



HEV infection in pregnancy

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OBJECTIVE(S): To determine the prevalence of hepatitis E virus (HEV) infection in pregnancy and to study the clinical outcome of this infection.

METHOD(S): During this one year prospective study there were 40 women with viral hepatitis during pregnancy of whom 25 were HEV positive. Prevalence of HEV infection, and maternal and fetal outcomes were studied.

RESULTS : Majority of the women were primigravidas in the age group of 20-25 years. Prevalence of HEV infection was found to be 62.5% (25/40) and maternal mortality 12% (3/25). Preterm delivery was the most common outcome leading to prematurity as the most common fetal problem with the birth weight ranging from 1.6 to 2 kg.

CONCLUSION(S): Hepatitis E was the commonest etiological agent in those who had viral hepatitis during pregnancy, with preterm delivery as the commonest complication. Maternal mortality was 12%.

Key words : HEV infection, pregnancy with hepatitis

Introduction

Viral hepatitis in pregnancy has been a subject of continuing interest and controversy. Acute viral hepatitis is a systemic infection predominantly affecting the liver, and is caused by six distinct types of viruses A,B,C,D,E and G ¹. Hepatitis E virus (HEV) that has a single and positive-strand RNA genome of approximately 7,200 nucleotides is one of the major causative agents of acute hepatitis in many developing countries in Asia, Africa and Central America ². It is also an important cause of morbidity and mortality in humans. It accounts for more than 50% of acute viral hepatitis in young adults in developing countries and carries a mortality rate of 20-30% among infected pregnant women, primarily those in their third trimester ³.

The present study was undertaken to evaluate the prevalence of HEV infection in pregnant women, to assess the maternal

and fetal outcomes in women infected with HEV, to determine the maternal mortality, and to compare it with other studies.

Methods

Sixty-five pregnant women admitted to our hospital with history of jaundice from 1st July, 2004 to 30th June, 2005 were prospectively studied. Personal, family and socioeconomic history was recorded in detail. Complete physical and obstetric examination was carried out. Complete blood counts, coagulation profile, liver function tests, and renal function tests were done. Viral serology for hepatitis A,B,C,D and E was performed. Serological titer of anti HEV IgM of more than 0.458 IU was taken as positive.

All women found to be HEV positive by serology were studied for maternal and fetal outcomes. Maternal outcome was noted in terms of complications like preterm delivery, premature rupture of membranes, pregnancy induced hypertension, intrauterine growth retardation, intrauterine fetal death, hepatic encephalopathy, organ failure, sepsis, and postpartum hemorrhage. Maternal mortality was calculated and compared with that reported in other studies. Fetal outcome was assessed in terms of birth asphyxia and birth weight.

Paper received on 03/08/2005 ; accepted on 05/12/2005

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Results

In the one year of study 65 pregnant women were admitted with jaundice. Of these, 40 (61.54%) had viral hepatitis and 25 (62.5%) of them had HEV infection. Majority (15/25, 60%) of them were in the age group of 20 to 25 years, the youngest being 20 years and the eldest 38 years. The mean age was 27 ± 2 years. Majority of the women were primigravidas (48%, 12/25) (Table 1).

Table 1. Age and parity (n=25).

Age years	Parity				Total
	0	1	2	3	
20-25	11	4			15
26-30	1	3	2	1	7
31-35		1	1		2
36-38				1	1
Total	12	8	3	2	25

Table 2 gives the gestation period at admission. Majority of them (13/25, 52%), were between 29-42 weeks of gestation and two were postterm. Seventy-five percent of the women were illiterate and belonged to a low socioeconomic strata. Preterm labor was the most common outcome, seen in 14 women (56%) followed by intrauterine fetal death in seven (28%). Intrauterine growth retardation and hepatic encephalopathy were seen in five women (20%) each. Four (16%) developed multiorgan dysfunction syndrome (Table 3). Premature rupture of membranes, puerperal sepsis, postpartum hemorrhage and pregnancy induced hypertension occurred in some women. The only woman presenting during the 1st trimester aborted and so did two of the nine (22.2%) presenting during 2nd trimester. Only two women (8%) did not have any complication. There were three maternal deaths (12%) (Table 3). All these three women had the hepatitis causing fulminating hepatic failure leading to hepatic encephalopathy and multiorgan dysfunction. Prematurity was the commonest morbidity in babies. Five of the 15 babies born alive after 26 weeks of gestation (33.3%) had moderate birth asphyxia with apgar score of < 7 at 1 and 5 minutes. The birth weight of the babies ranged from 1.6 to 2 kg. Table 4 compares the maternal mortality in HEV infection reported by various authors.

Table 2. Gestation period at admission.

Gestation Period (weeks)	Number
<12	1
12-24	4
25-28	5
29-36	11
37-42	2
>42	2
Total	25

Table 3. Maternal complications.

Complications	Number
Preterm labor	14
Intrauterine fetal death	7
Intrauterine growth retardation	5
Hepatic encephalopathy	5
Multiorgan dysfunction syndrome	4
Postpartum hemorrhage	3
Abortion	3
Maternal death	3
Premature rupture of membranes	2
Puerperal sepsis	2
Pregnancy induced hypertension	1
No complication	2

Table 4. Incidence of maternal mortality in HEV infected pregnant women.

Authors	Maternal mortality
Hussaini et al (1997) ⁷	20%
Beniwal et al (2003) ¹	39.1%
Kumar et al (2005) ⁵	27%
Present study	12%

Discussion

HEV is the major cause of acute, endemic non-A, non-B (NANB) hepatitis in the world, and occurs primarily in underdeveloped countries. It is spread by the feco-oral route, and is most often transmitted by contaminated drinking water, especially after major floods ⁴.

HEV infection is an important cause of morbidity and mortality in humans and is the commonest cause of hepatitis in pregnancy. The reported incidence of HEV infection in pregnancy ranges from 45% to more than 50% ^{1-3,5,6}. Our study had 40 cases of acute viral hepatitis out of which 25 (62.5%) were due to HEV. This is comparable with the findings of the above mentioned studies.

HEV hepatitis has a definite impact on maternal outcome. More than 90% of the women in our study had at least one obstetric complication. Preterm delivery (56%), intrauterine fetal death (28%), intrauterine growth retardation (20%), and fulminant hepatitis leading to encephalopathy (20%) and multiorgan dysfunction syndrome (16%) were the main complications. Majority of the women were in their third trimester, most of them being primigravidas in the age group of 20 to 25 years. Similar obstetric complications have been reported by Kumar et al ⁵, in whose study most of the women

were primigravidas presenting at 32-34 weeks and preterm delivery occurred in about two thirds while intrauterine growth retardation, premature rupture of membranes, placenta previa, retained placenta, and fulminant hepatic failure leading to hepatic encephalopathy were the other complications.

It was also observed in our study that 75% women were illiterate and belonged to low socioeconomic class, living in areas with poor sanitation. This accounts for a higher prevalence of HEV infection in these women. Malnutrition superimposed on the normal demands of pregnancy and inversion of T and B lymphocytes in early pregnancy have been postulated to be the contributing factors¹. HEV causes a more severe disease than hepatitis A virus, with mortality rates of 1-2% during epidemics⁴, and of 20-30% in pregnant women. Our study had a maternal mortality of 12% which compares well with that in other reported series (Table 4).

Prematurity was the commonest fetal outcome seen. Moderate birth asphyxia with an apgar score of <7 at 1 and 5 minutes was seen in one third of the babies born in the 3rd trimester. Average birth weight of these babies ranged between 1.6 and 2 kg. No other morbidity and mortality was noted. This could be attributed to an increased incidence of preterm deliveries.

It is not yet clear if infection with HEV confers lifelong immunity. No antiviral therapy has proved to be effective against HEV in vivo. Preliminary studies in cell cultures suggest that ribavarin and interferon alpha may have anti-

HEV activity⁴. However, a vaccine has been developed by recombinant technology and preliminary results of the first administration in man conducted in the US at Walter Reed Army Institute of Research indicate that the vaccine is safe and immunogenic³.

Conclusion

Hepatitis E virus account for 62.5% of viral hepatitis during pregnancy. It has 12% maternal mortality and high maternal morbidity. Premature delivery is the commonest fetal problem.

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