Maternal Plasma Lipid Concentration in Early Pregnancy and Risk of Preeclampsia

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ABSTRACT

Objective: To determine the relationship between maternal plasma lipid concentration in early pregnancy and risk of preeclampsia.
Study Design: Cross-sectional study.
Place and Duration of Study: Gynecology and Obstetrics Department Pak Emirates Military Hospital, Rawalpindi Pakistan, Jan 2019 to Jan 2020.
Methodology: A total of 500 pregnant women who came for routine antenatal checkup and underwent serum lipid profile testing at 13th week of pregnancy were included in our study. They were followed up till the end of pregnancy for any signs and symptoms of pre-eclampsia. Age and lipid profile parameters were correlated with the presence of preeclampsia in the study participants.
Results: Out of 500 pregnant women studied, 443(88.6%) had no preeclampsia during the course of pregnancy while 53(11.4%) had preeclampsia. Mean age of participants was 33.72±6.731 years. With binary logistic regression analysis, it was found that raised levels of total cholesterol, triglycerides and low density lipoprotein cholesterol at 13 weeks of pregnancy had statistically significant relationship with presence of preeclampsia later among the target population.
Conclusion: Deranged lipid profile emerged as strong predictor of preeclampsia in our target population. Raised total cholesterol level, triglyceride levels and low density lipoprotein levels were significantly more in patients who developed preeclampsia as compared to those who did not develop this condition.

Keywords: Lipid profile, Preeclampsia, Pregnancy.

INTRODUCTION

Pregnancy, though a physiological condition but still lead to multiple changes in various parameters of the human body predisposing it to all of pathological conditions during this time.[1] Women undergo a lot of metabolic and endocrine variations at different stages of pregnancy.[2] Glycemic, lipid and electrolyte abnormalities may occur at any point during the course of pregnancy and if not addressed in time may lead to long term untoward consequences both for the mother and baby.[3]

Blood sugars and lipid metabolism has been one of the most important physiological function of human body. Any alteration or problem in this metabolic pathway may lead to undesirable consequences. Pregnancy may affect the lipid metabolism in one way or the other. Number of conditions related to lipid metabolism and fat accumulation in various organs of the body have been reported during the pregnancy. [4,5]

Various studies done in the past have shown some correlation of abnormal lipid profile in early pregnancy with preeclampsia and adverse maternal and fetal outcomes. Enquobahrie *et al*. conducted a study in 2004 with the objective to study the impact of lipid abnormalities in early phase of pregnancy and risk of preeclampsia later on. They came up with the findings that these two parameters have a significant association and early recognition of lipid abnormalities may help in prevention of preeclempsia.[6] Spracklen *et al*. in 2014 published a met analysis in this regard and concluded that all parameters of cholesterol other than HDL cholesterol if elevated in early part of pregnancy may precipitate preeclampsia later on and cause various complications.[7] Jin *et al*. in 2016 published a study with the objective to investigate the associationsbetween lipid abnormalities during the pregnancy and complications among the mothers and babies. They revealed that among Chinese population, high level of triglycerides during the early part of pregnancy may be related to number of serious maternal and fetal complications.[8] Alahakoon *et al*. in 2020 after a similar study concluded that pathophysiology of preeclampsia may be related to abnormal lipid metabolism and that may be cause of preeclampsia

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symptoms among patients with lipid abnormalities. The lipid abnormalities of mother and babies may not be left unaddressed because they may have consequences related to heart problems.[9]

Prevention has always been the best and cost-effective strategy. Identifying the risk factors and addressing them in time may save the individual from grave consequences. In obstetric settings it is usually two individuals which are directly affected, the mother and baby which make the situation more delicate for the treating physicians. Nazli *et al*. in 2013 published a similar study in Khyber Pakhtunkhwa Province of Pakistan and concluded that serum lipids were found significantly higher among the patient suffering from pre-eclampsia and eclampsia, thus early assessment may be helpful in prevention of complications in these patients.[10] This study was planned with the rationale to determine the relationship between maternal plasma lipid concentration in early pregnancy and risk of preeclampsia.

METHODOLOGY

The study was cross-sectinal study conducted in Gynecology and Obstetrics Department Pak Emirates Military Hospital, Rawalpindi Pakistan, from January 2019 to January 2020. Ethical approval was obtained from Internal Review Board of Pak Emirates Military Hospital (IREB Letter no: A/28/Dated 28 Dec 2018). Study was explained and informed consent was taken. WHO Sample Size Calculator was used for sample size calculation with population prevalence proportion increased plasma lipids in pregnancy as 10%.[11] Non probability consecutive sampling technique used to gather the sample.

Inclusion Criteria: All the pregnant women between 18 and 45 years of age reporting for routine antenatal checkup at 13th week of pregnancy ready for follow up visits till he end of pregnancy were included.

Exclusion Criteria: Diagnosed cases of hypertension, type-II diabetes mellitus, gestational diabetes mellitus, ischemic heart disease, morbid obesity or any metabolic or endocrine disorder, Patients with history of preeclampsia or eclampsia in previous pregnancies were also excluded from the study. Patients with past or current history of lipid lowering drugs or any medications interfering with the blood pressure or lipid metabolism were also excluded from the study. Patients who could not be followed up till the end of pregnancy were also not included in the final analysis.

Pregnant women meeting the inclusion/ exclusion criteria coming for routine antenatal checkup underwent blood sampling at 13th week of pregnancy. Intravenous blood samples were collected from the cirrhosis patients with the help of 5ml syringe. Serum was separated and stored at −40°C until analyzed for lipid profile and fatty acids by micro-lab 300 and gas chromatography (GC 8700, Perkin–Elmer Ltd). Lipid profile performed by kit method (Merck, Germany) included total cholesterol (TC), triacylglycerol (TAG), high density lipoprotein–cholesterol (HDL-C), low density lipoprotein–cholesterol (LDL-C), very low density lipoprotein–cholesterol (VLDL-C) and total lipids.

Hypercholesterolemia in our analysis was defined as: TC >200 mg/dl and/or HDL-cholesterol >40 mg/dl and/or LDL-cholesterol >130 mg/dl and for hypertriglyceridemia value of TG >150 mg/dl.[12]

Patients were followed up till the end of pregnancy and looked for signs and symptoms of preeclampsia with relevant clinical and laboratory investigations.[13]

All statistical analysis was performed by using the Statistics Package for Social Sciences version 24.0 (SPSS-24.0). Mean and standard deviation for the age of study participants was calculated. Frequency and percentages for patients developing preeclampsia and patients with abnormal lipid profile were calculated. Chi-square was applied to look for any association between the variables and binary logistic regression analysis was applied to look for the extent of association of lipid profile parameters with preeclampsia. The *p*-value of less than or equal to 0.05 were considered as significant.

RESULTS

Target population was all pregnant women who underwent lipid profile assessment at 13th week of pregnancy and agreed to follow up till the end of pregnancy but with the application of inclusion and exclusion criteria and consent of the individuals 500 women were finally recruited in the study which were followed up and analyzed. Out of 500 pregnant women studied, 443(88.6%) had no preeclampsia during the course of pregnancy while 53(11.4%) had preeclampsia. Mean age of participants was 33.72±6.731 years. Table shows that raised total cholesterol, triglyceride and LDL cholesterol levels had statistically significant relationship with preeclampsia (*p*-value<0.05). With binary logistic regression analysis, it was found that these parameters of raised levels of total cholesterol, triglycerides and LDL cholesterol at 13 weeks of pregnancy had

statistically significant relationship with presence of preeclampsia later among the target population while age and HDL levels had no such association.

Table: Outcome of Various Variables Studied in the Analysis (n=500)

Variables	No preeclampsia	Preeclampsia	*p*-value
Age			
<35 years	210(47.4%)	25(43.8%)	0.613
>35 years	233(52.6%)	32(56.2%)	
Total cholesterol			
Normal level	340(76.7%)	34(59.6%)	0.007
>200mg/dl	103(23.3%)	23(40.4%)	
LDL cholesterol			
Normal level	259(58.4%)	23(40.3%)	0.010
>130mg/dl	184(41.6%)	34(59.7%)	
Triglyceride levels			
Within limit	302(68.2%)	25(43.8%)	<0.001
>150mg/dl	141(31.8%)	32(56.2%)	
HDL levels			
Within limit	277(62.5%)	42(73.7%)	0.092
Deranged	166(37.5%)	15(26.3%)	

DISCUSSION

Preeclampsia has not been an uncommon condition associated with pregnancy in all parts of the world. Multiple risk factors have already been identified which predispose a woman to develop this clinical condition during pregnancy.[14] Aziz *et al*. published a similar study in 2007 in Pakistan journal of medical sciences with the objective to evaluate the role of lipid profile alteration in thedevelopment of Pre-eclampsia. They studied only 32 cases and came up with the findings that the serum triglyceride concentrations increased significantly (232.18±106.41 vs. 113.12±21.3, *p*<0.01) while Serum HDL-cholesterol concentrations decreased significantly

(39.75±11.99 vs. 51.18±06.09, *p*<0.01) in pre-eclamptic group as compared to normal pregnant women.[15] Due to this significant association in or population we planned this study on a larger scale with more sample size to ascertain the relationship between maternal plasma lipid concentration in early pregnancy and risk of preeclampsia among pregnant women managed at our tertiary care teaching obstetric facility.

Gohil *et al*. in their study published in 2011 with the objective to evaluate lipid profiles in subjects with preeclampsia and to determine if there is any change in lipid profiles in subject of preeclampsia as compared to normal antenatal females, non-pregnant females and post-partum females. They concluded that dyslipidemia in the form of significantly decreased HDL concentration and significantly increased total cholesterol, LDL, VLDL & Triglycerides concentration is conspicuously evident in subjects of preeclampsia as compared to non-pregnant, normotensive pregnant and postpartum subjects.[16] Our results were abit different, total cholesterol, triglyceride and LD cholesterol levels emerged as a strong factors to predict the problemist but HDL levels had no significant relationship with presence of preeclempsia in our study.

Pusukuru *et al*. in 2016 performed a study with the objective to study the levels all the lipid profile parameters among pregnant ladies in last two trimesters. They concluded that total mean cholesterol levels, triglyceride levels, HDL cholesterol levels, VLDL cholesterol levels and LDL cholesterol levels get altered in second and third trimester and more in third trimester.[17] These results form the basis for our results as a huge percentage of our participants also had deranged lipid profile and if this has clear association with preeclampsia or other complications then this evil needs to be nipped in the bud by managing the lipids as early as possible.

Enaruna *et al*. in 2014 performed an interesting study and looked for the derangement in lipid profile and uric acid levels among the pregnant women suffering from preeclampsia. They came up with the findings that women with severe preeclampsia have higher uric acid levels as compared to women without preeclampsia stating that uric acid levels may get raised as cause or effect of preeclampsia. All the lipid profile parameters were also statistically significantly elevated among the patients with preeclampsia as compared to those without any signs or symptoms of preeclampsia.[18] We designed our study with a narrow cope and only studied the relationship of various lipid profile parameters with presence of eclampsia which turned out to be significant.

Study design posed a major limitation to this study. Follow up was very difficult and a lot of patients lost to follow up till the end of pregnancy. Patients developing preeclampsia may over represent as asymptomatic and healthy patients would be making most part of the patients who were lost of follow-up. Confounding factors which were not catered for in the study design may also hinder in generalization of results and concluding that abnormal lipid profile may be cause or risk factor for preeclampsia.

CONCLUSION

Deranged lipid profile emerged as strong predictor of preeclampsia in our target population. Raised total cholesterol level, triglyceride levels and LDL levels were significantly more in patients who developed preeclampsia as compared to those who did not develop this condition.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

FG & HS: Concept, Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

MAS & AMA: Data acquisition, data analysis, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Kepley JM, Mohiuddin SS. Physiology, Maternal Changes. [Updated 2019 Apr 24]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020.
2. Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. Cardiovasc J Afr 2016; 27(2): 89–94.
   https://doi.org/10.5830/CVJA-2016-021
3. Catalano PM, Thomas AJ, Huston LP, Fung CM. Effect of maternal metabolism on fetal growth and body composition. Diabetes Care 1998; 21 (Suppl 2): B85-90.
4. Grimes SB, Wild R. Effect of Pregnancy on Lipid Metabolism and Lipoprotein Levels. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext. South Dartmouth (MA): MDText.com, Inc.; 2000.
5. Wang J, Li Z, Lin L. Maternal lipid profiles in women with and without gestational diabetes mellitus. Medicine 2019; 98(16): e15320.
   https://doi.org/10.1097/MD.0000000000015320
6. Enquobahrie DA, Williams MA, Butler CL, Frederick IO, Miller RS, Luthy DA. Maternal plasma lipid concentrations in early pregnancy and risk of preeclampsia. Am J Hypertens 2004; 17(7): 574-581.
7. Spracklen CN, Smith CJ, Saftlas AF, Robinson JG, Ryckman KK. Maternal hyperlipidemia and the risk of preeclampsia: a meta-analysis. Am J Epidemiol 2014; 180(4): 346–358.
   https://doi.org/10.1093/aje/kwu145
8. Jin W, Lin S, Hou R, Chen XY, Han T, Jin Y et al. Associations between maternal lipid profile and pregnancy complications and perinatal outcomes: a population-based study from China. BMC Pregnancy Childbirth 2016; 16(60): 60-69.
9. Alahakoon TI, Medbury HJ, Williams H, Lee VW. Lipid profiling in maternal and fetal circulations in preeclampsia and fetal growth restriction-a prospective case control observational study. BMC Pregnancy Childbirth 2020; 20(61): 70-78.
10. Nazli R, Khan MA, Akhtar T,Lutfullah G, Mohammad NS, Ahmad J et al. Abnormal Lipid levels as a risk factor of eclampsia, study conducted in tertiary care Hospitals of Khyber Pakhtunkhwa Province - Pakistan. Pak J Med Sci 2013; 29(6): 1410–1414. https://doi.org/10.12669/pjms.296.3863
11. Ghodke B, Pusukuru R, Mehta V. Association of Lipid Profile in Pregnancy with Preeclampsia, Gestational Diabetes Mellitus, and Preterm Delivery. Cureus 2017; 9(7): e1420.
    https://doi.org/10.7759/cureus.1420
12. Artha IMJR, Bhargah A, Dharmawan NK, Pande UW, Triyana KA, MahariskiPA et al. High level of individual lipid profile and lipid ratio as a predictive marker of poor glycemic control in type-2 diabetes mellitus. Vasc Health Risk Manag 2019; 15(3): 149–157.
    https://doi.org/10.2147/VHRM.S209830
13. Duhig K, Vandermolen B, Shennan A. Recent advances in the diagnosis and management of pre-eclampsia. F1000Res 2018; 7(1): 242.
    https://doi.org/10.12688/f1000research.12249.1
14. Mayrink J, Souza RT, Feitosa FE,Filho EAR, Leite EF, Vettorazzi J et al. Incidence and risk factors for Preeclampsia in a cohort of healthy nulliparous pregnant women: a nested case-control study. Sci Rep 2019; 9(1): 9517.
    https://doi.org/10.1038/s41598-019-46011-3
15. Aziz R, Mahboob T. Pre-eclampsia and lipid profile. Pak J Med Sci 2007; 23(5): 751-754.
16. Gohil JT, Patel PK, Gupta P. Estimation of lipid profile in subjects of preeclampsia. J ObstetGynaecol India 2011; 61(4): 399–403.
    https://doi.org/10.1007/s13224-011-0057-0
17. Pusukuru R, Shenoi AS, Kyada PK, Ghodke P, Mehta V, Bhuta K et al. Evaluation of Lipid Profile in Second and Third Trimester of Pregnancy. J ClinDiagn Res 2016; 10(3): QC12–QC16.
    https://doi.org/10.7860/JCDR/2016/17598.7436
18. Enaruna NO, Idemudia JO, Aikoriogie PI. Serum lipid profile and uric acid levels in preeclampsia in University of Benin Teaching Hospital. Niger Med J 2014; 55(5): 423–427.
    https://doi.org/10.4103/0300-1652.140387

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