Original Article

Association of Liver Enzymes in the preeclampsia Patients Presenting In A Tertiary Care Hospital: Case Control Study

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Objective: To assess the association of preeclampsia with deranged liver enzymes of patients presenting in a tertiary care hospital.

Methods: It was case a control study including 100 females who fulfilled the inclusion criteria. They were enrolled in the study from OPD of Department of Obstetrics and Gynecology, Ghurki Trust Teaching Hospital, Lahore. Informed consent was obtained. Then two groups were formed i.e. cases with preeclampsia and controls without preeclampsia. Then blood sample was obtained in 3cc BD syringe. All samples were sent to the laboratory of the hospital for assessment of ALT and AST. Data was entered and analyzed by SPSS version 21.0. Odds ratio was calculated to find association between preeclampsia and deranged ALT and AST.

Results: The mean age of the patients was 33.30 (±4.45) years in cases and 32.96 (±4.72) in the control group. Mean gestational age was 33.88 (±4.07) weeks while 33.6 (±4.29) weeks in the control group. It was observed that body mass index was 28.90 (±2.32) in cases and 31.45 (±3.76). Parity was also almost similar in the both groups. It was observed that among cases 14 (28%) of the participants had deranged. ALT and AST value while 3 (6%) in the control group which was significant with Odds ratio >1.

Conclusions: Significantly deranged liver enzymes were observed in the eclampsia patients. There is a need to conduct further study to know its relationship with disease.

Keywords: preeclampsia, hypertension, liver function test, deranged liver function.

Introduction

Hypertension is the most common medical disorder in pregnancy. Hypertensive disorders of pregnancy are responsible for significant maternal and perinatal morbidity and the third leading cause of pregnancy related deaths (14.4%), superseded only by haemorrhage and sepsis. Preeclampsia is a multisystem disorder, unique to pregnancy that is usually associated with raised blood pressure and proteinuria after 20 weeks of gestation.[1] Maternal mortality ratio in 2015 was 178 per 100,000 live births in Pakistan.[2] In Pakistan, pre-eclampsia /eclampsia deaths represent one-third of maternal deaths reported at the tertiary care hospital settings.[3] Gestational hypertension and preeclampsia /eclampsia are hypertensive disorders induced by pregnancy; both disorders resolve postpartum. Gestational hypertension is the most common cause of hypertension in pregnant women.[4] The syndrome of hemolysis, elevated liver enzymes and low platelets (HELLP) is a severe manifestation of preeclampsia and complicates approximately 0.5-0.9% of all pregnancies and 10%-20% of cases with severe preeclampsia.[5]Ten to 50 percent of women initially diagnosed with gestational hypertension go on to develop preeclampsia in one to five weeks. HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) probably represents a subtype of preeclampsia with severe features in which hemolysis, elevated liver enzymes, and thrombo- cytopenia are the predominant features, rather than hypertension or central nervous system or renal dysfunction, although the latter do occur.

The majority of patients, but not all, have hypertension (82 to 88 percent) and/or proteinuria (86 to 100 percent).[6] Several studies have suggested that liver involvement in preeclampsia is serious and frequently accompanied by evidence of other organ system involvement, especially the kidney and brain along with hemolysis and thrombocytopenia.[7] The diagnostic work-up of abnormal liver function tests (LFTs) in pregnancy is challenging, as the condition peculiar to pregnancy have to be considered in addition to the causes affecting the non-pregnant population. The spectrum of disease is varied and the abnormal LFT can be mild with no long-term consequences, or it can be severe, leading to both maternal and fetal mortality.[6,7] AST is found in liver, cardiac muscles, brain, skeletal muscles, erythrocytes and kidney. ALT is found predominantly in liver. Therefore, increases in ALT are more specific than AST for hepatobiliary disease. In the hepatocytes, AST is cytoplasmic while ALT is intra-mitochodrial. A typical hepatitis picture therefore comprises ALT rise, accompanied by lesser elevation in AST. Here is

no agreement on the effect of pregnancy on serum AST and ALT. In a few studies, AST and/ or ALT levels slightly increase in the third trimester. However, in most studies, AST and ALT levels remain within the normal range for non-pregnant state.[8] As such, gastroenterologists and obstetricians are often faced with the dilemma of whether the abnormal LFT are related to pregnancy and whether immediate obstetric intervention in necessary.[9] In routine, LFTs are not evaluated in early stage, till the female is symptomatic. This may be due to lack of local evidence. So we conducted this study to find the association and prevent the life threatening consequences of liver dysfunction and preeclampsia.

Methods

This was a Case control study conducted in department of obstetrics and gynecology, Ghurki Trust Teaching Hospital Lahore from June 2019 to December 2019. 100 pregnant females were included; 50 females in each group. Non-probability, consecutive sampling technique was used. Inclusion criteria was decided preeclampsia females of age 18-40years, parity<5, presenting at gestational age>20 weeks (on LMP) presenting for antenatal check-up. While females with chronic hypertension, chronic, or gestational diabetes, anemia, eclampsia and abnormal LFT before pregnancy (on medical record), were excluded from study. Two groups were formed Group A cases (with preeclampsia) and Group B controls (without preeclampsia). Then blood samples were obtained by using 3cc BD syringe. All samples were sent to the laboratory of the hospital for assessments of ALT and AST. Females with abnormal results were managed as per hospital protocol. Data analysis: Data was entered and analyzed by SPSS version 21. Mean and SD ratio was calculated for quantitative variables like age, gestational age and BMI. Frequency and percentage was calculated for qualitative variables like abnormal ALT and AST. Parity will also be presented as frequency. Odds ratio was calculated to find association between preeclampsia and abnormal ALT and AST. OR>1 was taken as significant. Data was stratified for age, gestational age, parity and BMI. Post-stratification, adjusted OR was calculated with aOR>1 considered as significant.

Results

The mean age of the patients was 33.30±4.45 years in cases and 32.96±4.72 in the control group. Mean gestational age was found to be almost same in both group 33±4 weeks and body mass index was 28.90±2.32 in cases and 31.45±3.76 in control.

Table-1: Comparison of the Abnormal ALT and AST in the cases versus control

	Normal ALT & AST	
Group	Yes	No
Cases	14 (28.0%)	36 (72.0%)
Control	03 (6.0%)	47 (94.0%)

Odds Ratio=6.09

Table-2: Stratification of the abnormal ALT and AST in the cases versus control with respect to the age.

	Abnormal ALT & AST			Odds
Group of age	Yes	No	P-Value	Ration
18-30 Cases	5 (37.5%)	09 (64.3%)	0.20	3.0
Control	02 (12.5%)	41 (87.5%)		
>30 Cases	09 (25.0%)	27 (75.2%)	0.01	11.0
Control	01 (2.9%)	33 (97.1%)		

Table-3: Stratification of the Abnormal ALT and AST in the cases versus control with respect to the Parity.

			Abnormal ALT & AST				
Parity			Yes	No	Total	P-Value	Odds Ration
1.00	Group	Cases	02 (50.0%)	02 (50.0%)	04 (100.0%)	0.53	3.50
		Control	02 (22.2%)	07 (77.8%)	09 (87.5%)		
2.00	Group	Cases	04 (21.1%)	15 (78.9%)	19 (100.0%)	0.11	0.78
		Control	0 (.0%)	15 (100.0%)	15 (100.0%)		
3.00	Group	Cases	07 (35.0%)	13 (65.0%)	20 (100.0%)	0.20	5.38
		Control	01 (9.1%)	10 (90.9%)	11 (100.0%)		
4.00	Goup	Cases		09 (100.0%)	06 (100.0%)	-	-
		Control		10 (100.0%)	10 (100.0%)		
5.00	Goup	Cases	01 (100.0%)	0 (.0%)	01 (100.0%)	0.16	-
		Control	0 (.0%)	05 (100.0%)	05 (100.0%)		

It was observed that among cases 14(28%) and among control group3 (6%) had abnormal ALT and AST which was significant with Odds ratio of 6.09. Data was stratified for age, gestational age, body mass index and parity. Comparison of abnormal ALT and AST in both groups

Discussion

Pre-eclampsia occurs in 2%-8% of all pregnancies, with the incidence of severe pre-eclampsia being around 1%. In the U.K, an estimated incidence is 2.7 per 10,000 births(9, 10).The risk of pre-eclampsia is 4.1% in women in their first pregnancy and 1.7% in later pregnancies overall. However, this risk rises to 14.7% in the second pregnancy in women who had pre-eclampsia in their first pregnancy and 31.9% in women who had pre-eclampsia in their previous two pregnancies.[11]Pregnancy induces physiological, hormonal and physical changes. These changes may be responsible for the incidence of acute hepatic failure (AHF) in pregnancy both pre and post partum.[12,13] Acute fatty liver of pregnancy (AFLP), pre eclampsia and HELLP (haemolysis, elevated liver enzymes, and low blood platelet count) syndrome have been demonstrated as being the main causes of severe hepatic failure in pregnancy. They are thought to represent a spectrum of the same pathological process.[14,15] They are described as being specific to the trimester in which they appear, but this is not always the case.In a study, serum bilirubin and plasma levels of liver enzymes ALT, AST and ALK were measured. The mean BMI of the cases was 29.04±3.97 and that of controls was 26.54±3.11. The mean value of serum bilirubin in cases was 10.78±3.74 micromol/L and in controls it was 7.92±2.42 micromol/L (p< 0.001). The mean values of enzyme ALT in cases was 55.81±31.93 U/L while in the controls it was 15.22 ±3.30 U/L (p < 0.001). Mean serum AST in the cases was 41.34±10.76 U/L and in the controls it was 24±2.54 U/L (p<0.001). Mean ALK level of cases before delivery was 454.16±243.69 U/L, and in controls it was 181.34±66.76 U/L (p<0.001). Raised levels of serum bilirubin and liver enzymes ALT, AST and ALK were found in preeclampsia cases, Which was consistent with the findings of the current study. We also found a significant increase in Liver enzyme level in eclamptic females.[2,16] In another study, there was significant increase (p<0.001) in the levels of serum ALT and ALP in preeclampsia group compared to control and between high risk and PET group. Levels of AST also increased significantly (p<0.05) when preeclampsia group was compared with control and high risk group.[17] This study has limitations that it was a single centered study and the institute was a public institute. Majority of the patients were poor with bad hygienic conditions so similar studies are required in a controlled environment.

Conclusion

Conclusively, it is stated that there are high chances of raised liver enzymes levels in the patients presenting with preeclampsia. So it is needed to monitor the blood profile in such cases during and after pregnancy so that early on mortality or morbidity could be safeguarded.

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References

1. Anthony J, Damasceno A, Ojjii DJCjoA. Hypertensive disorders of pregnancy: what the physician needs to know. 2016;27(2):104.
2. World Health Organization: Trends in maternal mortality: 1990 to 2015 estimates by WHO, UNICEF, UNFPA, The World Bank and the United Nations Population Division. 2015. http://www.who.int/reproductivehealth/publications/monitoring/maternal-mortality-2015/en/. Accessed 17 Aug 2016.
3. Sheikh S, Qureshi RN, Khowaja AR, Salam R, Vidler M, Sawchuck D, et al. Health care provider knowledge and routine management of pre-eclampsia in Pakistan. 2016;13(2):104.
4. ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. Obstet Gynecol 2019; 133:e1.
5. Khowaja AR, Qureshi RN, Sheikh S, Zaidi S, Salam R, Sawchuck D, et al. Community's perceptions of pre-eclampsia and eclampsia in Sindh Pakistan: a qualitative study. 2016;13(1):36.
6. Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. Obstet Gynecol 2004; 103:981.
7. Salam RA, Das JK, Ali A, Bhaumik

S, Lassi ZSJJofm, care p. Diagnosis and management of preeclampsia in community settings in low and middle income countries. 2015;4(4):501.
8. Grant CJ, Wilkes EAJM. Liver disease in pregnancy. 2019.
9. Zhuang X, Cui A-M, Wang Q, Cheng X-Y, Shen Y, Cai W-H, et al. Liver dysfunction during pregnancy and its association with preterm birth in China: A prospective cohort study. 2017;26:152-6.
10. Mutua DN, Mwaniki Njagi EN, Orinda G (2018) Liver Function Tests in Normal Pregnant Women. J Liver 7: 228.
11. Hazari N, Hatolkar V, Munde SJIJoCM, Sciences A. Study of serum hepatic enzymes in preeclampsia. 2014;2(1):1-8.
12. Steegers EA, Von Dadelszen P, Duvekot JJ, Pijnenborg RJTL. Pre-eclampsia. 2010;376(9741):631-44.
13. Knight MJBAIJoO, Gynaecology. Eclampsia in the united kingdom 2005. 2007;114(9):1072-8.
14. Hernández-Díaz S, Toh S, Cnattingius SJB. Risk of pre-eclampsia in first and subsequent pregnancies: prospective cohort study. 2009;338:b2255.
15. Knight M, Nair M, Tuffnell D, Kenyon S, Shakespeare J, Brocklehurst P, et al. Saving lives, improving mothers' care. 2016.
16. Broekhuijsen K, van Baaren G, van Pampus M, Ganzevoort W, Sikkema J, Woiski M, et al. Immediate delivery versus expectant monitoring for hypertensive disorders of pregnancy between 34 and 37 weeks of gestation (HYPITAT-II): an open-label, randomised controlled trial. 2016;387:848.
17. White WM, Mielke MM, Araoz PA, Lahr BD, Bailey KR, Jayachandran M, et al. A history of preeclampsia is associated with a risk for coronary artery calcification 3 decades later. 2016;214(4):519. e1-. e8.
18. Salomon C, Guanzon D, Scholz-Romero K, Longo S, Correa P, Illanes SE, et al. Placental exosomes as early biomarker of preeclampsia: potential role of exosomal microRNAs across gestation. 2017;102(9):3182-94.
19. Girling J, Dow E, Smith JJBAIJoO, Gynaecology. Liver function tests in pre□ eclampsia: importance of comparison with a reference range derived for normal pregnancy. 1997;104(2):246-50.
20. Mei-Dan E, Wiznitzer A, Sergienko R, Hallak M, Sheiner EJTJoM-F, Medicine N. Prediction of preeclampsia: liver function tests during the first 20 gestational weeks. 2013;26(3):250-3.1.