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Original Research Article

Role of liver function tests among pregnant women with respect to feto-maternal outcome in third trimester: an analytical cross-sectional study

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ABSTRACT

Background: Liver disease occurs in approximately 3% of pregnant women so it has adverse effect on feto-maternal outcome. Diseases specifically related to pregnancy are intra-hepatic cholestasis of pregnancy, acute fatty liver of pregnancy, abnormal liver function with preeclampsia, HELLP syndrome and hyperemesis gravidarum. Aim was to determine prevalence of liver disease in pregnancy and the impact of abnormal liver function tests on feto-maternal outcome

Methods: It was an analytical cross-sectional study conducted in the department of obstetrics and gynecology, UISEMH, GSVM Medical College, Kanpur for a period of 2 years. All antenatal patients between the ages of 18-40 years who presented with abnormal liver function tests in third trimester were enrolled. Socio demographic and detailed clinical history was taken from all such patients and they were followed till delivery for feto-maternal outcome.

Results: Hypertensive disorders in pregnancy were the most common cause of abnormal liver function tests in pregnancy (55.25%), followed by intrahepatic cholestasis in pregnancy (23.91%). Acute viral hepatitis was present in 8% patients. In 39% patients, preterm delivery was documented about 43.7% babies had birth weight less than 2.5 kg. Maternal mortality was 15.3% and perinatal mortality was 24.7%.

Conclusions: Deranged liver function in pregnancy is associated with significant maternal and perinatal morbidity. Early diagnosis and appropriate intervention can improve feto-maternal outcome.

Keywords: HELLP syndrome, Hyperemesis gravidarum, Intrahepatic cholestasis of pregnancy, Preeclampsia

INTRODUCTION

Liver plays an important role for various metabolic changes during pregnancy. Pregnancy causes very few alterations in the results of standard liver function tests. It occurs in approximately 3% of all pregnant patients.[1-6] Abnormal liver function tests (LFTs) in pregnancy require proper interpretation in order to make correct diagnosis at right time.

Liver diseases complicating pregnancy can be divided into three broad categories- diseases specifically related to pregnancy (resolve spontaneously or following delivery) are hepatic dysfunction from hyperemesis gravidarum, intrahepatic cholestasis, acute fatty liver of pregnancy, and hepatocellular damage with preeclampsia.

Acute hepatic disorders that is coincidental to pregnancy, such as acute viral hepatitis.

Chronic liver diseases that predate pregnancy, such as chronic hepatitis, cirrhosis, or esophageal varices.

This study was done with an aim to determine the prevalence of liver diseases specific and non-specific to pregnancy, role of liver function tests in diagnosis of liver diseases in pregnancy and to study the impact of abnormal liver function tests on feto-maternal outcome.

METHODS

This was an analytical cross-sectional study conducted in the department of obstetrics and gynecology, UISEMH, GSVM Medical College Kanpur for a duration of 2 years from January 2021 to January 2023. Ethical clearance for the study was taken from ethical committee, GSVM Medical college, Kanpur.

Inclusion criteria

All antenatal patients of age group 18-40 years and gestational age from 26 weeks to 36 weeks. Antenatal patients who presented to our side with abnormal liver function test results. Patients who were willing to participate in the study and follow up.

Exclusion criteria

Antenatal patients on drugs affecting liver enzymes. Antenatal patients with history of chronic illnesses like chronic kidney disease, chronic liver diseases, autoimmune diseases. Patients who were not willing to follow up.

All antenatal patients of age group 18-40 years with abnormal liver function tests in third trimester were enrolled in our study. Socio demographic features and detailed clinical history was taken from all such patients. All the antenatal patients enrolled were followed till delivery to determine the fetomaternal outcomes. In all the antenatal patients besides doing the routine ANC investigations following test were done- serum bilirubin (total, direct, indirect); serum proteins; serum albumin; serum albumin globulin ratio; alkaline phosphatase; LDH; SGOT; SGPT.

After obtaining the demographic, menstrual and obstetrics details, the specific symptoms related to liver dysfunction such as pruritus, persistent vomiting, yellowish discoloration of urine, blurring of vision, diminished urine output, upper abdominal discomfort and anorexia were asked. A detailed history of any drug intake such as anti-tubercular drugs, oral contraceptive and history of sickling was noted. History of blood transfusion, tattoos, alcohol consumption was taken.

Statistical analysis

Data was compiled using Microsoft excel and analysed using IBM statistical package for social sciences (SPSS) version 26 software.

RESULTS

In our study 17441 antenatal patients came to OPD and labour room emergency at our hospital in the duration of January 2021 to January 2023 (2 years) out of which 5286 patients were delivered in this duration. Amongst all these antenatal patients fulfilling our inclusion criteria and with abnormal liver function tests i.e. 325 patients were enrolled in our study.

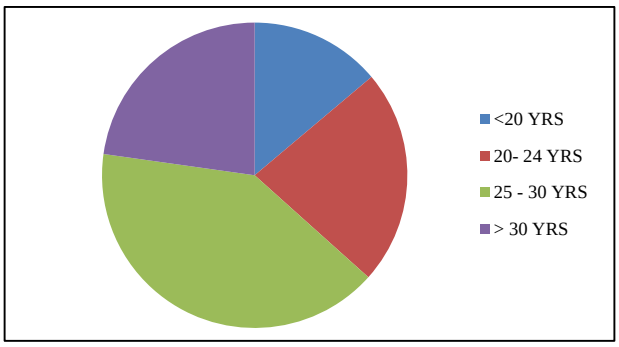

Figure 1: Age wise distribution of pregnant women with abnormal LFT.

Out of these 325 patients 05 patients lost to follow up hence excluded from study (2 of viral hepatitis, 3of hypertensive disorders of pregnancy) in statistical data analysis. Amongst these 320 patients 47 patients were absolutely asymptomatic and liver function tests were mildly deranged in them. Rest 273 patients presented were symptomatic.

Table 1: Distribution of pregnant female with abnormal LFT in terms of area, parity and socioeconomic status.

Area	n=320	%
Rural	248	76.8
Urban	75	23.2
Parity		
Primigravida	169	52.81
Multiparity	151	47.18
Socioeconomic status		
Upper class	1	0.3
Upper middle class	7	2.1
Middle class	144	45
Lower middle class	56	17.5
Lower class	111	34.7

Majority of pregnant women who came to our hospital with abnormal liver function test were of age group 25-30 years as shown in Figure 1. Majority of pregnant women who came to our hospital with abnormal liver function test were primigravidas, belonged to middle class and were resident of rural areas as shown in Table 1.

The most common presenting symptoms in pregnant women with abnormal liver function test was edema followed by high blood pressure. Causes specific to pregnancy were the most important cause of abnormal liver function test in pregnancy amongst which Hypertensive disorders of pregnancy were the most common cause of abnormal liver function tests.

Table 2: Role of liver function test in screening liver disease in third trimester of pregnancy.

	Liver disease present	Liver disease absent	Total	Significance	Prevalence odds ratio (POR)
Abnormal LFT	171	22	193		
Normal LFT	24	2969	2993	P value <0.0001	961.55
Total	195	2991	3186		

Table 3: Maternal outcome in pregnant women with abnormal liver function test in terms of maternal complications.

	Complications present	Complications absent	Total	Prevalence	POR
Abnormal LFT	99	221	320		
Normal LFT	654	4312	4966	P value <0.0001	2.95
Total	753	4533	5286		

Table 4: Maternal mortality in pregnant women with abnormal liver function test.

	Maternal mortality	Maternal survival	Total	Significance	POR
Abnormal LFT	49	271	320		
Normal LFT	43	4923	4966	P value <0.0001	20.7
Total	92	5194	5286		

In this study 3186 were the total number of antenatal patients who came to our side and were screened for liver disease in third trimester. The sensitivity and specificity of LFT in diagnosing liver disease in pregnancy in third trimester is 87% and 99% respectively. Prevalence odds ratio 961.55, 95% CI- 528.39 to 1749.78, Z statistic- 22.486, prevalence ratio- 110.49. P value of role of LFT in diagnosing liver diseases in third trimester was <0.0001 which was highly significant as shown in Table 2.

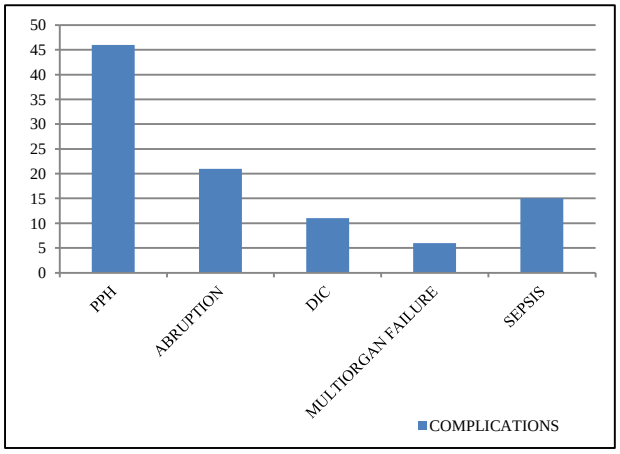

Figure 2: Complications in pregnant women with abnormal liver function test.

Figure 2 shows the complications in pregnant women with abnormal LFT. The most common complication in patients with abnormal liver function test was PPH followed by abruption. Here 5286 are the total number of deliveries conducted in our study duration i.e. 18 months at our center. Prevalence odds ratio of developing complications was 2.95, 95% CI- 2.29 to 3.79, Z statistics- 8.46. P value calculated was <0.0001 that means that the complications in pregnant women with abnormal liver function test was highly significant as shown in Table 3.

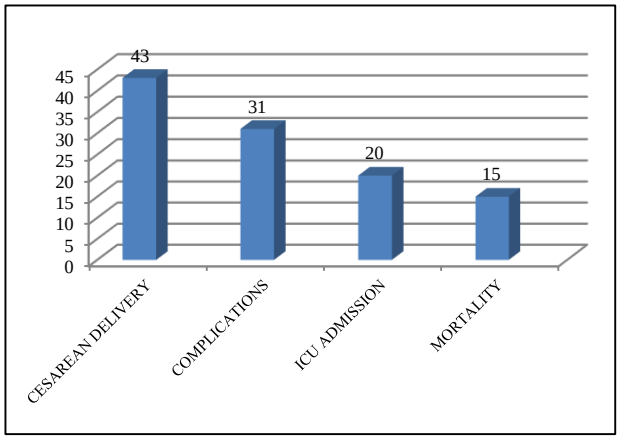

Figure 3: Maternal outcomes in pregnant women with abnormal LFT.

In 42.8% of women with abnormal liver function test the mode of delivery was caesarean delivery. Maternal outcomes LSCS (42.8%), maternal complications (31%), ICU admission (20%), maternal mortality (15.3%) of pregnant women with abnormal liver function test as shown in figure 3.5286 are the total no. of deliveries conducted in our study duration i.e. 24 months at our center. Prevalence odds ratio of maternal mortality due to abnormal was- 20.7, 95% CI- 13.5 to 31.7, Z Statistics- 13.98, significance- p value <0.0001. P value calculated was <0.0001 that means that the maternal mortality due to

abnormal liver function test in pregnancy was highly significant as shown in Table 4.

Table 5: Fetal outcome in terms of birth weight and APGAR score.

Birth weight	n=320	%
>2.5 kg	177	56.19
2.5-1.5 kg	49	15.5
<1.5 kg	89	28.2
Apgar score	**n=248**	**%**
>7	153	61.6
4-7	56	22.5
<4	39	15.7

The Table 5 shows that in 39% of pregnant women with abnormal liver function tests delivery occurred before 37 weeks of gestation and amongst all cases of abnormal liver function test 43.7% women gave birth to newborn with birth weight less than 2.5 kg. Amongst all the newborn babies born to pregnant women with abnormal liver function test 38.2% babies were born with APGAR score of <7. In our study the most common cause of NICU admission in newborn was prematurity and low birth weight followed by meconium aspiration.

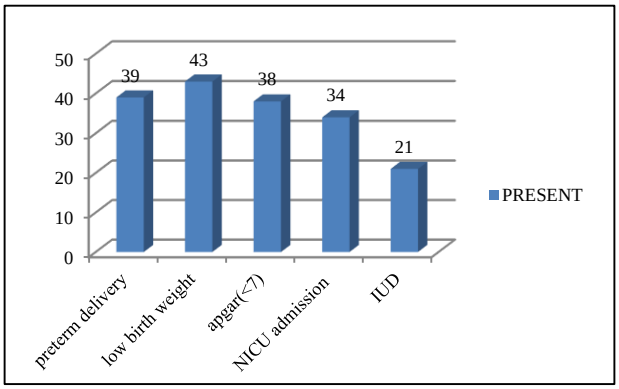

Figure 4: Fetal outcome in pregnant women with abnormal liver function test.

Table 6: Fetal outcome in pregnant women with abnormal liver function test in terms of perinatal mortality.

	Perinatal mortality	Alive newborn	Total	Significance	POR
Abnormal LFT	74	241	315		
Normal LFT	340	4795	5135	P value <0.0001	4.33
Total	414	5036	5450		

5450 were the number of babies born during our study duration. Prevalence odds ratio of perinatal mortality in patients with abnormal liver function test was 4.33, 95% CI- 3.26 to 5.74, Z statistics- 10.159, p value of perinatal mortality in patients of abnormal liver function test was <0.0001 which was highly significant as shown in Table 6. In our study we found that there was a direct correlation between highly deranged liver function tests and adverse fetomaternal outcome.

DISCUSSION

Liver diseases in pregnancy are associated with various complications in both mother and fetus. The present study documented prevalence of 1.56% of liver disease in pregnancy. However Rathi et al in their study reported prevalence of (0.9%) of liver disease in pregnancy.[21] Mishra et al documented 0.9% incidence and Tripathi et al also reported the incidence of 1.68% in their study.[10,19] On the other hand Tiwari et al reported a much higher incidence 2.37% of liver disease in pregnancy while Vinayachandran et al documented much lower incidence of 0.22%.[9,18] The observed discrepancy in incidence rate of liver disease between present study and reference studies could be due to difference in inclusion criteria. All the patients with abnormal liver function test excluding chronic liver disease were included in our study. Mishra et al also excluded chronic liver disease patients while Tiwari et al included cases of chronic liver disease in their study.[18,19]

In our study majority of patients were resident of rural area (76.8%), belonged to middle (45%) and lower (34.7%) socioeconomic class, not booked for antenatal care and generally got admitted in the hospital as emergency cases. Similar findings were observed in other Indian studies like Mishra et al, Rathi et al and Tripathi et al.[10,19,21]

In our study maximum numbers of patients (40.9%) of abnormal liver function tests belonged to 25-29 years of age group. These findings were in concordance to study by Mishra et al in which Majority of the patients (55%) were in the age group 21-30 years.[19] Patra et al also reported the most common age group of abnormal liver function test as 21-25 years.[7] Present study documented maximum number of cases i.e. 52.8% of abnormal liver function tests in primigravidas. Mishra et al and Patra et al also reported similar findings in which majority of patients of abnormal liver function test were primigravidas.[7,19] Therefore we can say that abnormal liver function tests are more common in primigravidas than multigravidas and the reason behind this could be that the hypertensive disorders of pregnancy (most common cause of abnormal LFTs) are more common in primigravidas.

Patients with liver disease in pregnancy usually present with non-specific symptoms. In our study edema (83.1%)

followed by high blood pressure (43.7%) were the most common presenting symptoms. Itching without rash was the chief complaints among all patients with intrahepatic cholestasis of pregnancy. Similar findings were noted by Mishra et al and Tripathi et al where edema was present in 25% cases and 18.3% cases respectively Patra et al reported high blood pressure (46.8%) followed by pruritis (30.6%) as the most common symptom in their study while Choudhary et al noted yellow discoloration as the most common (91%) symptom.[7,10,17,19] In our study, As the hypertensive disorders of pregnancy were found to be the most common cause of abnormal liver function tests due to which edema and high blood pressure were the most common symptom in our study.

In the present study the most common cause of abnormal liver function tests was causes specific to pregnancy (87%). Mishra et al also noted causes specific to pregnancy as most common cause (83.7%).[19] These findings were also concordant with Chang et al who reported causes specific to pregnancy in 76% of cases of liver disease in pregnancy in their study.[1] In our study most common cause of abnormal liver function tests was hypertensive disorders of pregnancy (55.25%). This is similar to findings reported in Patra et al study where pregnancy induced hypertension was the most common (46.6%) cause of abnormal liver function test during pregnancy.[7] Mishra et al also documented pregnancy induced hypertension as the most common cause of abnormal LFT.[19]

In our study abortion occurred in 1.5% of cases and 42.8% of cases with liver disease underwent caesarean section. The prevalence odds ratio of caesarean section in patients of abnormal liver functions test was 115.57. The calculated Z statistics was 17.26 and p value <0.0001 which is highly significant. Vaginal deliveries were conducted in 55.62% patients of abnormal liver function test. This corresponds to study of Mishra et al and Tripathi et al in which 30% and 36.7% patients respectively underwent caesarean section.[10,19] The reason behind this could be the induction failure and emergency caesarean sections done in patients of preeclampsia, eclampsia, HELLP syndrome in order to terminate the pregnancy. In present study Induction was done in 47.7% of cases for termination of pregnancy and out of this 40.4% of cases underwent caesarean section due to induction failure and fetal distress.

Maternal complications were observed in 30.9% of cases in our study. The prevalence odds ratio of developing maternal complications in patients with abnormal liver function test was 2.95. The calculated Z statistics was 8.46 and p value <0.0001 which is highly significant. Most common complication noted was postpartum haemorrhage (14.35%) followed by abruption in 6.5% of cases. Patra et al observed maternal complications in 37% of cases amongst which eclamptic convulsions were the most common intrapartum complication and PPH followed by acute kidney injury as most common postpartum complication.[7] Mishra et al observed maternal complications in 28.7% cases and PPH was the most common complication amongst them.[19] The reason behind high percentage of PPH and abruption in our study may be deranged coagulation factors in patients of abnormal liver function tests. On the other hand Patra et al reported much higher percentage (11%) of acute renal failure in their study.[7]

In our study ICU admission was required in 20% cases and similar findings were documented by Tiwari et al in which ICU admission was required by 26.5% of cases.[18] The most common cause of ICU admission was DIC and multiple organ failure syndrome.

In our study the maternal mortality was 15.3% amongst patients of abnormal liver function test. The prevalence odds ratio of maternal deaths in patients with abnormal liver function test is 20.7. The calculated Z statistics is 13.98 and p value was <0.0001 which is highly significant. However, Rathi et al and Changede et al observed a higher maternal mortality of 20% and 40% respectively while Mishra et and Tripathi et al reported a much lower maternal mortality of 5% and 2% respectively.[10,14,19,21] And this variation in maternal mortality at various centers is because of difference in referral pattern in various institutes. In contrast Ch'ng et al reported no maternal mortality in their study.[1]

Birth weight is an important predictor of perinatal mortality and morbidity. In our study 43.7% of patients with abnormal LFT delivered low birth weight babies. In 15.5% of cases birth weight was between 1.5-2.5 kg and in 28.2% cases birth weight was <1.5 kg. Patra et al documented much higher incidence i.e. 63% of newborn with low birth weight and Kumar et al documented about 50% of new born with birth weight 1.5-2.5 kg.[7,23] Similarly Singhal et al reported higher prevalence of low birth weight in women with hypertensive disorders of pregnancy.[22] Reason behind this is that In majority of patients in our study with hypertensive disorders of pregnancy immediate termination was done for management which lead to delivery of low birth weight babies.

Apgar score at 5 minutes was <7 in 38.2% cases of abnormal liver function test. Similar results were observed by Tripathi et al and Patra et al in which apgar score <7 was observed in 36% and 28.5% of cases.[7,10] We observed that women with PIH and cholestasis had low Apgar score in present study.

In our study NICU admission was required in 33.7% of cases. Patra et al documented NICU admission in 42.4% of cases and on the other hand Mishra et al and Tiwari et al documented NICU admission in 27.5% and 24.47% of cases.[7,18,19] Prematurity and low birth weight (11.2%) followed by meconium aspiration (6.8%) were the most common causes of NICU admission in our study.

In our study the perinatal mortality was documented in 24.7% of cases. The prevalence odds ratio of perinatal

mortality in patients with abnormal liver function test was 4.33. The calculated Z statistics was 10.16 and p value was <0.0001 which was highly significant. Similar results were seen in Patra et al in which perinatal mortality was documented in 23% of cases and Tiwari et al documented perinatal mortality in 29.17% of cases.[7,18] However Mishra et al documented much higher perinatal mortality of 41.25% in their study and similarly Choudhary et al documented perinatal mortality in 38 % of cases.[17,19]

The main limitation of our study was that the duration of our study was small and was conducted in a single center. Also the sample size was small. COVID-19 pandemic and lockdown have further hampered our study results. Further studies should be conducted with bigger sample sizes and for a longer duration and it should be multicentric for better results.

CONCLUSION

Abnormal liver function test had adverse effect on both the mother and the fetus. Causes specific to pregnancy remains the most common cause of abnormal liver function tests. Amongst them hypertensive disorders of pregnancy followed by intrahepatic cholestasis of pregnancy were the most common causes of abnormal liver function test. Abnormal liver function test in pregnancy is associated with poor maternal and perinatal outcomes. Regular antenatal checkup, screening, diagnosing liver disorder as early as possible, proper treatment and timely referral to higher centers can improve the feto-maternal outcomes and decrease the maternal and perinatal mortality in patients with abnormal liver function tests.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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