



## A Study on Acute Viral Hepatitis in Pregnancy; Seroprevalence and Fetomaternal Outcome in a Tertiary Care Hospital

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### Abstract

**Background:** Viral hepatitis is the major cause of jaundice in pregnancy. It can lead to coagulation defects, postpartum haemorrhage, organ failure and high maternal mortality and poor outcomes of their newborns, so early diagnosis and treatment is required for better management of the patients.

**Objective:** To assess the prevalence of viral hepatitis in pregnant women and their fetomaternal outcome. **Methods:** A total of 293 pregnant women presented with clinical and biochemical evidence of jaundice in Obstetric and Gynaecology Department were included in this study. All the patients were followed during their hospital stay and maternal morbidity, mortality and fetal outcome were recorded. **Results:** Out of 293 women, 178 (60.8%) were serologically diagnosed for AVH in pregnancy. HEV was the major cause of viral hepatitis 67.98% (121/178) followed by HAV 22.47% (40/178), HBV 8.43% (15/178), HCV 1.12% (2/178). No case of HDV and co-infection was found. Maternal mortality rate was 14.61%. **Conclusions:** HEV is found to be the common cause of AVH in pregnancy and was associated with high maternal mortality and poor fetal outcome. Through better sanitation, safe potable water supply, personal hygiene and awareness regarding substance abuse, viral hepatitis infection can be minimized in pregnant women.

**Keywords:**-Acute Viral Hepatitis, Maternal Mortality, Pregnancy.

### INTRODUCTION

Acute viral hepatitis (AVH) is a systemic infection affecting liver predominantly. It is characterized by serum aspartate aminotransferase elevation of atleast five-fold or

clinical jaundice or both. AVH is the most common cause of jaundice in pregnancy among all causes affecting fetuses as abortion, stillbirths, NICU admission and neonatal death.<sup>[1]</sup> Pregnancy appears to be a potential



risk factor for viral replication and leads extreme low immune status of pregnant women and presents as a challenging disease to obstetrician. Most developing countries have a high birth rate and a large pool of hepatotropic viruses causing hepatitis in pregnancy.

HEV infection is a public health issue in several countries where safe drinking water is a problem. It is responsible for worst maternal and fetal outcome in pregnant women compared to other types of viral hepatitis.<sup>[2]</sup> The uniqueness of hepatitis E is its transformation from a relatively self-limiting disease in non-pregnant state to a highly virulent disease during pregnancy. In India, hepatitis E infection is the most common cause of fulminant hepatic failure and it is so severe that it often leads to mortality which may go upto 75%.<sup>[3]</sup> Fulminant hepatitis was seen in high percentage in third trimester pregnant women with high maternal mortality ranging from 15-45%.<sup>[4]</sup> Obstetric and fetal outcome in HEV infected pregnant women is also not favourable.

HAV infection is a self limiting disease characterized by complete recovery and rarely, a rapidly fatal fulminant hepatitis may follow.<sup>[5]</sup> The course of the disease during pregnancy is generally similar to that in non-pregnant patients, with excellent maternal and fetal outcomes in developed nations. HCV infection gets transmitted vertically and the virus may lead to hepatocellular carcinoma in the mother as well as the child. Studies suggest prevalence of HCV among pregnant females to be 0.6% to 2.4%, with overall mother to infant transmission varying from 8% to 15%.<sup>[2]</sup>

Hepatitis B during pregnancy has its role in the perpetuation of chronic infection through vertical transmission.<sup>[6,7]</sup> Mothers with a reactive serum test for HBeAg have more circulating virus and higher rates of perinatal transmission than mothers without detectable serum HBeAg and a reactive serum test for anti-HBeAg.<sup>[4]</sup> HBV infection does not appear to be teratogenic but there could be a higher incidence of low birth weight among infants born to mothers with acute HBV infection during pregnancy. Approximately 20-25% of chronic hepatitis B virus carriers are ultimately co-infected with hepatitis D virus.<sup>[8]</sup> Perinatal transmission is uncommon but identifying pregnant patients with chronic HDV infection is important because of the increased likelihood of underlying advanced liver disease.

The prevalence and etiology of viral hepatitis still remains debatable in developing and developed countries and available review of literature showed that there is wide variation in clinical course and fetal outcome of viral hepatitis in pregnancy. Therefore, this study was undertaken to evaluate its clinical course, fetomaternal outcome in cases of acute viral hepatitis in pregnancy.

### **Aims & Objectives**

The study was conducted to know the prevalence of Acute Viral Hepatitis (AVH) caused by hepatitis A, E, B, D, C viruses in pregnant women and to evaluate the clinical course, maternal and fetal outcome in cases of AVH in pregnancy.

### **MATERIAL AND METHODS**

A prospective observational study was conducted in the Department of Microbiology, Government Medical College, Amritsar during the period of one and a half year (from 1st January 2019 to 30th June, 2020). All pregnant women visiting to the Obstetric and Gynaecology Department, presenting with clinical and biochemical evidence of Hepatitis were included, irrespective of gestational age and parity.

### Inclusion criteria

Recent onset of jaundice (< 6 months), serum bilirubin level > 2.5 mg/dl with an increase in serum transaminase level more than two times the normal, fever in absence of chronic liver disease or past history of jaundice.

### Exclusion criteria

History of chronic liver disease or past history of jaundice with duration of illness more than 6 months, HELLP syndrome (Hemolysis, elevated liver enzymes, low platelet count), acute fatty liver of hepatitis, intrahepatic cholestasis of pregnancy, drug induced jaundice, any clinical or laboratory evidence of chronic liver disease

In each case, detailed history and examination, biochemical results along with viral serology for hepatitis A, B, C, D, E viruses were assessed. After obtaining the written informed consent of the patients along with completely filled patients' history form, 5 mL blood samples with universal precautions were collected by venipuncture, from 293 patients presenting with jaundice. Serum was separated from blood samples after centrifugation at 3,000 rpm for 3 minutes. The serum samples were analysed for the detection of IgM

antibodies for HAV and HEV, anti-HCV antibodies for hepatitis C virus, surface antigen and IgM anti-HBc of hepatitis B virus and IgM anti-HDV in HBsAg positive cases. The procedures were followed as per the manufacturer's instructions mentioned in the literatures provided within the ELISA kits.

All the patients were followed throughout the pregnancy and intrapartum period. Clinical course, maternal and fetal morbidity, mortality and perinatal outcome were recorded on the proforma. The data thus obtained were compiled and tabulated to obtain valid results.

## RESULTS

A total of 293 pregnant women presented with clinical and biochemical evidence of jaundice were included in this study. Out of which 178 (60.8%) women were serologically diagnosed for Acute Viral Hepatitis in pregnancy. Majority of the patients of AVH belonged to the age group of 25-29 years (46.63%) and were from rural area (61.80%). Most of these patients were literate (71.91%) and 61.80% of the patients were from lower socio-economic class. Primigravida (40.45%) constituted the largest group of pregnant population with viral hepatitis and majority were in their third trimester (80.89%).

Out of 178 patients, 121 cases (67.98%) were of hepatitis E virus, 40 cases (22.47%) were of hepatitis A virus and 15 cases (8.43%) were of hepatitis B virus. There were only 2 cases (1.12%) of hepatitis C virus obtained in this study. Out of 15 cases of hepatitis B virus (HBV), 13 were positive for HBsAg and 2 were positive for HBc-IgM antibodies. No case of hepatitis D virus and co-infection of two or more viruses was found in the study [Table2].

Majority of the patients with acute viral hepatitis had vaginal (79.78%) and preterm deliveries (55.1%). Hepatic encephalopathy was the most common (12.36%) complication seen in the patients of hepatitis followed by DIC (1.68%), postpartum hemorrhage (1.12%) and acute renal failure (0.56%). Only 24 (13.48%) were admitted in ICU. Out of 178 patients, 26 (14.61%) died and 152 (85.39%) were recovered as shown in [Table 3].

Majority of the preterm (39.89%) delivery cases were found in HEV patients followed by HAV (8.43%) and HBV (5.62%) patients. Maximum number of complications were seen in HEV patients (i.e 20 cases of hepatic

encephalopathy, 2 cases of DIC, 2 cases of postpartum hemorrhage and 1 case of acute renal failure). Maximum mortality was seen in HEV (25/121) patients followed by HAV (1/40) [Table 4].

Out of 178 deliveries, 150 (84.27%) were born alive, 18 (10.11%) were intrauterine deaths and 10 (5.62%) cases were stillbirths. Out of 150 live births, 25.33% cases were of low birth weight and 54% cases were admitted in NICU [Table 5].

Maximum cases of intrauterine deaths (18 cases) and stillbirths (9 cases) were seen in HEV patients followed by HAV patients (1 case of stillbirth) [Table 6].

**Table 1: Demographic profile**

| Parameter             |               | Number of patients (n=178) | Percentage (%) |
|-----------------------|---------------|----------------------------|----------------|
| Age group (years)     | <20           | 5                          | 2.81           |
|                       | 20-24         | 77                         | 43.26          |
|                       | 25-29         | 83                         | 46.63          |
|                       | ≥30           | 13                         | 7.30           |
| Type of Parity        | Primigravida  | 72                         | 40.45          |
|                       | Gravida 2     | 63                         | 35.39          |
|                       | Gravida 3     | 23                         | 12.92          |
|                       | Gravida 4     | 20                         | 11.24          |
| Duration of pregnancy | Trimester I   | 0                          | 0              |
|                       | Trimester II  | 34                         | 19.11          |
|                       | Trimester III | 144                        | 80.89          |

**Table 2: Distribution of type of hepatitis virus in pregnant women**

| Viral marker                        | Number of patients | ELISA assay done      | Percentage (%) |
|-------------------------------------|--------------------|-----------------------|----------------|
| Hepatitis E virus                   | 121                | IgM anti-HEV          | 67.98          |
| Hepatitis A virus                   | 40                 | IgM anti-HAV          | 22.47          |
| Hepatitis B virus                   | 15                 | HBsAg and IgM ant-HBc | 8.43           |
| Hepatitis C virus                   | 02                 | IgM anti-HCV          | 1.12           |
| Hepatitis D virus                   | 0                  | IgM anti-HDV          | 0.00           |
| Co-infection of two or more viruses | 0                  | -                     | 0.00           |



|       |     |   |        |
|-------|-----|---|--------|
| Total | 178 | - | 100.00 |
|-------|-----|---|--------|

**Table 3:** Maternal complications and outcome

| Parameter                         |                        | Number of patients | Percentage (%) |
|-----------------------------------|------------------------|--------------------|----------------|
| Mode of delivery                  | Vaginal delivery       | 142                | 79.78          |
|                                   | Cesarean section       | 36                 | 20.22          |
| Gestation at the time of delivery | Preterm delivery       | 98                 | 55.1           |
|                                   | Fullterm delivery      | 80                 | 44.9           |
| Maternal complications            | Hepatic encephalopathy | 22/178             | 12.36          |
|                                   | DIC                    | 3/178              | 1.68           |
|                                   | Postpartum hemorrhage  | 2/178              | 1.12           |
|                                   | Acute renal failure    | 1/178              | 0.56           |
|                                   | ICU admission          | 24/178             | 13.48          |
| Maternal Outcome                  | Recovered              | 152                | 85.39          |
|                                   | Died                   | 26                 | 14.61          |

**Table 4:** Correlation of viral markers with maternal complications and outcome

| Parameter              |                        | HEV | HAV | HBV | HCV |
|------------------------|------------------------|-----|-----|-----|-----|
| Preterm delivery       |                        | 71  | 15  | 10  | 2   |
| Maternal complications | Hepatic encephalopathy | 20  | 1   | 1   | 0   |
|                        | DIC                    | 2   | 1   | 0   | 0   |
|                        | Postpartum hemorrhage  | 2   | 0   | 0   | 0   |
|                        | Acute renal failure    | 1   | 0   | 0   | 0   |
|                        | ICU admission          | 17  | 6   | 1   | 0   |
| Maternal Outcome       | Died                   | 25  | 1   | 0   | 0   |

**Table 5:** Fetal outcome

| Fetal outcome             | Number (n) | Percentage (%) |
|---------------------------|------------|----------------|
| Live                      | 150/178    | 84.27          |
| Intra-uterine Death (IUD) | 18/178     | 10.11          |
| Stillbirth                | 10/178     | 5.62           |
| Low birth weight          | 38/150     | 25.33          |
| NICU admission            | 81/150     | 54.00          |

**Table 6:** Distribution of type of hepatitis virus involved in Fetal outcome

| Parameter  | HEV | HAV | HBV | HCV |
|------------|-----|-----|-----|-----|
| IUD        | 18  | 0   | 0   | 0   |
| Stillbirth | 9   | 1   | 0   | 0   |
| Live       | 94  | 39  | 15  | 2   |

## DISCUSSION

Acute viral hepatitis (AVH) is the most common form of liver disease worldwide and

it frequently affects women of childbearing age, either as an acute infection or as a chronic disease.<sup>[2]</sup> It is still a major public health concern of developing countries such as India, despite improving socio-economic condition, sanitation, and health awareness.<sup>[9]</sup> HEV infection occurring in young adults is a known phenomenon with a predisposition to pregnant women.<sup>[10]</sup> Most of the cases of hepatitis in India have been attributed to Hepatitis E, for which it is an endemic zone.<sup>[11]</sup> HEV and HBV infections during pregnancy are associated with fulminant hepatic failure and high mortality rate.<sup>[2]</sup> The present study comprised of 293 pregnant women presented with clinical and biochemical evidence of jaundice. Out of which 178 (60.8%) women were serologically diagnosed for Acute Viral Hepatitis in pregnancy.

Out of 178 pregnant women, age group most commonly affected was 25-29 years (46.63%). Same age group was reported by Jethwa DK et al (46%) and by Madan et al (50.7%) in their respective studies.<sup>[2,3]</sup> Primigravidae constituted the largest group (40.45%) of pregnant women with viral hepatitis in our study. Similarly, Shukla et al, Madan et al and Jethwa DK et al observed 41%, 39.68% and 42% of infected pregnant women to be primigravidae respectively.<sup>[2,3,4]</sup> In our study, 80.89% of pregnant women with acute viral hepatitis were found to be in third trimester of pregnancy. This may correlate with the growing demands of the fetus as the pregnancy advances and due to which there is a consequent burden on the maternal metabolism to meet the requirements. Patil M et al (82%),<sup>[12]</sup> Singh S et al (71.4%) and Patra S et al (67%) reported similar results of high

prevalence of viral hepatitis in third trimester.<sup>[6,7]</sup>

A higher prevalence of viral hepatitis was observed in rural population (61.80%) which is consistent with the study conducted by Jethwa DK et al (92% in rural population).<sup>[2]</sup> A higher viral hepatitis positivity was observed in literates (71.91%) which is similar to the observations of Kumar A et al (73.8%).<sup>[13]</sup> Majority of the cases (61.80%) were from lower socio-economic class which is consistent to the findings of Jethwa DK et al (89%).<sup>[2]</sup>

In our study, HEV was responsible for the maximum cases (67.98%) of acute viral hepatitis. Similar higher prevalence of HEV as a causative factor of viral hepatitis was found in the studies done by Jethwa DK et al,<sup>[2]</sup> (68.4%), Patra S et al (60%),<sup>[7]</sup> Jaiswal SP et al (57.5%) and Banait et al (55.76%).<sup>[14,15]</sup> Hepatitis A virus was found to be the second most common (22.47%) cause of acute viral hepatitis which is consistent with Jethwa DK et al,<sup>[2]</sup> who reported HAV to be second most common infection (22.8%) followed by HEV (68.4%). As most of these cases were from lower socio-economic class, poor sanitation and unsafe drinking water may had contributed the higher rate of HAV in the present study.

Prevalence of hepatitis B virus infection was found to be 8.43% in the present study which is in consistent with the observations of Beniwal M et al,<sup>[16]</sup> Singh S et al and Jethwa DK et al who reported 7.2%,<sup>[2,6]</sup> 10% and 8.8% of HBV seropositivity in their studies respectively. No case of HBV-HDV co-infection was detected in our study which is similar to the study conducted by Kose V et al.<sup>[17]</sup> Prevalence of 1.12% of hepatitis C virus infection was detected in the patients of viral hepatitis which

is similar to Jaffery T et al (1.03%).<sup>[18]</sup> There was a no case of co-infection of two or more viruses found in our study, which is in accordance with the studies of Sahai S et al and Chaitra S et al.<sup>[11,19]</sup>

Among all patients of acute viral hepatitis, jaundice (100%), fever (65.17%), loss of appetite (61.79%) were the common clinical features which is in accordance with the study conducted by Shukla S et al,<sup>[4]</sup> in which they reported yellowish discoloration of sclera and urine (100%), loss of appetite (62%) and fever (43%) as the common complaints among the patients of acute viral hepatitis. In the present study, serum bilirubin, AST (>40 IU/L) and ALT (>40 IU/L) levels were raised in all cases (100%) of viral hepatitis which is similar to the results reported by Birajdar SV et al and Suresh et al in their respective studies.<sup>[20,21]</sup>

In the our study, majority of pregnant mothers with viral hepatitis had vaginal delivery (79.78%) and cesarean section was done in 20.22% cases. Cesarean section was done due to obstetric indications or worsening maternal conditions, however, vaginal delivery is preferred due to the fear of increased bleeding tendency in these patients. This is consistent with the results of Madan A et al,<sup>[3]</sup> in which they reported 77.78% cases of vaginal delivery and 15.87% cases of cesarean section.

Out of 178 pregnant mothers infected with AVH, 98 (55.1%) had preterm deliveries. Similar results were observed in the studies by Veronica et al,<sup>[22]</sup> (56%) and Beniwal M et al (66.6%).<sup>[16]</sup> Majority of preterm delivery cases in our study were found in HEV patients (39.89%) which is comparable to 29% cases of preterm delivery reported by Jain P et al.<sup>[23]</sup>

Among maternal complications, hepatic encephalopathy (12.36%) was the most common complication seen in pregnant women with acute viral hepatitis followed by DIC (1.68%). Patil M et al,<sup>[12]</sup> also reported hepatic encephalopathy (18%) and coagulopathy (16%) as common complications in their study. Majority of these complications were seen in HEV patients in our study i.e 16.53% of hepatic encephalopathy, 1.65% of DIC and PPH and 0.83% of acute renal failure. This is in accordance with the results of Jethwa DK et al,<sup>[2]</sup> who reported hepatic encephalopathy (15%), DIC (10.3%) and PPH (5.1%) in HEV patients.

A prevalence of 14.61% maternal mortality due to acute viral hepatitis was observed in our study which is comparable to the study conducted by Sahai S et al,<sup>[11]</sup> and Shrestha et al,<sup>[24]</sup> in which they reported 19.1% and 19.35% of maternal mortality rate respectively. The reason for low mortality rate in our study can be due to the better antenatal health facilities at the periphery and tertiary care centers as well as the proper awareness among the population these days.

The mortality rate in pregnant mothers infected with HEV as reported by other studies ranges between 14-45% and may be as high as 70%.<sup>[4]</sup> HEV infection was found to be associated with high maternal mortality in our study as 25 out of 121 (20.66%) HEV infected mothers died. Out of 25 deaths, 20 were due to hepatic encephalopathy, 4 were due to DIC (2) & PPH (2) and 1 was due to acute renal failure. Similarly HEV was the main causative agent for maternal mortality in the studies done by Patil M et al (16.3%), Ahmed RE et al (25%),



Shukla S et al (33.3%) and Madan A et al (45.8%).<sup>[3,4,12,25]</sup>

In the present study, 1 out of 40 (2.5%) pregnant mothers infected with HAV infection expired due to hepatic encephalopathy as a complication. Maternal outcome due to HBV and HCV infection was found to be favourable in this study as no case of maternal mortality was observed which is similar to the observations of Patil M et al and Madan A et al.<sup>[3,12]</sup>

Current study shows that 18 out of 178 (10.11%) pregnant women with viral hepatitis had intrauterine death which is consistent with the study conducted by Wani S et al (11% IUDs).<sup>[26]</sup> All of these mothers had HEV infection, underwent hepatic encephalopathy and died. Prevalence of 5.62% stillbirth and 84.27% live births was observed which is similar to the results reported by Patil M et al (3% of stillbirth and 73.77% of live births).<sup>[12]</sup> Low birth weight (25.33%) formed the bulk of NICU admission (54%) which is similar to the results reported by Jethwa DK et al,<sup>[2]</sup> in their study (25% of low birth weight and 33.3% of NICU admission).

Poor fetal outcome was observed in HEV infected mothers in our study. Intrauterine deaths and stillbirths were observed in 14.88% (18/121) and 7.44% (9/121) of these patients respectively. This is comparable to the studies conducted by Prasad et al (9.09% IUDs and 4.08% stillbirths) and Ahmed RE et al (17.8% IUDs).<sup>[25,27]</sup> Reasons for the poor fetal outcome with HEV infection can be due to low birth weight, preterm deliveries, vertical transmission and general poor sanitation. In HAV infected patients, 2.5% prevalence (1/40) of stillbirth was observed which is in

accordance with the results of Kumar N et al who reported 2 out of 8 stillbirths in their study.<sup>[28]</sup>

Favourable fetal outcome of HBV positive patients was observed in our study which is in disparate to the studies done by Thakur HS et al (4.5% stillbirth) and Chaitra S et al (4.7% IUD and 0.8% stillbirth).<sup>[1,19]</sup> This variation can be explained on the fact that they have done screening of patients using rapid HBsAg kits instead of ELISA based kits in their studies and missed out some of the HBV infected patients. All HCV infected patients had favourable fetal outcome which is similar to the results reported by Thakur HS et al Chaitra S et al.<sup>[1,19]</sup>

In spite of the above results, there were some limitations to our study. Firstly, we cannot deny the possibility of referral bias in our study. Pregnant women with jaundice and early preterm deliveries requiring NICU facility were commonly referred to our institution from primary health centers. Furthermore, follow-up of virus positivity in neonates was not done in this study. Intrauterine deaths were not investigated with viral RNA testing/autopsy which could have given us an insight into the possible etiology of the affected fetus.

## CONCLUSIONS

Acute Viral Hepatitis during pregnancy is the most common cause of jaundice. HEV and HAV are found to be common causes of Acute Viral Hepatitis in pregnancy. Maternal morbidity and mortality with poor fetal outcome is highly associated with HEV infection. Thus, it is suggested that pregnant women should be periodically screened for clinical features of acute viral hepatitis during



antenatal visits. Pregnant women with suspected hepatitis should be timely diagnosed and closely monitored for fetal well-being and signs of fetal distress, as this disease also adversely affect the fetal outcome. Through better sanitation, safe potable water supply, personal hygiene and awareness regarding substance abuse, viral hepatitis infection can be

minimized in pregnant women especially in the endemic areas. Following a multipronged approach of active screening, adequate treatment, educational counselling and complete immunization against viral hepatitis in all women of reproductive age group can help decrease the burden of acute viral hepatitis.

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