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ORIGINAL ARTICLE

Materno-Fetal Outcomes with Viral Hepatitis in Pregnancy

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Abstract

Objective To evaluate materno-fetal outcomes in pregnant women with jaundice.

Methods A prospective study was conducted over a period of 6 months in a tertiary care hospital of Delhi, India. 82 pregnant women with jaundice were included. The serum was screened for viral markers, liver function tests, and coagulation status.

Results The mean age of women was 27.3 ± 4.3 years. 43.9 % ($n = 36$) women were HEV positive, 36 % ($n = 27$) HBsAg positive, 4 % ($n = 3$) HAV positive and 1.3 % ($n = 1$) HCV positive. Intrahepatic cholestasis was diagnosed in 10.8 % ($n = 8$) of women. Maternal morbidity was evaluated in terms of chorioamnionitis (5.4 %, $n = 3$), encephalopathy (26.8 %, $n = 15$), and coagulopathy (67.9 %, $n = 38$). There were five maternal deaths, and all were unbooked with HEV-positive status and a bilirubin >15 mg/dl with deranged coagulogram and encephalopathy and IUDs. 79 women delivered vaginally, and three had cesarean section. Of the vaginal deliveries, 59.8 % ($n = 49$) went into spontaneous labor, and 25.5 % ($n = 21$) were induced for varied reasons (BPS < 6/10 (38 %, $n = 8$)) and progressive derangement of LFT (38 %, $n = 8$). Among the 71 deliveries, 29 (40.8 %) were IUD and 42 (59.1 %) were live born. On analyzing the morbidity data, it was found that HEV-positive women (deranged coagulogram 71.05 %, IUD 75.86 %, encephalopathy 80 %) had a poorer outcome as compared to their HBsAg positive counterparts (deranged coagulogram 10.52 %, IUD 13.79 %, encephalopathy 6.66 %).

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Conclusion Urgent redressal of issues pertaining to sanitation and provision for clean drinking water for citizens of India is the need of the hour as HEV is fecooral in transmission.

Keywords Hepatotrophic viruses · Pregnancy · Hepatitis E · Hepatitis B · Fecooral transmission · Coagulopathy · Encephalopathy

Introduction

Opinions differ over the materno-fetal outcomes of pregnancy associated with acute viral hepatitis (AVH) [1–7]. Observations from developed countries show that pregnant state per-se has no adverse effect on the course of hepatitis, provided the nutrition is adequate [5–7], though many groups from the developing countries have reported increased maternal and fetal mortality [2, 3].

Viral hepatitis is a major public health problem in India which is hyperendemic for hepatitis A virus (HAV) and hepatitis E virus (HEV). In pregnancy, greater morbidity and mortality of hepatitis, especially during epidemics, have been noticed as a consequence to poor prenatal care and maternal nutrition [1–3, 8–11].

The epidemiology of sporadic AVH and its association with pregnancy have not been well elucidated, though HEV-mediated hepatitis during pregnancy was assumed to lead to severe disease with poor prognosis in India [2, 8]. The reason for increased incidence and severity of hepatitis E in pregnancy is not known. In view of the above-stated facts, we planned to study the incidence of hepatitis caused by different viral agents, the patient profile, and the materno-fetal outcome of these pregnancies.

Methodology

This was a prospective observational study which was conducted in a tertiary care hospital of Delhi, India. All pregnant women with jaundice were recruited in the study. A total of 82 women were evaluated over a period of 6 months (Jan 2011–June 2011). Cases of severe pre-eclampsia with HELLP, Acute fatty liver, and drug hepatitis were excluded. After admission, all patients had a thorough history and clinical examination. The period of gestation was calculated on the basis of last menstrual period (LMP) and early ultrasound which ever was available. The blood sample was collected and was sent for biochemical studies for liver function test, coagulation profile, and serological tests for IgM anti-HAV, HBs antigen, IgM anti-HEV, and IgM anti-HCV using commercially available ELISA kits.

The management approach adopted was conservative with monitoring of clinical, biochemical, and hemodynamic parameters. No attempts were made to terminate the pregnancy unless otherwise indicated on the standard obstetric practices.

Criteria for diagnosis of AVH were

(1) Recent onset of jaundice in the absence of prior history of jaundice or chronic liver disease
(2) No other cause to account for jaundice
(3) Serum bilirubin >1.2 mg/dl with an increase in serum transaminases 2½ times above upper limit (normal values AST 6–18 IU/l, ALT 3–26 IU/l).

Intrahepatic cholestasis was diagnosed when otherwise unexplained pruritus and abnormal liver function test and/or raised bile acids occured in pregnancy and both resolved after delivery.

Fulminant hepatic failure (FHF) was defined as the occurrence of hepatic encephalopathy in patients of AVH within 8 weeks of onset of disease. A PT INR >1.5 was taken as deranged coagulogram and mandated transfusion of blood products (FFP).

Results

During the study period, a total of 82 patients were recruited. Table 1 shows the demographic profile of these patients.

Of 82 patients, 10 (12.1 %) patients were in 2nd trimester, 71 (86.5 %) in 3rd trimester, and 1 (1.2 %) immediate postpartum, while no patient presented in the 1st trimester. Majority of our patients presented in the third trimester in both HBV and HEV groups ($n = 26$ vs. $n = 34$).

Mean bilirubin level was 8.04–9.05. The biochemical parameters are shown in Table 2.

Etiologies of AVH were HAV in 3 (4 %), HBV 27 (36 %), HCV 1 (1.3 %), HEV 36 (48 %), HAV + HEV 5 (6.66 %), HBV + HEV 2 (2.66 %), and HAV + HEV + HCV 1 (1.3 %). Intrahepatic cholestasis was diagnosed in 7 (8.5 %) of the patients (Table 3).

Maternal morbid events were analyzed in terms of FHF, coagulopathy, and fatal hepatitis. 68 % ($n = 38$) women had coagulopathy, 27 % ($n = 15$) FHF, and 6.1 % ($n = 5$) had fatal hepatitis. Of the above, 80 % of patients of FHF were HEV group as against 6.66 % in HBV group. Deranged coagulogram was present in 71.05 % of HEV versus 10.52 % in HBV group. No patient with HAV or HCV had either FHF or coagulopathy (Table 4).

Fatal hepatitis was diagnosed in five patients. All these women received no antenatal care and were HEV positive with a high bilirubin level (17.87 ± 2.10 mg/dl) and coagulopathy.

Table 1 Demographic profile

Mean age (years)	27.3 ± 4.3
Parity	
Primi	44 (53.65)
Second gravida or more	37 (45.12)
Postpartum	1 (1.21)
Status	
Booked	14 (17)
Unbooked	68 (83)

Table 2 Biochemical characteristics

Parameter	Mean ± SD	Range(mg/dl)
Total bilirubin	8.04 ± 9.05	1.2–21
AST	363.66 ± 564.07	17–3,450
ALT	350.30 ± 433.26	36–1,740

Table 3 Viral markers

Etiology	No. of patients (%)
HAV	3 (4)
HBsAg	27 (36)
HCV	1 (1.3)
HEV	36 (43.9)
HAV + HEV	5 (6.66)
HBsAg + Anti-HEV	2 (2.66)
HAV + HEV + HBsAg	1 (1.3)

Table 4 Maternal morbidity

	HAV	HBV (%)	HCV	HEV (%)
FHF	–	6.66	–	80
Coagulopathy	–	10.52	–	71.05
Maternal death	–	–	–	5

Table 5 Neonatal outcome

	HAV ($n = 3$) (%)	HBV ($n = 27$) (%)	HCV ($n = 1$) (%)	HEV ($n = 36$) (%)
Preterm	33.3	40.62	100	31.2
IUD	–	17.24	–	68.9

Although a conservative policy was adopted for these patients, 59.8 % ($n = 49$) went into spontaneous labor and 25.5 % ($n = 21$) patients were induced for varied reasons (BPS < 6/10—38 %, oligohydramnios—3.8 %, and progressive derangement of LFT—38 %). 67 patients delivered vaginally, whereas three had cesarean section (two in the induced group and one in the spontaneous group). Table 5 elicits the percentage of preterm and intrauterine deaths among various hepatic viral agents.

Discussion

In this prospective study of 82 pregnant women with jaundice and AVH admitted to a tertiary care hospital in Delhi, we found that HEV infection accounted for 43.9 % of cases. FHF, maternal mortality, obstetric complications, and adverse fetal outcomes were more in the HEV subgroup as compared to AVH caused by other hepatic viruses.

Materno-fetal outcome in pregnancies complicated with AVH has been a matter of considerable debate with studies from developed and developing countries showing conflicting results [5, 7, 8]. The plausible cause of this difference may be related to the differing etiologies of AVH and FHF in these countries.

The etiology of AVH in developed versus developing countries is HAV 40 versus 4 %, HBV 30 versus 22 %, HCV 25 versus 9 %, and HNAE 2 versus 25 % [12, 13]. The incidence of HAV, HCV, HAV, and HEV co-infections was low in our study, which is similar to the study by Jaiswal et al. [14].

Hepatitis E in the developed world is seen as an imported disease usually in travelers from endemic and constitutes <1 % of all cases of sporadic AVH, though it is as high as 40 % in the third world countries. In our study, HEV as cause of jaundice and AVH were seen in 43.9 % of cases. This is in congruence with the observation of Jaiswal et al. from India and Aziz et al. from Pakistan, who reported an incidence of 58 and 62 %, respectively, for the same [14, 15]. The rate of FHF in the present study was 68 %. Our observation that HEV was associated with FHF in higher proportion of cases is supported by various studies. Jaiswal et al. [14] found that FHF was more common in pregnancy than in nonpregnant state lending support to the fact that pregnancy increases the severity of HEV infection and not susceptibility to the virus. Similar results were reported by Khuroo et al. [2] in which forty-seven (61.8 %) of the 76 pregnant women developed FHF, 69.2 % in HEV group, and 10 % in non-HEV group ($P < 0.001$). Thirty-four (10.1 %) nonpregnant women developed FHF, 10 % in HEV group, and 9.7 % in non-HEV group ($P = 0.86$).

Furthermore, the mortality among pregnant women with FHF progressively increased with gestational age and appeared to be maximum in the third trimester, and was exclusively limited to the HEV subgroup; these observations are similar to those reported by Khuroo et al. [2] and Mirghani et al. [10] suggesting that HEV in pregnancy is an explosive disease. An important observation made in the present study was the occurrence of coagulopathy more so in the HEV-positive women (71.05 %) vis-à-vis HBV-positive group (10.52 %), which was in correlation with those reported by Khuroo et al. [12].

Not many studies have reported fetal outcomes in pregnant women with AVH. Of the 70 deliveries in our study, 76.1 % were preterm of which 68 % went into spontaneous labor, though preterm delivery was noted to be slightly higher in the HBV group compared to the HEV group (40.62 vs. 31.25 %) which was not statistically significant. Other studies have shown preterm rates varying between 65 and 70 % [16, 17]. Intrauterine deaths also have been reported more in the HEV group in various studies including our study [18].

To summarize, HEV was the most common hepatotrophic virus associated with FHF, maternal mortality, and adverse obstetric and fetal outcomes. Urgent redressal of issues pertaining to sanitation and provision for clean drinking water is the need of the hour in developing countries as HEV is fecooral in transmission. Further research is needed to determine how best these adverse outcomes can be prevented.

Compliance with ethical statement and Conflict of interest It was an observational study, and patients were managed according to the routine obstetric and hospital protocol so the ethical committee clearance was not sought. The authors has no conflict of interest.

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