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Abnormal Liver Function Test in Pregnant Females attending a Tertiary Care Hospital in Lahore

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ABSTRACT

Background: To avoid diagnostic blunder, abnormal liver function tests (LFTs) related to pregnancy must be carefully evaluated. The underlying condition may have a significant impact on the results for both the mother and the foetus. **Objective:** Examining the clinical traits, frequency, and potential causes of anomalies in liver function tests was the aim of the current study. **Study Design:** Cross-sectional study. **Settings:** Obstetrics and Gynecology Department, in collaboration of Department of Gastroenterology, Services hospital, Lahore Pakistan. **Duration:** Six months from July to December 2020. **Methods:** 85 pregnant females with abnormal liver function tests. Drug induced abnormal liver function tests and women with chronic liver disease were excluded. **Results:** Total 85 patients were included. The incidence of abnormal LFT was 0.98%. The mean age was 33.40 ± 12.3. Most of the females 46 (54.1%) were young with age less than 30 years. Oedema 21 (24.7%) was the most common presenting complain. Liver disorder in this study was found in 15 (17.64%) women which was not specific to pregnancy & consisted of infective hepatitis, sickle cell disease & malaria whereas 70 (82.3%) women had1pregnancy-specific liver dysfunction. Four cases of diffuse intravascular coagulopathy were complex, and two of them were treated by transfusing blood components; the other two succumbed to AFLP and placental abruption, respectively. There were a total of seven maternal fatalities in the study. The remaining two, one with hepatitis E and the other with HELLP syndrome, both passed away from multi-organ failure. There were 34 (38.8%) females with intrauterine death inclusive of three cases of 2nd trimester with early onset1pre-eclampsia. Number of preterm births was 8 that accounted for 9.41% of total 52 live births, 21 (24.7%) had intrauterine growth retardation and 23 (27%) were neonatal admissions. **Conclusion:** The most common reason for abnormal liver function tests during pregnancy, particularly in the third trimester, is pregnancy-specific diseases. The pre-eclampsia-related condition is the most prevalent of these diseases. If there is unawareness, abnormal LFT may go undetected, especially if jaundice is not the presenting symptom.

Keywords: *Abnormal liver function test, Preeclampsia, Fatty liver disease.*

INTRODUCTION

The liver is an important organ for maintaining the physiology of body & provides support for each organ. It must work properly during1pregnancy for a good fetal & maternal outcome. Liver should be normally functioning especially in pregnancy.[1] Hemodynamic, hormonal, & immunological changes that are specific to pregnancy may affect the progression of both acute and chronic liver disorders. Therefore, having a liver with abnormal functions may increase pregnancy complications and sometimes result in maternal death. Pregnancy-related abnormal liver function tests (LFTs) must be properly interpreted to prevent diagnostic pitfalls. An urgent diagnostic workup must be started because the underlying disease may have a major effect on both maternal and foetus outcomes. A symptomatic pregnant woman may have abnormal liver function tests,

while a life-threatening issues may be resulted by the fulminant type.[2,3]

The treating doctor may be confused by some of the physical changes in pregnant women, which are non-specific i.e. nausea, vomiting and abdominal pain. Alkaline phosphatase levels and clotting factor production both increase three to fourfold during pregnancy, while protein S, serum albumin and total proteins decrease. These variations in laboratory test findings reflect the physiological changes of pregnancy. The liver enzyme transaminase level, serum bilirubin level & prothrombin time have not changed significantly.[4] Pregnancy-related pathological liver dysfunction may or may not coexist with other conditions, and it can be divided into 3 groups.[4,5] The first group of pregnancy-specific liver issues includes acute fatty liver of pregnancy, pre-eclampsia, intrahepatic cholestasis, eclampsia, syndrome of hemolysis, elevated liver enzymes and low platelets (HELLP) & other liver issues. Most of these disorders are trimester1specific. The 2nd category consists of pregnancy-related incurrent liver diseases such viral hepatitis & herpes simplex.[6] Pregnancy with1pre-existing liver disease like Wilson's disease, chronic active hepatitis, cirrhosis of the liver, portal hypertension & hepatic tumor, is included in the third group.

The rationale of the study was to determine the frequency, clinical profile & possible causes of derangements of liver function test at1the tertiary care hospital and as well as to study the foeto-maternal outcome1in these women.

METHODS

This cross-sectional study was conducted in the Obstetrics and Gynecology Department, in collaboration of Department of Gastroenterology, Services hospital, Lahore. Sample size 85 was calculated with 80% power of test & 8% margin of error and percentage of abnormal liver function i.e. 83.25% in pregnancy. The study included all pregnant patients admitted to the obstetric unit of a hospital with abnormal liver dysfunction. Women with chronic liver disorders & those whose liver1function tests were abnormal due to the use of medicines were excluded. The symptoms of liver dysfunction like pruritus, yellowish coloring of urine, prolonged vomiting, decreased urine output, anorexia & upper abdominal distress were then1discussed after the demographic & obstetric data was collected. The usage of any drugs in the past, including paracetamol, anti-tubercular drugs, oral contraceptives, and sickle cell history, was noted. Given the poor liver function, history of blood transfusions, piercings, previous surgeries & hyperlipidemia was sought.

Every patient got thorough general and obstetric examination. LFT were requested in cases of pre-eclampsia & gestational hypertension or clinical signs & indicators of ICP, infectious hepatitis or other diseases. Additional definitive tests, such as platelet count, viral serological testing for hepatitis &s hemoglobin electrophoresis, were carried out as necessary to help identify the underlying cause. The diagnostic standards for the numerous underlying disorders were based on the following elements. HELLP disorder: high bilirubin level, low platelet count (<100,000/lL), increased AST (>70 IU/L), hemolysis. Partial increase in AST (>400IU/L), low platelet count (\150000/lL), whether or not hemolysis is present. Preeclampsia-related liver dysfunction: high transaminases or bilirubin when there is hypertension that is 140/90 mmHg or higher on two separate occasions that are more than six hours apart, and proteinuria after 20 weeks of pregnancy.

Data was entered and analyzed in SPSS 25 V. Age and LFT laboratory values were presented as Mean & SD. Diagnosis, Abnormal LFT values and fetal outcome were presented as frequency and Percentage.

RESULTS

Total 85 patients were enrolled. In our study, 85 women out of 8590 admissions had deranged liver enzymes, with an incidence of 0.98%. The mean age was 33.40 ± 12.3. Most of the females 46 (54.1%) were young with age less than 30 years. There were 44 (51.7%) low parity, 25 (29.4%) booked and 60 (70.5%) were un-booked. Majority of females were belonging to lower socioeconomic status. Majority of the women were in 3rd trimester of pregnancy (84.7%). Oedema 21 (24.7%) was the most common presenting complaint, followed by yellowish urine & visual symptoms, shown in Table 1.

Diagnosis found in first trimester of pregnancy, hepatitis 2 (2.35%), in second trimester, preeclampsia 4 (4.7%) & sickle cell disease 2 (2.3%) and Pre-eclampsia and HELLP syndrome was most common diagnosis in third trimester of pregnancy. In this study, 15 (17.64% %) women had liver disorder that were not specific to pregnancy & consisted of infective hepatitis, sickle cell disease & malaria whereas 70 (82.3%) women had pregnancy-specific liver dysfunction. Of these, 67 (87.5%) women with liver dysfunction had pre-eclampsia,12 with HELLP syndrome & 5 women with eclampsia. There were 49 women who had pre-eclampsia in the absence of eclampsia or HELLP syndrome (Table: 2)

According to LFT abnormalities, mostly females 55 (64.7%) had serum LDH value greater than 600. The majority 38(44.7%) females had AST elevation and 41 (48.23%) with ALT elevation between the 100-500 I.U range. The commonest value of bilirubin level was

between 1 and 2.5 mg/dL found in 39 (45.8%) cases. A range of 141 to 564 IU/L of alkaline phosphatase was observed in 71 (83.5%) females. (Table: 3)

Table 1: Demographic Characteristics

Age	<20	19 (22.3%)
	21-30	46 (54.1%)
	>30	20 (23.5%)
Parity	Primigravida	44 (51.7%)
	Primiparous	26 (30.5%)
	Parity 2 or above	15 (17.6%)
Socioeconomic Status	Low	15 (17.6%)
	Middle	59 (69.4%)
	High	11 (12.9%)
ANC	Booked	25 (29.4%)
	Un-booked	60 (70.5%)
Gestational Age	I	4 (4.7%)
	II	9 (10.5%)
	III	72 (84.7%)
Presenting Complain	Fever	5 (5.8%)
	Vomiting	10 (11.7%)
	Yellow Urine	13 (15.29%)
	Epigastric Pain	8 (9.41%)
	Headache	12 (15.29%)
	Oedema	21 (24.7%)
	Visual Symptoms	10 (11.7%)
	Miscellaneous	6 (7.05%)

Table: 2 Distribution of Diagnosis

	Diagnosis	Frequency (%)
1st	Hepatitis	2 (2.35%)
2nd	Pre-eclampsia	4 (4.7%)
	Sickle Cell Disease	2 (2.3%)
	Hepatitis	4 (4.7%)
3rd	Acute Fatty Liver	1 (1.17%)
	HEELLP Syndrome	11 (12.9%)
	Hepatitis	6 (7.0%)
	Intrahepatic cholestasis of pregnancy	1 (1.17%)
	Eclampsia	6 (7.05%)
	Pre-eclampsia	47 (55.2%)
	Malaria	1 (1.17%)
Causes specify to pregnancy		70 (82.3%)
Preeclampsia related disorder		67
Pre-eclampsia		49
HELLP syndrome		12
Eclampsia11		6
Others		
Acute fatty liver of pregnancy		2
Intrahepatic1cholestasis of pregnancy		1
Causes non-specify to pregnancy		15 (17.6%)
Hepatitis		11
HEV		5
HBV		1
HAV		4
Miscellaneous		4
Malaria		3
Sickling		1

Table 3: LFT values for pregnant patients with different disorders

	Serum Bilirubin		AST	ALT	Alkaline Phosphate	Serum LDH
	Total	Direct				
Pre-eclampsia	1.65	1.46	123.04	125.22	249.56	725.54
Eclampsia	1.78	1.44	120.71	107.65	231.8	644.1
HELLLP	3.99	3.82	175.1	166.1	307.3	990.1
Viral Hepatitis	12.3	9.5	741.39	813	663.2	163.2
ICP	3.9	3.42	100	113.9	1749	380.1
Miscellaneous	4.13	90.62	102.6	92.11	316	769
AFLP	6.12	7.1	672	777	500.1	901

There were 55 (64.7%) women who gave birth vaginally, and 31 (36.4%) experienced spontaneous onset. A total of 24 (28.2%) women received labour induction because of obstetric indications, while 10 (11.7%) of this group underwent caesarean birth due to diverse obstetric indications, requiring an emergency delivery because of worse foetomaternal state in severe pre-eclampsia. (Table: 4)

Table 4: Frequency of Female according to Range of Abnormal LFT

Alkaline Phosphate (IU/L)	
42-141	14 (16.4%)
141-564	71 (83.5%)
564-1000	0
>1000	0
SLDH	
<230	3 (3.52%)
230-460	13 (15.29%)
461-600	14 (16.4%)
>600	55 (64.7%)
AST	
<100	37 (43.5%)
100-500	38 (44.7%)
500-1000	6 (7.05%)
>1000	4 (4.70%)
ALT	
<100	35 (41.1%)
100-500	41 (48.23%)
500-1000	9 (10.5%)
>1000	
Total Bilirubin	
<1	16 (18.8%)
1-2.5	39 (45.8%)
2.6-5	13 (15.29%)
5.1-10	8 (9.4%)
>10	9 (10.5%)

Overall, 32 (37.6%) women suffered from1adverse outcome. Four cases of diffuse intravascular coagulopathy were complex, and two of them were treated by transfusing blood components; the other two

succumbed to AFLP and placental abruption, respectively. (Table: 5)

In addition to these two, there were a total of seven maternal fatalities in the study. The remaining two, one with hepatitis E and the other with HELLP syndrome, both passed away from multi-organ failure. The maternal1morbidity was observed in 25 (29.4%) women. The common complication was postpartum hemorrhage, which was treatable with medical procedures. (Table: 5)

Table 5: Maternal Outcome Distribution

	Maternal Outcome (Mode of Delivery)				Outcome	
	Abortion 4 (4.70%)	**Vaginal 55 (64.7%)**		**LSCS 24 (28.2%)**	**Mortality 7 (8.2%)**	**Morbidity 25 (29.4%)**
		Spontaneous (31)	Induced (24)			
Preeclampsia (49)	4 (4.7%)	18	17	10 (11.7%)	-	8 PPH=3, ARF=1, Ascites=4
Eclampsia (6)	-	2 (2.3%)	1 (1.17%)	3 (3.%)	-	5 Ascites=1, ARF=2, Pulmonary Oedema=2
HELLP (12)	-	2 (2.3%)	2 (2.3%)	8 (9.4%)	4 (4.7%)	8 PPH=3, ARF=2, APH=1, DIC=2
Viral Hepatitis (12)	-	6 (7.0%)	3 (3.5%)	2 (2.3%)	2 (2.3%)	3 PPH=2, Ascites=1
ICP (1)	-	-	1 (1.17%)	-	-	1 Sickle Disease=1
Malaria (3)	-	3	-	-	-	-
Sickle Cell (1)	-	-	-	1	1	-

There were 34 (38.8%) females who had intrauterine fetal demise including three cases of 2nd trimester with early onset of pre-eclampsia. Out of 52 live births, 8 (9.41%) preterm, 21 (24.7%) intrauterine growth retardation and 23 (27%) were neonatal admission. Table: 6

Table 6: Distribution of participants as per foetal outcomes

Foetal Outcome	Frequency (%)
Intrauterine Foetal Death	34 (38.8%)
Fresh	7 (8.2%)
Macerated	27 (31.7%)
Live Birth	52 (61.1%)
Preterm	8 (9.41%)
Intrauterine Growth Retardation	21 (24.7%)
Neonatal Admission	23 (27.0%)

DISCUSSION

Liver illness in pregnancy is understudied and presents a challenge to the gynecologist and hepatologist in consultation. Over 3% of pregnancies are affected by some forms of liver disease, and serious pregnancy-related liver issues can be fatal for both the mother and the foetus. Rapid diagnosis is necessary in serious cases since the decision to deliver the baby right away will determine the outcome for both the mother and the foetus. Options for diagnosis and treatment must consider the possible consequences for both the mother and the kid.[7-9]

The LFT abnormalities in pregnancy are more common in younger age groups. Most of the women in our study had poor socioeconomic status, had not booked1antenatal care, and were typically only admitted to the hospital in cases of emergency. Similar data is seen in other studies as well.[10-13] The third trimester was the common gestational time for abnormal liver function tests, and pregnancy-related factors were most commonly to cause, particularly the condition known as pre-eclampsia. This explains why oedema remains a significant clinical feature of pre-eclampsia despite the fact that it is no longer a diagnostic criterion and is instead the most common presenting symptom.

In our study, only 1.0(1.25%) woman had intrahepatic1cholestasis of pregnancy. ICP can occur in between 0.1 and 1.5% of pregnancies.[13] When our case was examined in the laboratory, her alkaline phosphatase & serum bilirubin level both were significantly increased at 38 weeks of gestation. Many pregnant women with impaired liver function don't experience symptoms, and early diagnosis and appropriate care in these cases only occur about when the clinician is aware of the possibility of a liver problem.

The most frequently used indicators of hepatocyte damage are ALT and AST. The liver and numerous other tissues contain AST, which is found in both cytosolic & mitochondrial isoenzymes forms. For the liver, it is less sensitive and focused. The liver contains the largest quantities of ALT, a cytosolic enzyme that is specify to the liver.[14] Level of AST & ALT are related to a number of liver disorders. ALT levels may increase to numerous

thousand units per liter in those with acute viral hepatitis. As a sign of hepatocyte damage, lactate1dehydrogenase (LDH) is less sensitive than AST & ALT. However, it significantly increases following an ischemic liver injury.[13]

A poor prognosis for both the mother and the foetus is related to HELLP syndrome. These patients are more at risk of problems like acute kidney failure, liver damage, and disseminated intravascular coagulation. Along with all of these complications, we also had a significant frequency of ascites, which was a factor in eight out of 25 (29.4%) of the severe morbidities. Additionally, all eight had general oedema. Ascites may form in these women due to water retention and an increase in renin-angiotensin-aldosterone system activity.[7] The increased spectrum of the same disease process is called AFLP.[15] The death rates in the other studies were high, ranging1from 31 to 100%.[16,17] There was only one woman with AFLP who passed away from multi-organ failure in our study. Also, hepatitis E is reported to have1highest mortality rate during pregnancy.[18-20]

Poorer prognosis for the foetus was also associated with pre-eclampsia-related obstetric problems; the perinatal mortality rate reported ranges from 24.6 to 62.0%.[21] In this study, in 34 cases (38.8%), the foetus died intrauterine, among those who were born alive, preterm were 8 (9.4%) and intrauterine growth retardation was found in 21(24.7%). This may be due to the fact that the most of the cases had obstetric problems connected to preeclampsia, which in and of itself may result in these unfavorable outcomes & that the women exhibiting abnormal LFT represent severe variants of the disease spectrum.

The lack of facilities, ignorance of pregnancy-specific conditions that may worsen the outcome of pregnancy, especially when there is poor nutrition and abnormal1liver function and higher frequency of anemia, The factors that seem to be accountable for higher incidence of maternal & foetal morbidity or fatality include the delay in obtaining medical advice and in referral to the tertiary care hospital. When these women are taken to the referral hospital, many of them are already dead, and they frequently do not response to treatment.

CONCLUSION

Pregnancy-specific disorders are the leading cause of abnormal liver function test during pregnancy especially in the third trimester. The pre-eclampsia-related condition is the most prevalent of these diseases. Due to unawareness, abnormal LFT may go undetected, especially if jaundice is not the presenting symptom. Gestational age may define initial stage especially in the absence of significant clinical symptoms. This stage appears to be the best indicator to confirm the diagnosis, followed by the relative values of liver function tests in different pregnancy-specific & nonspecific diseases.

LIMITATIONS

This study is conducted in only one tertiary care hospitals of Lahore, Punjab.

SUGGESTIONS / RECOMMENDATIONS

The inclusion of other Tertiary care Hospitals all over the Pakistan can be involved to get larger sample. This can help in developing national Guidelines.

CONFLICT OF INTEREST / DISCLOSURE

No conflict of interest

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