

Prevalence of raised Alanine Amino transaminase (ALT) in pregnant mothers: A Cross-sectional Study

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Author's Contribution

¹ Conception of study

^{1,4} Experimentation/Study conduction

^{1,3} Analysis/Interpretation/Discussion

¹ Manuscript Writing

^{2,3} Critical Review

^{2,3} Facilitation and Material analysis

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Abstract

Objective: To determine the prevalence of raised ALT, common causes, and associated fetomaternal morbidity in pregnant mothers presenting, at cantonment general hospital Rawalpindi

Materials and Methods: This was a cross-sectional study conducted at cantonment general hospital Rawalpindi from July 2016 till June 2017.

Results: Out of 1924 women, 102 were identified with raised ALT making a prevalence of 5.3%. Sixty-one (59.8%) were booked. The hypertensive group which included severe preeclampsia, chronic hypertension with superimposed preeclampsia/eclampsia were 55 (53.9%), intrahepatic cholestasis of pregnancy(ICP) 32 (31.7%), acute viral hepatitis 9 (8.8%), Acute fatty liver of pregnancy(AFLP) 2 (1.96%), and unknown cause in 4 (3.92%). Mean ALT levels were 54.1 ± 6.94 , 71.28 ± 23.25 , 84.22 ± 27.82 , 231.5 ± 47.37 respectively. In four cases no definitive cause could be identified with the available tests were labeled as an unknown group, having a mean ALT level of 79.25 ± 10.07 . (**p=0.01**).

Term delivery occurred in 71 (69.6%), while 31 (30.39%) were preterm. There was one termination of pregnancy. Vaginal birth occurred in 42 (42.2%), and 53 (51.9%) underwent emergency cesarean. There was one peripartum hysterectomy. Meconium stain of liquor was 19 (18.6%). The birth weight of most babies 73 (71.5%) was between 2-3 kilograms only three were ≤ 1 kilograms.

Eight cases of postpartum hemorrhage, three maternal deaths, and six perinatal/early neonatal deaths were observed.

Conclusion: Raised ALT in pregnancy leads to increased fetomaternal complications. Severe preeclampsia and obstetric cholestasis were the commonest causes. Women of younger age groups were having acute viral hepatitis. Timely recognition and diagnosis are essential to institute appropriate management strategies.

Keywords: Liver dysfunction, pre-eclampsia, acute fatty liver of pregnancy, cholestasis of pregnancy.

Introduction

Liver function tests (LFTS) are measured clinically as a biomarker for liver health. Alanine amino transaminase (ALT) is a transaminase enzyme is found in plasma, various body tissues, and mostly the liver. Hepatic damage causes the release of these intracellular enzymes, leading to raised levels. Interpretation of abnormal liver function tests is crucial, considering the widespread maternal adaptive response to an ongoing pregnancy. According to study pregnancy, related liver dysfunctions are reported to affect 3% of pregnancies.¹ Gestational hypertensive disorders, acute fatty liver of pregnancy, intrahepatic cholestasis of pregnancy (ICP) are the major causes of liver derangements.²

Hypertensive disorders (Preeclampsia/eclampsia) are recognized causes of the maternal mortality rate of 15.5% according to a Turkish study.³ Increasing number of obstetric patients are admitted to intensive care units due to complications of preeclampsia.⁴ A multicentre trial in china showed 58.7% of obstetric patients in intensive care units had pregnancy-related hypertensive disorders.⁵

Our Pakistani study also reported the profound effect of preeclampsia on liver function tests when compared to normal pregnancies. The mean ALT was 55.81 ± 31.93 compared to control 15.22 ± 3.30 .⁶ HELLP syndrome (hemolysis, elevated liver enzymes, low platelet) is a serious condition with a high rate of maternal mortality. Disseminated intravascular coagulation (DIC), acute renal failure, and major postpartum hemorrhage (PPH) are the feared complications⁷

The incidence of ICP is also high compared to the other populations. According to our local study it affects around 3.1% of our obstetric patients.⁸ Patients with high ALT are at 3.54 fold increased risk of adverse perinatal outcome. Potential fetal risks include iatrogenic /spontaneous preterm birth, meconium, and fetal death.⁹ Ursodeoxycholic acid (UDCA) has been shown to improve pruritis and liver function tests^{10,11}. Early induction of labor after 37 weeks, can cause a major reduction in the stillbirth rate.¹²

Acute Viral infections such as hepatitis A, B, C, and E are unfortunately very prevalent in our country. According to our Pakistani study vertical transmission of Hepatitis B and C as the mode of exposure accounted for one-quarter of children under five years of age and the majority (72.5%) occurred in Punjab province.¹³ Another local study showed Hepatitis E (53.8%), Hepatitis B (17.3%), Hepatitis C in 7 (13.5%)

HELLP syndrome in (13.5%), and Acute fatty liver of pregnancy (AFLP) in (3.57%) cases. Maternal mortality of (28.8%) and fetal mortality (77%).¹⁴ In chronic liver disease, liver function tests may not worsen during pregnancy. However, in chronic hepatitis B, flares in ALT (99-2522U/L) were seen in 6% during pregnancy and 10% within three months after delivery.¹⁵ An Indian study showed the study frequency of chronic liver disease in pregnancy (0.4%), hepatic decompensation in 16%. A live birth rate of 76% was being better and complications such as variceal bleeding or decompensation of liver disease were less common than previously reported.¹⁶

Acute Fatty liver of pregnancy (AFLP) is a rare but life-threatening emergency, characterized by microvesicular fatty infiltration of the liver, attributed to defect in mitochondrial beta-oxidation of fatty acids.¹⁷ Raised bilirubin, transaminase, and coagulopathy occurring in 100%, hypoglycemia in 53%.¹⁸

Liver dysfunction in pregnancy with markedly raised transaminase can lead to a severe adverse fetomaternal outcome. Early diagnosis and prompt management can markedly improve fetomaternal morbidity and mortality.

Materials and Methods

This cross-sectional study was conducted at Cantonment general hospital Rawalpindi from July 2016 till February 2017.

We recruited our pregnant patients whose ages ranged from 17-36 years, parity from 0-5, no history of prior cesarean delivery, with raised ALT using a cut-off value of 45 IU/L. Only those cases that had persistently raised levels at least on two or more occasions on serial monitoring were included.

Cases of chronic liver disease and chronic hepatitis, alcoholism, drug-induced hepatic dysfunction, hyperemesis gravidarum, and autoimmune causes were not included.

The decision for induction, delivery, termination, etc was purely based on standard obstetric indications, and no upper limit of ALT was defined for any intervention.

Each case was analyzed in detail, regarding maternal demographic characteristics (age, parity, booking status), the mean level of ALT, gestational age at initial diagnosis, the possible cause of derangement in ALT, mode and time of delivery, the incidence of meconium staining of liquor, birth weight, maternal morbidity mortality, perinatal /early neonatal deaths.

The collected data was analyzed using Statistical Package for Social Sciences version 20. One way Anova, with a Post hoc test (welch's test) was applied to see the statistical significance in ALT levels among various groups.

Results

Out of 1924 women delivered during the study period, we found 102 were having raised ALT levels making a prevalence of 5.3%. Their ages ranged from 17-36 years, and parity from 0-5. We found that younger women and low parity were at risk as 92 (90.1%) women below 31 years of age, and 86 (84.3%) women had parity between 0-3.

Gestational hypertensive disorders affected 55 (53.9%), mean ALT was 54.10 ± 6.94 , presented at a mean gestational age of 35.5 weeks, and delivered at a mean gestational age of 36.8 weeks. Headache was the predominant symptom, uncontrolled blood pressure, vertigo, and visual symptoms. There were two cases of seizures. This group had the highest emergency cesarean section rate. Out of 53 emergency cesarean sections, 28 (52.8% of total emergency cesarean sections) were performed in this group, out of which 9 were preterm. Two of maternal deaths and three fetal/early neonatal deaths were observed in this group. One peripartum hysterectomy due to postpartum hemorrhage was performed in this group. ICP was found in 32 (31.7%), with a mean ALT level of 71.28 ± 23.25 . Pruritis was the chief complaint. One patient reported the recurrence of cholestasis in her all three pregnancies. One intrauterine fetal death was observed in this group. Em LSCS were 16, the main indications were failed induction, fetal distress, and meconium.

Acute viral hepatitis was seen in 9 (8.8%), five were having acute hepatitis B; three had hepatitis E, and one hepatitis A viral infection. THE mean ALT level being 84.22 ± 27.82 , women in this group were younger mean age 22.55 ± 3.04 , presented in early pregnancy mean gestational age at diagnosis was 29.08 weeks. Nausea and abdominal pain were the main complaints. One termination of pregnancy was done due to hepatitis E infection with the worsening of maternal symptoms and liver dysfunction. There were two emergency cesarean for fetomaternal indication.

We had only two cases of AFLP (1.96%), who presented at a mean gestational age of 35.7 weeks. Mean ALT was highest in this group 231.5 ± 47.37 . Unfortunately, two fetal deaths and one maternal death occurred in this group.

In four patients the cause of persistently raised ALT could not be explained with available investigations in our hospital and was labeled as the unknown cause group. However, no significant fetomaternal morbidity was seen except one case of the meconium stain of liquor and emergency cesarean.

There were 8 cases of postpartum hemorrhage, but 4 patients required extensive blood transfusion (>6 units) and blood products. Eighteen women were admitted to the intensive care unit (ICU) for monitoring and surveillance. Nine stayed for 7 days or more.

Meconium stain of liquor was seen in 19 (18.6%), out of which 9 (8.8%) were in ICP, 4 (3.92%) inactive viral hepatitis, 3 (2.9%) in hypertensive, 2 (1.96%) in AFLP 1 (0.98%) in an unknown group.

The birth weight of three babies was less than 1 kg, 73 were between 2-3 kg, 18 were between 3-3.5 kg, and 7 were above 3.5 kg. Twenty-three babies were retained in the Neonatal intensive care unit for observation, seventeen were admitted. However, only five remain stayed for 7 days or more.

Six perinatal/early neonatal deaths were reported, three in the hypertensive group, two in AFLP, and one in the ICP group.

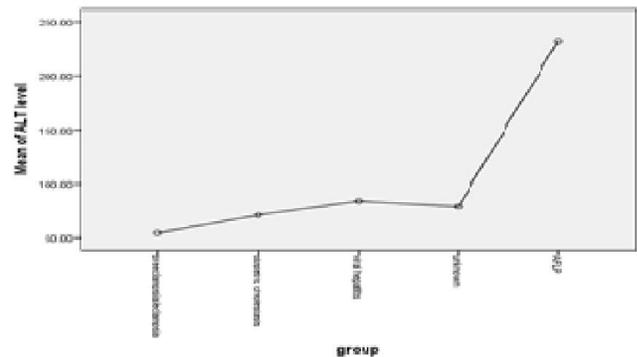


Figure 1: Mean ALT levels in various groups

Table 1: Gender and age distribution of subjects

Group	N=102	Mean ALT	Std deviation
Preeclampsia/eclampsia	55	54.10	6.94
ICP	32	71.28	23.37
Acute viral hepatitis	9	84.22	27.82
AFLP	2	231.50	47.37
Unknown cause	4	79.25	10.07

Outcome: Mean ALT Levels

P=0.01

Table 2: Mean, the standard deviation for age, parity, gestational age at diagnosis and delivery

Groups		Age in years	Parity	Gestation at diagnosis in weeks	Gestation at delivery in weeks
Preeclampsia/ eclampsia	Mean	23.60	1.78	35.52	36.83
	Std dev	4.23	1.34	1.49	0.79
ICP	Mean	25.19	2.19	32.47	36.98
	Std dev	3.31	1.36	1.77	0.62
Acute viral hepatitis	Mean	22.55	1.00	29.08	37.86
	Std dev	3.04	1.22	8.15	0.77
AFLP	Mean	28.50	3.00	35.70	35.70
	Std dev	4.24	1.41	0.56	0.63
Unknown cause	Mean	27.50	2.75	30.20	37.72
	Std dev	4.20	0.95	8.95	0.47

Table 3: Clinical presentation

Complain/symptom	Frequency	Percentage
Headache	27	26.5
visual/vertigo	12	11.8
uncontrolled B.P	10	9.8
Decreased fetal movements	12	11.8
Abdominal pain	9	8.8
nausea/vomiting	9	8.8
abnormal bleeding	6	5.9
Pruritis	15	14.7
Seizures	2	2.0

Table 4: Maternal morbidity and mortality

Group	Maternal morbidity	Maternal mortality
Preeclampsia/eclampsia	Em Lscs	29
	APH/PPH	4
	Hysterectomy	1
ICH	EmLscs	18
	APH/PPH	2
AFLP	EmLscs	2
	APH/PPH	2
Acute viral hepatitis	EmLscs	3
	TOP	Nil
Unknown cause	EmLscs	1

TOP= Termination of pregnancy

Table 5: Fetal morbidity and mortality

Group	Meconium stain	Fetal mortality
ICP	9 (8.8%)	1
Acute viral hepatitis	4 (3.92%)	Nil
Preeclampsia/eclampsia	3 (2.9%)	3
AFLP	2 (1.96%)	2
Unknown cause	1 (0.98%)	Nil

Discussion

Our study showed that ALT was raised in 5.3% (102/1924) women using a cut-off value of 45 IU/L. Raised levels of Aspartate aminotransaminase (AST) are modestly predictors of adverse maternal outcomes. A study conducted in Bangladesh Mondal BR, Ahmed S and et al showed mean levels of total bilirubin and ALT was found significantly high in both preeclampsia and eclampsia group as compared to controls.¹⁹ Kojic R and et al found absolute magnitude of AST, ALT, and Lactate dehydrogenase (LDH) as predictor of adverse maternal complications (AST: ROC AUC 0.73 [95% CI 0.67 to 0.97]; ALT: ROC AUC 0.73 [95% CI 0.67 to 0.79]; LDH: ROC AUC 0.74 [95% CI 0.68 to 0.81]).²⁰

Elad mei Dan et al found ALT level of 50 IU/L having a sensitivity of 3.3% (despite a specificity of 97%) in predicting severe preeclampsia.²¹ Turkmen GG et al have shown mean ALT, AST, and bile acids are significantly raised in the cholestasis group than the control.²² Our local study using ALT cut off level of 95IU/L level to predict adverse perinatal outcomes in intrahepatic cholestasis of pregnancy found a sensitivity of 76.47% and specificity of 78.8%.²³ Kondrackiene J, Zalinkevicius R et al showed using the

cut-off value for ALT (31 IU/L) results in an increase of sensitivity to 92.2% vs 90.1% in diagnosing ICP.²⁴ Early-onset ICP patients presented with more worsening symptoms, leading to more premature deliveries and fetal distress. However difference in mean ALT levels in early-onset cholestasis 159 ± 50 , and late-onset cholestasis 142 ± 52 U/L was not statistically significant ($p > 0.05$).²⁵

Our study had certain limitations. Our inferences depend on hospital record, their accuracy about diagnosis and management, and records on birth certificates and discharge forms. We tried our best to countercheck and recheck to minimize the bias. Secondly, the number of cases for some groups was very small e.g. AFLP. We used ANOVA with post hoc Welch's correction to find the p-value.

We could not address the impact of chronic liver disease on ALT during pregnancy. Most of our obstetric patients do not maintain their previous antenatal records, so we cannot compare from previous ALT levels. Secondly, although screening for viral hepatitis is performed in our hospitals but liver function tests such as bilirubin, ALT, AST, LDH are not done as a routine unless clinically indicated. So only acute cases with clinical features were recruited.

Cases of hyperemesis gravidarum, alcoholism, drug-induced abnormality in liver function tests, and autoimmune causes were also not included.

Conclusion

AFLP cases presented with the highest ALT levels. Severe pre-eclampsia/eclampsia affected the majority of our patients with high fetomaternal morbidity when compared to the cholestasis and viral hepatitis patients. While younger women were having viral hepatitis. Early diagnosis of the cause and prompt management can improve fetomaternal outcome.

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