

Maternal and Perinatal Outcome of Pregnancy with Hepatitis E Infection

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ABSTRACT

Objective: To see the prevalence of HEV infection in the cases of acute hepatitis among pregnant women, and maternal and perinatal outcome of pregnancy complicated by HEV infection.

Methods: This was a descriptive study done at two tertiary care hospital in Kathmandu, Nepal between July 2006 and June 2007. Women presenting with acute hepatitis were tested for HEV using commercial rapid HEV test kit (assure HEV IgM Rapid test by MP diagnostics). Pregnant women, who tested positive for HEV, were enrolled as study group. Maternal and perinatal outcome of these women were analyzed.

Results: Ninety-three pregnant women with acute hepatitis due to HEV were admitted during the study period. Of these 93 cases, acute liver failure occurred in 24 (25.8%), acute renal failure in eight (8.6%) and maternal mortality occurred in 18 (19.35 %). Five women (5.4%) had miscarriage and 79 delivered (53 preterm and 26 term). Pregnancy continued in nine. Perinatal mortality occurred in 16 (20.2%) of which nine were still birth and seven neonatal deaths.

Conclusion: Hepatitis E virus infection is a major cause of acute hepatitis in pregnant women with adverse maternal and perinatal outcome.

Keywords: Hepatitis, Pregnancy, Hepatitis E virus, Acute liver failure.

INTRODUCTION

Hepatitis E virus (HEV) is a single-stranded positive sense RNA virus and a major cause of enterically transmitted hepatitis in many countries of Asia and Africa.¹ The main source of transmission of HEV is contaminated drinking water.² Nepal is highly endemic for HEV causing acute sporadic cases and periodic outbreaks.³ It is the commonest cause of acute viral hepatitis in Nepal.⁴ HEV infection has been seen to have high attack rate in pregnant women and associated high maternal mortality and perinatal mortality rate.⁵ The actual cause of high mortality in pregnant women is still not known. It may be due to an altered status of hormones and immunity, which was observed during pregnancy in a study done by Jilani et al.⁶ HEV infection is emerging as a number one killer of pregnant women in Kathmandu, Nepal.⁷ Recently, an epidemic of hepatitis E virus with high maternal mortality was reported among Sudanese women in Darfur as well as in India.^{8,9} However, despite the evidence of high mortality of pregnant women with HEV infection, Bhatia et al observed that outcome of HEV infection during pregnancy is not different when compared with age matched nonpregnant women and men.¹⁰ There are conflicting reports also from developed countries where no adverse effect has been observed on the course of infection during pregnancy.¹¹

This multicentre study was done to find out the prevalence of HEV infection among the hospitalized cases of acute hepatitis during pregnancy, and maternal and perinatal outcome of pregnancy complicated by HEV infection in Kathmandu, Nepal.

MATERIALS AND METHODS

This was a cross-sectional study, done between July 2006 and June 2007, conducted at the Department of Obstetrics and Gynecology, Kathmandu Medical College Teaching Hospital (KMCTH) and Paropkar Maternity and Women's Hospital in collaboration with Sukraraj Tropical and Infectious Disease Hospital, Teku and Bir Hospital. All the pregnant women at any gestational age who presented during the study period with acute hepatitis were tested for HEV infection by commercial rapid HEV test kit (assure HEV IgM Rapid test by MP diagnostics). Those with acute hepatitis due to HEV infection were enrolled as a study case. Demographic and clinical information of the cases were obtained. Management of the cases was done as per the respective institutions protocol. Induction of labor was done only for obstetric indication. None of the pregnancy was terminated for acute hepatitis or ALF. Patients with acute hepatitis were given standard care. If their conditions improved, they were discharged and instructed to return for regular follow-up visits until delivery. Critically ill

patients requiring multidisciplinary care from Paropkar Maternity and Women's Hospital were referred to Sukraraj Tropical and Infectious Disease Hospital, Teku and Bir Hospital. At KMCTH, cases with ALF were managed at ICU set up in collaboration with the Department of Internal Medicine and Anesthesiology. All the cases were followed-up till discharge or death. Maternal and perinatal outcome was noted.

Gestational age was confirmed clinically. In doubtful cases, help of USG was taken. Acute hepatitis was diagnosed when a patient presented with recent onset of jaundice with total serum bilirubin level equal to or above 2 gm/dl and ALT more than 2.5 times upper limit of normal. Acute liver failure (ALF) was diagnosed when hepatic encephalopathy developed in patient with acute hepatitis within 4 weeks of onset of jaundice.¹² Hepatorenal syndrome was diagnosed when acute renal failure occurred in patient with acute hepatitis. Coagulation failure was diagnosed when there was bleeding from multiple sites (skin, mucosa, venipuncture sites, etc.) and international normalized ratio was more than 2.

Approval of the study protocol from head of departments/hospital and director of respective institutes was taken before starting this study. Only verbal consent was taken from patient, as this was just an observational study and their care was not influenced by their inclusion in the study. Data were collected, recorded and analyzed with total anonymity of the patients.

The commercial rapid HEV test kit (assure HEV IgM Rapid test by MP diagnostics) was provided to the participating institute by Walter Reed/AFRIMS Research Unit, Nepal.

Data were entered into the computer database using Microsoft Excel spreadsheet, and statistical analysis was performed. Results are presented as frequencies, percentages and descriptive statistics.

RESULTS

During the study period, total 124 cases of pregnancy with acute hepatitis was admitted, and out of this 93 (75%) cases were diagnosed to be due to HEV.

The median age of the patient was 22 with range between 17 and 36. More than 75% of the cases were from age group 25 or less.

Forty-two cases (45.16%) were primigravida, 34 (36.55%) second gravida, 15 (16.12%) third gravida, and two cases (2.15%) were gravida five.

Eighty-four cases (90.3%) were in their third trimester at the time of hospital admission, and mean gestational age of the cases were 31 week (Table 1).

Obstetric complications like antepartum hemorrhage occurred in four (4.3%), postpartum hemorrhage in 27 (29%), prelabor rupture of membrane in nine (9.7%), intrauterine fetal death in five (5.37%), and spontaneous miscarriage occurred in five (5.37%) cases (Table 2).

Of the total 93 cases, 79 delivered (53-preterm, 26-term), five cases had miscarriage, and nine were undelivered. Of these nine cases, two mother died in antepartum period and the

Table 1 Patient characteristics

Variables	Values
Median age in years (range)	22 (17-36)
Median gravida—n (range)	2 (1-5)
Mean gestational—age in week	31
<i>Trimester distribution—n (%)</i>	
First trimester	5 (5.37)
Second trimester	4 (4.3)
Third trimester	84 (90.32)

Table 2 Obstetric complication and fetal outcome

Variables	Values
<i>Obstetric complication</i>	
APH	4 (4.3)
PPH	27 (29)
PROM	9 (9.7)
IUFD	5 (5.37)
Miscarriage	5 (5.37)
<i>Fetal outcome</i>	
Total delivery	79 (84.95)
Preterm delivery	53 (67)
Still birth	9 (11.4)
Neonatal death	7 (8.86)
Live birth	63 (79.8)
Perinatal mortality	16 (20.2)

remaining seven who improved were discharged with their pregnancy continuing. Perinatal mortality occurred in 16 (20.25%) cases out of 79 deliveries of which nine were still birth and seven neonatal deaths (Table 2).

Acute liver failure occurred in 24 (25.8%), acute renal failure in eight (8.6%), coagulation failure in 52 (55.91%), and maternal mortality occurred in 18 (19.35%). Of the 18 cases of maternal mortality almost 89% of the death occurred in postpartum period. Maternal mortality was very high and occurred exclusively in the cases of ALF. Of the 24 cases of ALF, 18 (75%) had mortality (Table 3).

DISCUSSION

In this study, HEV infection was the cause of acute hepatitis during pregnancy in 75% of the cases, which is higher than the prevalence of HEV infection during pregnancy in an Indian study by Patra et al (60%).⁹ Similar prevalence (62%) was reported in Pakistan by Aziz and associate.¹³ However, a study of sporadic HEV infection in the context of multiple HEV epidemics in Kashmir reported a prevalence of 86% among pregnant patients with acute viral hepatitis.¹⁴ These difference in prevalence may be due to regional difference in HEV prevalence. Relatively high prevalence in this study is in accordance with the findings of study by Shrestha SM et al, who had reported 86% of the sporadic hepatitis in Kathmandu in their study, was due to HEV infection.¹⁵ In this study, more than 75% of the women were of age group 25 or less, which is similar to the finding of Clayson et al who had noted

Table 3 Maternal morbidity and mortality

Variables	Values
<i>Medical complication</i>	<i>n (%)</i>
ALF	24 (25.8)
Coagulation failure	52 (55.91)
Acute renal failure	8 (8.6)
<i>Total maternal mortality</i>	<i>n (%)</i>
First trimester	18 (19.35)
Second trimester	1 (5.55)
Third trimester	1 (5.55)
Postpartum	16 (88.88)
Among patient with ALF (%)	75

ALF—acute liver failure

that the rate of infection was higher in adolescent and young adults.¹⁶

Most of the cases in this study were in their third trimester, similar to the finding of Shams et al who had observed that HEV infection affected more women in their last trimester.¹⁷

Acute liver failure occurred in 25.8% of the HEV infected cases in this study, similar to the findings of Khuroo et al.¹⁸ Other studies have documented the development of ALF in 32 to 69% of HEV infected pregnant women with acute hepatitis in sporadic settings.^{14,19,20}

This study noted high rate of maternal mortality similar to the findings of several other studies.^{5,6,8,9,18,20} In previous studies from Kathmandu, maternal mortality was reported to be 23.5% in the epidemics of HEV in Nepal.¹⁵

Maternal mortality occurred exclusively in the cases of ALF, and 75% of the cases of ALF had mortality. This finding was similar to the findings of Indian studies where mortality rate of HEV associated ALF was seen to be between 52 and 74%.^{6,9,10,14} The reasons for high frequency of ALF and maternal mortality in HEV infected pregnant women are unclear. Researches are being done which suggest that diminished cellular immunity (indicated by a decrease in CD4, an increase in CD8 cell counts and lowered CD4/CD8 cell ratio), and a high level of steroid hormones that influence viral replication/expression during pregnancy may be the plausible reason for severity of the disease.⁶ In most of the cases, condition deteriorated after delivery and mortality occurred in postpartum period and reason behind this is not yet clear.

Obstetric and fetal outcome in HEV infected women is also not favorable as reported by some studies.^{9,18,20} Of the 79 deliveries in this study, 53 (67%) delivered preterm similar to the finding of Patra⁹ and A Kumar et al.²⁰

High perinatal death was also noted in this study, which was also seen in other studies.^{9,18}

The reason behind the high perinatal death is also not very clear, but vertical transmission which occurs in approximately 90% of pregnancy might be a cause.²¹ Increased rate of preterm deliveries, which was seen in this study as well as several other studies,^{9,20} also may be the contributing factor in high perinatal death.

CONCLUSION

Hepatitis E virus infection is a major cause of acute hepatitis in pregnant women with adverse maternal and perinatal outcome.

RECOMMENDATIONS

Appropriate preventive measures against HEV, mainly during pregnancy, are warranted to reduce maternal and perinatal mortality in HEV endemic country like Nepal. Provision of safe drinking water and sanitation should be given priority. Voice should be raised for commercial production of HEV vaccine which was successfully tested in Nepal.²² More research should be directed towards finding out the pathogenesis of HEV infection in pregnancy and reason for high frequency of ALF in pregnancy.

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