



"LIVER DISORDER DURING PREGNANCY: A STUDY OF CLINICAL PROFILE IN A TERTIARY CARE HOSPITAL"

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ABSTRACT

Background: The spectrum of liver disorder during pregnancy is varied from asymptomatic pregnant woman to a fulminant form with life threatening complications. Commonly liver disorder manifests as jaundice. This study aims to analyze the incidence, risk factors, causes of liver disease, clinical presentation, complications and maternal-fetal outcome.

Methods: A prospective observational type of study conducted on 100 patients with jaundice attending antenatal clinic in our hospital over a period of one year.

Results: A total 100 cases of liver diseases complicating pregnancies were recorded out of 30,096 deliveries (0.33%). Viral hepatitis (71%) and HELLP syndrome (21%) accounted for majority of cases. Hepatitis E (38%) was the most common cause of liver disease and leads to high maternal-fetal morbidity and mortality.

Conclusion: Liver disease in pregnancy have a non specific presentation. Appropriate supportive management and policy of early delivery will help in improving maternal and fetal outcomes in pregnant women with liver disease.

KEYWORDS : viral hepatitis, HELLP syndrome, Hepatitis E

INTRODUCTION

The spectrum of liver disorder during pregnancy is varied from asymptomatic pregnant woman to a fulminant form with life threatening complications. HELLP syndrome, preeclampsia-eclampsia, Acute fatty liver of pregnancy, viral hepatitis and cholestasis of pregnancy are unique to pregnancy while several medical disorders like sickle cell disease, malaria, leptospirosis, terminal sepsis too affects liver. Commonly liver disorder manifests as jaundice. Non specific symptoms at presentation like vomiting, nausea and pain in abdomen increase the likelihood of delay in diagnosis in the absence of strong clinical suspicion. Timely intervention and termination of the pregnancy in cases of liver diseases attributable to pregnancy forms the main stay of treatment.

The incidence of liver diseases in pregnancy is 2.9% of which 0.32% presented with jaundice. The overall incidence of liver disease in pregnancy is 3.2% out of which preeclampsia with hepatic dysfunction encountered 1.8%, followed by eclampsia 0.6%, HELLP syndrome 0.24%, viral infection 0.19%, intrahepatic cholestasis of pregnancy 0.13%, chronic liver disease 0.03%. In the study from southern India, the commonest causes of liver disease in pregnancy are acute fatty liver of pregnancy (15%) and PIH-associated liver dysfunction.

Maternal mortality in pregnancy with liver disease has dropped to 1.1% in recent studies from west. Pereira et al reported 13% maternal as well as perinatal mortality rate among pregnant women with severe liver disease. Tank et al included patients with only severe liver disease and had found higher maternal and perinatal mortality rates (42% and 62% respectively). The southern Indian study showed overall mortality of 20.2% and perinatal mortality of 24.6%.

Liver disorder during pregnancy is challenging for obstetrician as it involves multidisciplinary approach including the facilities of liver transplant surgery. Ours being the largest tertiary care referral unit in central India with limited resources, gets lot many critical cases of jaundice. High prevalence of sickle cell disease in this geographic location makes things more complicated. We observed in death meets that HELLP syndrome, Acute fatty liver of pregnancy and Viral hepatitis contributes to most of the maternal mortality, while cholestasis of pregnancy majorly affecting neonatal morbidity. It was thus decided to carry out a prospective observational study and analyse the incidence, spectrum, clinical presentation and outcome of liver diseases complicating pregnancy in our hospital.

METHODS

This was a prospective observational study carried on 100 pregnant women of all gestational age group with jaundice and abnormal liver function tests out of 30,096 women attending antenatal clinic during one year period from Feb 2016 to Jan 2017 at GMCH Nagpur. Women attending antenatal clinics and antenatal referrals from peripheral hospital were included in the study. These patients were followed up prospectively till delivery and data collected in excel as age of subjects, parity, gestational age, associated risk factors, range of abnormal LFT and other investigations, diagnosis, maternal-fetal outcome and complications.

Diagnosis was based on clinical presentation, liver function tests, USG abdomen and postmortem liver biopsy. The following are the criteria used for the diagnosis of these diseases in our hospital.

HELLP syndrome

Diagnosed based on the peripheral smear, platelet count ($<1,50,000/\text{mm}^3$), LDH ($>600\text{IU/L}$), and Liver enzymes (AST and ALP $>70\text{IU/L}$), as partial or complete.

Acute viral hepatitis

Clinical features of hepatitis, elevated liver enzymes and viral markers positive for hepatitis A, B, C and E.

Acute fatty liver of pregnancy

Diagnosed mainly by exclusion with strong clinical suspicion, laboratory findings of abnormal liver function tests, USG abdomen and postmortem liver biopsy.

Intra hepatic cholestasis of pregnancy (IHCP)

IHCP is diagnosed on clinical findings of pruritis in the absence of skin disease, abnormal liver function tests, USG abdomen.

INCLUSION CRITERIA

All pregnant women at any gestational age admitted with jaundice and abnormal liver function tests are included in this study.

EXCLUSION CRITERIA

- Pregnant women with chronic liver disease
- Pregnant women with drug induced abnormal liver function tests
- known case of hemolytic anemia
- Diagnosed case of Dengue, complicated malaria, Leptospirosis
- known case of platelet disorder (ITP)
- Hyperemesis gravidum

G) Patient's having terminal Sepsis

Statistical analysis:

Continuous variables were presented as Mean SD. Categorical variables were expressed in frequency and percentages. Categorical variables were compared by performing chi-square test. For small numbers, Fisher exact test was applied wherever applicable. All the test were 2 sided. P<0.05 was considered as statistical significance. Statistical software STATA version 14.0 was used for data analysis.

RESULTS

Out of 30,096 patients 100 patients were identified with liver disorder during pregnancy making incidence of liver disease to 0.33%in hospital population.

Table No.1 Demographic profile.

	Number of patients	Percentage
Age		
≤20	7	7.0
21-25	51	51.00
26-30	36	36.0
31-35	6	6.0
Period of gestation		
24-28	19	19
29-32	22	22
33-36	16	16
37-40	43	43
Gravidity		
G1	66	66.0
G2	28	28.0
G3	6	6.0

Maximum cases were primigravida 66% followed by second gravida 28% (Table 1). 51% were in age group 21-25 years. 43% were in 37-40 weeks of gestation at the time of delivery.

Table 2: spectrum of liver disease

Disease	Number of cases	Percentage
Hepatitis A	12	12
Hepatitis B	19	19
Hepatitis C	2	2
Hepatitis E	38	38
Hepatitis	71	71
IHCP	7	7
HELLP	21	21
AFLP	1	1

(Hepatitis includes Hepatitis A, Hepatitis B, Hepatitis C and Hepatitis E)

Hepatitis was a most common disease found in study subjects (71%) followed by HELLP syndrome (21%), Cholestasis of pregnancy (7%) and AFLP (1%).Hepatitis E was the most common cause of liver disorder in our study (38%).

Table 3: Risk factors

Risk factors	No. of patients	Percentage
Thrombocytopenia	38	38.0
Anemia	68	68.0
Diabetes	8	8.0
Obesity	16	06.0
Preeclampsia	21	21.0
Eclampsia	13	13.0

Anemia was a major risk factor in our study (68%) followed by thrombocytopenia (38%) and Preeclampsia (21%).

Table 4: Delivery outcome

Mode of delivery	Number of cases	Percentage
Vaginal delivery	74	74
Preterm	38	38
Term	36	36
Caesarean	26	26
Preterm	10	10
Term	16	16

Table 5: Perinatal outcome

	Number of cases	Percentage
Live birth	72	72
Still birth	28	28
Preterm	48	48
Term	52	52
NICU admission	31	31
Birth weight	No. of patients	Percentage
≤1500	23	23
1501-2000	30	30
2001-2500	24	24
>2500	23	23

Commonest mode of delivery in our study was vaginal delivery (74%) out of this 38% were preterm and 36% were term (Table3).There were 26% caesarean out of this 10% were preterm and 16% were term. 28% patients had still birth out of which 17% were due to hepatitis and 8% were due to HELLP syndrome. Out of this 28% still birth 9% were preterm and 2% were having growth restriction.

Table 4 shows the perinatal outcome. Of the total 100 births 72% were live and 28% were stillbirths. 48% babies were preterm and 52% were term.31% babies required NICU admission.77% babies had birth weight less than 2.5 kg.

Table 6: Distribution of neonatal outcome in different types of hepatitis

Neonatal outcome	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis E
Live	11	16	2	25
Still Birth	1	3	0	13

Maximum still births were present in hepatitis E infection (13%), followed by hepatitis B infection (3%).So in our study most common cause of still birth was hepatitis E.

Table 7: Maternal outcome

Maternal outcome	Number of cases	Percentage
Live	81	81
Death	19	19

81% patients were live and 19% maternal deaths observed in study population.

Table 8: Maternal outcome and their diagnosis

Maternal outcome	HELLP	Hepatitis	AFLP	IHCP
Live	19	56	1	5
Death	2	15	0	2

Maximum maternal deaths occurred in hepatitis infection (15%), especially in hepatitis E (12%).

Table 9: Maternal Complications.

Complications	Number of cases
APH	6
PPH	12
DIC	14
Puerperal Sepsis	2
Hepatic encephalopathy	23

ARF	7
Esophageal Varices	3
MODS	10
Ventilator required	9
ICU admission	14

14% patients required ICU admission. Most common complication was hepatic encephalopathy constituting (23%).DIC (14%) and postpartum hemorrhage (12%) were some of the major contributors of maternal morbidity.

Table 10: Maternal Complications and their diagnosis

Complication	HELLP	Hepatitis	AFLP	IHCP
APH	3	3	0	0
PPH	6	5	0	1
DIC	2	11	0	1
Puerperal Sepsis	1	1	0	0
Hepatic encephalopathy	2	18	0	3
ARF	3	3	0	1
Varices	0	3	0	0
MODS	1	8	0	1
Ventilator required	3	4	0	2
ICU admission	4	8	0	2

Hepatitis (18%) was the most common cause for hepatic encephalopathy. Most of the maternal complications were due to hepatitis and HELLP syndrome.

Table 11: Maternal Complications in different types of hepatitis

Maternal Complications	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis E
APH	0	0	0	3
PPH	0	0	1	4
DIC	1	0	1	9
Puerperal Sepsis	0	0	1	0
Hepatic encephalopathy	1	0	1	16
ARF	0	0	0	3
Esophageal Varices	0	0	1	2
MODS	0	0	2	6
Ventilator required	0	0	1	3
ICU admission	0	1	1	6

All maternal complications were more common in Hepatitis E infection.16% patients of Hepatitis E were having hepatic encephalopathy. 9% patients went into DIC.6% patients required ICU admission.

DISCUSSION

Liver disorder in pregnancy has different outcomes in western and Indian studies. We tried to find out incidence of different liver disorder during pregnancy, study risk factors affecting maternal and fetal outcome and it's complications, so as to help in early diagnosis and prompt treatment of such patients to overall reduce maternal and perinatal mortality.

Incidence of liver disorder during pregnancy in our study was 0.33%.In a study from Northern India D' Souza et al reported an overall incidence of 3.3%.Sharma et al reported an incidence of 1.9% of liver disease in pregnancy from central india⁶.The incidence of jaundice in pregnancy was reported as 0.4% by Acharya et al and 0.9% by Rathi et al⁷.

Primigravida and patients aged 21-15 years accounted most cases. This was similar to the findings of other studies from India^{8,9,10,11}.This is explained as this is the most common age group for pregnancies in India.

In our study maximum number of study subjects were in gestational age group 37-40 weeks (48%) and there was no statistically significant difference between the groups which was found in similar studies^{9,10}.In our study anemia was the most common associated risk factor (68%) which is also found in above study. Second most common risk factor was thrombocytopenia (38%) followed by preeclampsia (21%) which is similar to Indrajit et al study¹².

In our study most common cause of liver disorder during pregnancy was viral hepatitis (71%) that was similar to Meena N. Satia et al study (62%)¹¹.second most common cause was HELLP syndrome (21%).IHCP was the third most common cause of liver disorder (7%).In 1% of study subjects AFLP was the cause of liver disorder.

Present study differs from Nalini Mishra et al¹¹, Indrajit Suresh et al¹² and Uttara Kohli et al¹ because most of the infective hepatitis patients were referred to our hospital from peripheral hospitals. We found that hepatitis E was the most common cause of viral hepatitis in pregnancy (38%).Similar results found in Nalini Mishra et al¹⁰, Gowri Prasad et al⁹ and Meena N.Satia et al¹¹ study.

In our study vaginal delivery was mode of delivery in 74% of cases which similar to other studies^{8,9,10}. In our study we found that hepatic encephalopathy was most common maternal complication (23%).Similar results found in other studies^{11,13}. DIC was the second most common maternal complication (12%). In our study we found that Low birth weight was most common fetal complication (64%) which is similar to Indrajit suresh et al study¹². In our study we observed that there were 19% maternal death. Similar results seen in Meena N.Satia et al¹¹ study. In our study we found that there were 28% still birth. Similar results found in Meena N.Satia et al¹¹ study.

Conclusions

Liver disorder during pregnancy is an important obstetric problem on account of high associated perinatal mortality and morbidity. Such disorder have non-specific presentation. Course of disease is rapid and in short period it may affect the fetus. Overall, there is an increased incidence of fetal adverse events in pregnant females with liver diseases. The impact of hepatic disorders on the mother is also significant. In a country like India, beginning from health education to the pregnant mother regarding warning signs and immediate visit to doctor, to medical personnel at primary health centre for early transfer can go long way in lowering maternal and perinatal morbidity.

Thus, we conclude from our study that high suspicion of liver disorder during pregnancy based on subtle signs and symptoms should encourage liver function tests immediately. Cases diagnosed at periphery should be immediately referred to tertiary care centre. Appropriate supportive management and policy of early delivery will help in improving maternal and fetal outcomes in pregnant women with liver disease.

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