, out of a total of 111, belonged to the age group of 26 to 30 years [13]. The present findings indicated that most women with preeclampsia delivered between the gestational ages of 34+1 and 36+6 weeks (preterm), which aligns with the results of the study by Suksai M et al., The present study confirmed that women who develop preeclampsia are more likely to deliver at an earlier gestational age [14].

In the present study, the incidence of preeclampsia was higher in Group 2 (women with high serum triglyceride levels) compared to Group 1 (women with normal serum triglyceride levels). Similarly, the study by De J et al., showed that the preeclampsia group was associated with a significant increase in triglycerides and VLDL cholesterol, along with a decrease in HDL concentration ($p<0.05$) [15]. In the studies by Mukherjee R et al., and Gohil JT et al., serum Triglycerides (TG), Total Cholesterol (TC), Low-density Lipid (LDL), and Very Low-density Lipid (VLDL) levels were significantly higher, while HDL levels were significantly lower in preeclamptic women compared to normotensive pregnant women [16, 17]. The present results align with a study by Singh U et al., which demonstrated that women with preeclampsia had 25.3% higher triglyceride concentrations than normotensive women [18]. A meta-analysis of 24 case-control studies indicated that preeclampsia is associated with hypertriglyceridaemia ($p<0.001$), and a meta-analysis of five prospective cohort studies confirmed the link between hypertriglyceridaemia and preeclampsia ($p<0.001$) [19]. Poornima IG et al., also concluded that hypertriglyceridaemia is associated with the development of preeclampsia [20].

The present study revealed that out of 24 preeclamptic women, 15 experienced poor neonatal outcomes (IUGR, asphyxia, or both). This indicates that IUGR and birth asphyxia are more common in patients with hypertriglyceridaemia. A review article by Bashir M et al., which included various studies and meta-analyses, contradicted the present findings, showing that maternal hypertriglyceridaemia is associated with large-for-gestational-age babies [21]. In the present study, IUGR was primarily due to the development of preeclampsia. Overall, the present findings suggest that high serum triglyceride levels during the antenatal period are statistically significant predictors of preeclampsia occurrence during pregnancy.

Limitation(s)

The size of the study population was small, which may have led to erroneous interpretations of the results. The study duration was limited, and being a hospital-based study, it may not represent the entire population of the region. Additionally, since the present study was conducted in a teaching institution and blood pressure measurements were taken by different doctors, there may have been inter-observer variations. Another significant limitation is that measuring serum triglycerides only once (in the early mid-trimester) may not capture dynamic lipid changes throughout pregnancy, potentially underestimating or overestimating the predictive value.

CONCLUSION(S)

Higher serum triglyceride levels were found to be associated with an increased incidence of preeclampsia. Therefore, serum triglyceride levels in early second trimester can be established as a predictor for the development of HDP. This allows for earlier management of HDP, which poses significant challenges to obstetricians.

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