

Association Of Raised Serum Triglycerides With Incidence Of Pre-Eclampsia

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Abstract

Background: Pre-eclampsia, a serious multi-systemic pregnancy complication is estimated to occur in 5-10% of pregnancies worldwide.

Objective: To determine the frequency of pre-eclampsia in pregnant females with hyper-triglyceridemia and to study its associations.

Methodology: This Cross-sectional study was conducted at Gynecology Dept. Poly Clinic Hospital, Islamabad (March - Sept. 2022). Pregnant females of age 15-40 years, gestational age 13-20th weeks and singleton pregnancy were included. Known hypertensives, receiving lipid-lowering or anti-hypertensives, chronic kidney or liver disease, teenage pregnancies, primigravida, history of CVA, IHD, epilepsy or endocrine disorders were excluded. After the detailed clinical evaluation, fasting serum triglyceride levels were checked. A total of 225 cases with elevated serum triglycerides were finally selected and evaluated for the presence of pre-eclampsia by monitoring the blood pressure, cardiovascular, gynaecological examination and urine for the presence of proteinuria. Patients were followed till the development of pre-eclampsia or completion of pregnancy. Results: Among 225 pregnant females with raised serum triglycerides, the mean age was 24.28±5.5 years. Pre-eclampsia was observed in 47(20.89%) of patients. The Chi-square tests of association between pre-eclampsia and each of parity, residential status, and socio-economic status were insignificant while BMI and Gestational age were significant. **Conclusion:** There is a high prevalence of pre-eclampsia in pregnant women with hypertriglyceridemia. Serum triglyceride levels may predict the women at risk for pre-eclampsia. The risk of preeclampsia in women with hyper-triglyceridemia is independent of parity, and socioeconomic or residential status. Hypertriglyceridemia may predispose to pre-eclampsia even at lower BMI levels. The development of hypertriglyceridemia in early gestation may be an additional risk factor. Early screening of women at risk may lead to better outcomes.

Keywords: Pre-eclampsia. Triglycerides. Hypertension. Proteinuria.

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1. Introduction

Pre-eclampsia is an idiopathic disorder of pregnancy characterized by proteinuria and Hypertension. Recent estimates indicate that over 30,000 women die worldwide each year because of pre-eclampsia and its complications, with 98% of those occurring in developing countries. Globally pre-eclampsia has been estimated to cause between 10-25% of perinatal loss. In Pakistan, the prevalence of pre-eclampsia has been estimated at around 19%. Up to 5% of women develop pre-eclampsia in the first pregnancy and although the overwhelming majority of these have successful pregnancy outcomes, still it has considerable adverse impacts on maternal, fetal, and neonatal health including cerebral haemorrhage, and renal and liver dysfunction. The exact mechanism of pre-eclampsia is not known but endothelial dysfunction in the placental vasculature is considered

a widely accepted theory for the etiology and the pathogenesis of the disease. Several other factors including genetic, immune, vascular and oxidative stress are also implicated in the pathogenesis of pre-eclampsia.

An abnormal lipid profile especially raised triglyceride is known to be strongly associated with atherosclerosis cardiovascular diseases and has a direct effect on endothelial dysfunction. There is growing evidence indicating that the risk of pre-eclampsia is increased in women with significantly elevated levels of triglyceride. Among pre-eclamptic patients, serum triglyceride concentration increases much more notably, two or three times more and the triglycerides are likely to be accumulated in vessels like uterine spiral arteries and contribute to endothelial damage by generating small, dense low-density lipoprotein particles. This accumulation decreases the release of prostacyclin,

resulting in oxidative stress via endothelial dysfunction, a key mechanism in the proposed Pathos physiology of pre-eclampsia. Both increased hepatic triglyceride synthesis and decreased peripheral metabolism could contribute to exaggerated triglyceride rise in pre-eclampsia. , Ahmed et al assessed the maternal lipid profile as a risk factor for pre-eclampsia and they found that the mean serum level of TG in severe pre-eclamptic women was higher, i.e., 210.57 mg/dl compared to normotensive having 152.30 mg/dl). The rise in serum TG was significantly higher in pre-eclamptic patients. Recently, in another cross-sectional study, Xue R. et al, reported that 6.48% of patients with raised triglyceride develop preeclampsia. Based on the findings of different studies in cardiovascular research, it has been established that endothelial dysfunction is associated with raised serum triglycerides. Recent studies show that there exists a consistent positive association between elevated maternal triglycerides and the risk of pre-eclampsia. However, rare information on this important obstetric issue is available to our local population. So, the present study is planned to determine the impact of high triglyceride levels during pregnancy on the occurrence of pre-eclampsia in our local population. If our results found a respectable frequency of pre-eclampsia in women with elevated triglyceride, it would be routinely performed in future during early work up for pregnancy. It would help the clinician devise preventive strategies for these women at early stages that would eventually reduce the overall associated morbidity and mortality in our local pregnant women.

2. Materials & Methods

This Cross-sectional study was conducted at Gynecology Dept. Poly Clinic Hospital, Islamabad over 6 months duration (4th March – 3rd Sept. 2022) after ethical approval. The sample size of 146 cases was calculated by using the WHO sample size calculator taking a Confidence level of 95%, anticipated population proportion at 6.48% and precision at 4%. 225 cases meeting the inclusion-exclusion criteria were selected by non-probability consecutive sampling. Operational definitions: Preeclampsia is a disorder of widespread vascular endothelial malfunction and vasospasm that

occurs after 20 weeks' gestation, clinically defined by hypertension and proteinuria, with or without pathologic edema. Eclampsia, which is considered a complication of severe preeclampsia, is a new onset grand mal seizure activity and/or unexplained coma during pregnancy or postpartum in a woman with signs or symptoms of preeclampsia. Pregnant females who presented with raised serum triglycerides, age 15-40 years gestational age 13-20th weeks and singleton pregnancy were included. Patients who were known hypertensive before pregnancy, patients already receiving lipid-lowering medications or anti-hypertensives, known chronic kidney or liver disease, teenage pregnancies, primigravida, history of CVA, IHD, epilepsy or endocrine disorders were excluded. After the detailed history and examination, the fasting serum triglyceride levels were checked. A total of 225 cases were finally selected and evaluated for the presence of pre-eclampsia by monitoring the blood pressure and other vital signs, cardiovascular, and gynecological examination and urine for the presence of proteinuria/ Patients were followed till the development of pre-eclampsia or completion of pregnancy. The data was analyzed using SPSS Version 20.0. Mean and standard deviation were determined for the quantitative variables (i.e., age, gestational age, parity, BMI and triglyceride levels). Frequency and percentages were calculated for residential status, socio-economic class and pre-eclampsia. Effect modifiers such as age, parity, BMI, gestational age (at the time of enrolment for the study), residential status and socio-economic status were controlled by stratification for raised serum triglyceride. Post-stratification Chi-square tests of association were applied. Data is presented as tables and graphs. P-value <0.05 was taken as statistically significant.

3. Results

A total of 225 patients, the mean age was 24.28±5.5 years (15-40 years range). 146(4.9%) cases were 21-30 years, while 48(21.3%) were ≤ 20 years and 31 (13.8%) were more than ≥ 30 years. 82(36.44%) cases were primipara, while 143(63.56%) cases were multipara. Amongst the pregnant women that presented with raised triglyceride levels, during the follow-up pre-eclampsia was observed in 47(20.89%) patients while 178(79.11%) were free of pre-eclampsia (fig 1).

Pre-eclampsia was seen in 29.2% (age group < 20 years), 17.1% (age group 21-30 years), and 25.8% (age group >

30 years). Pre-eclampsia was not found to be significantly associated with age groups ($p=0.157$).

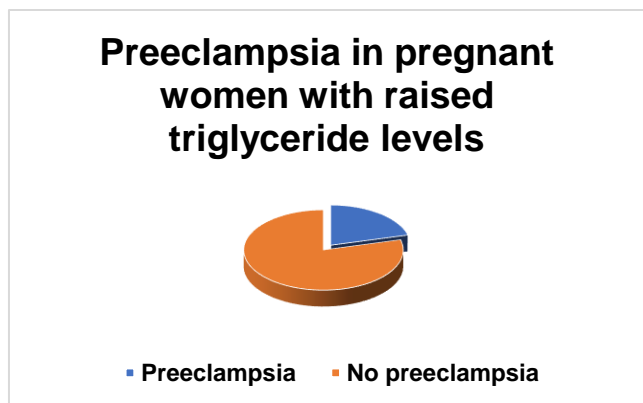


Figure-1 Pie chart presenting Preeclampsia in pregnant women with elevated serum triglyceride levels (n=225).

Concerning parity, preeclampsia was observed in 14(17%) primipara vs., 33(23%) multipara women ($p=0.286$). Concerning BMI, 23(29.9%) of BMI <25 Vs. 24(16.2%) of BMI > 26 developed pre-eclampsia ($p=0.017$).

The females with gestational age (GA) < 16 weeks had preeclampsia in 33(26%) while GA > 17 weeks had 14(14.3%) ($p=0.032$; table 1)

There were 23(22.3%) rural residents with preeclampsia Vs, 24(19.7%; $p=0.625$). Regarding the socio-economic class, lower socioeconomic class cases had preeclampsia in 10(23.8%), the middle class had 33(21%), while the upper class had 04(15.4%) preeclampsia cases ($p=0.706$; table 1).

5. Discussion

Pre-eclampsia is one of the leading causes of maternal morbidity and mortality in the world. In developing countries, women are at 14 times higher risk of dying from obstetric complications compared to developed countries. Pregnancy complications caused around 289,000 deaths of women worldwide in 2013 and 99% of them were from developing countries. Globally, about 50,000 mothers die only from pre-eclampsia. As estimated by WHO, the occurrence of pre-eclampsia is seven times higher in developing countries compared to developed countries. The prevalence of pre-eclampsia ranges between 1.8 and 16.7% in developing countries.

Pre-eclampsia with a frequency of 3.7% is a pregnancy-related disorder constituting one of the leading causes of fatal and maternal morbidity and

mortality world wide. Hypertension is considered among the category of common medical disorders in Pregnancy. PIH constitutes many hypertensive disorders which are initiated after the gravid state of 20 weeks in pregnancy. Gestational hypertension including pre-eclampsia and pre-eclampsia comprises 70% of total cases; while chronic hypertension constitutes 30% of total hypertension abnormalities in pregnancy.

Table 1: Presenting the preeclampsia concerning demographic variables, BMI and gestational age. (n=225)

Variables	Pre-Eclampsia N=47	No-Preeclampsia N=178	P-Value
PARITY			
Primipara	14(17.1%)	68(82.9%)	0.286
Multipara	33(23.1%)	110(76.9%)	
BMI			
≤25	23(29.9%)	54(70.1%)	0.017
>26	24(16.2%)	124(83.8%)	
RESIDENTIAL STATUS			
Rural	23(22.3%)	80(77.7%)	0.625
Urban	24(19.7%)	98(80.3%)	
SOCIOECONOMIC CLASS			
Lower	10(23.8%)	32(76.2%)	0.706
Middle	33(21%)	124(79%)	
Upper	04(15.4%)	22(84.6%)	
GESTATIONAL AGE			
≤16 weeks	33(26%)	94(74%)	0.032
>17weeks	14(14.3%)	84(85.7%)	

(Test of significance Chi-square test; significant $p<0.05$)

As for developed countries incidence of pre-eclampsia is reported to be 1 in every 2000 deliveries when a comparison is done to developing nations, where incidence is 1 in every 100 subjects to 1 in every 1700 subjects. Eclampsia and pre-eclampsia constitute almost >50,000 maternal mortalities globally. In the

pathogenesis of pre-pre-eclampsia, the initiating event has been postulated to be the reduced placental perfusion that leads to widespread dysfunction of the maternal vascular endothelium by mechanisms that are not well defined. Hence, the increased serum triglyceride levels lead to its increased endothelial accumulation, that results in endothelial dysfunction in pregnancy. Increased triglycerides in pre pre-eclampsia are likely to be deposited in uterine spiral arteries and contribute to the endothelial dysfunction, both directly and indirectly through generation of small, dense LDL.

The prevalence of pre-eclampsia in the present study is higher compared with the global average, which is around 20%. However, the prevalence ranges from 1.8 to 16.7% in developing countries, and thus our finding falls in the upper side of this range. A study conducted in our neighboring country India reported the prevalence of pre-eclampsia as about 28% with a variation in the prevalence across the states or regions, which is high to our results. A review covering larger data sets reported the prevalence of pre-eclampsia 0.2–6.7% in Asia, 0.5–2.3% in Africa, 2.8–5.2% in Europe, 2.8–9.2% in Oceania, 1.8–7.7% in South America and the Caribbean, and 2.6–4.0% in North America. Another review summarized the data for the Asian regions and reported the prevalence of pre-eclampsia 2.07% in China, 1.19% in Japan, 2.22% in Thailand and 0.59% in Nepal. In a review of 22 studies, Ray et al reported that women with elevated triglycerides had twice the risk of pre-eclampsia, and the four studies that adjusted for confounders (age, BMI and parity) indicated that the risk was four times higher, compared with women with normal triglycerides. It was also suggested that triglyceride assessment between 28 and 32 weeks could be predictive of preeclampsia. Several other investigators have reported that hypertriglyceridemia could be involved in the pathogenesis of hypertensive disorders during pregnancy. Meta-analysis of 15 studies were included to compare the serum triglyceride levels between pre-eclamptic and normotensive pregnant women. Thirteen of the included studies showed significantly higher serum triglyceride level in pre-eclamptic group as compared with normotensive pregnant women but two studies did not show significant association between serum triglyceride level and pre-eclampsia.

Although it is still unclear whether hypertriglyceridemia becomes a risk factor for pre-eclampsia or whether there is any causal association between them, high triglyceride levels seem to increase the risk of placental vascular disorders, which trigger endothelial dysfunction, atherosclerosis and thrombosis. The development of atherosclerosis in the placental spiral arteries of pre-eclamptic women indicates that elevated levels of triglycerides are involved in this disorder.

Current study may help us identify the cases at risk of pre-eclampsia. Along with the routine workup, triglyceride levels should be checked to identify the high-risk cases. The data of this study may be beneficial for comparison with international figures. Current study finds that raised triglycerides are associated with pre-eclampsia even in women who are non-obese and have normal BMI levels. Further studies are suggested at a larger scale and multiple centres to verify the results of this study.

5. Conclusion

Significant pre-eclampsia was found in patients with raised serum triglycerides levels in this study. Elevated serum triglycerides may be involved in endothelial damage leading to pre-pre-eclampsia. The risk of preeclampsia in women with hypertriglyceridemia is independent of parity, socioeconomic or residential status. Hypertriglyceridemia may predispose to pre-eclampsia even at lower BMI levels. Development of hypertriglyceridemia in early gestation may be additional risk factor. Therefore, these women should receive adequate counselling to urge them to adopt healthier habits and lifestyles and to seek periodic check-ups.

CONFLICTS OF INTEREST- None

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Contributions:

S.S - Conception of study

S.S, S.M - Experimentation/Study Conduction

S.M, Q.U.A - Analysis/Interpretation/Discussion

Q.U.A, N.F - Manuscript Writing

N.S, L.M - Critical Review

N.F, N.S, L.M - Facilitation and Material analysis

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