ORIGINAL ARTICLE

Fetomaternal Outcome with Hepatitis E in Pregnancy

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ABSTRACT

Objective: To assess the maternal morbidity and mortality and fetal outcome with hepatitis E (HEV) in pregnancy.
Study Design: Cross-sectional study.
Place and Duration of Study: Liaquat National Hospital, Karachi, from May 2008 to April 2010.
Methodology: Thirty patients admitted at Gynae Ward with serologically proven HEV in pregnancy were included in the study. All these patients were followed during their hospital stay with liver function tests and coagulation profile. Maternal morbidity and mortality and fetal outcome were recorded.
Results: Maximum maternal morbidities were noted in patients who presented in 3rd trimester, both clinically and derangement of haematological and biochemical tests. Out of 30 patients, 08 patients expired with maternal mortality rate of 29.3% and rest were discharged safely. Perinatal mortality rate was 30.3 per 1000 live births.
Conclusion: Hepatitis E runs a fulminant course during pregnancy with very high mortality rate especially during third trimester and postpartum period.

Key Words: *Hepatitis E. Maternal mortality. Perinatal mortality. Fulminant hepatic failure.*

INTRODUCTION

Hepatitis in pregnancy presents challenging disease to the obstetrician. Most Asian countries have a high birth rate and a large pool of hepatotropic viruses causing hepatitis in pregnancy. Pakistan is endemic for all types of hepatitis and both epidemic and sporadic forms have been reported. Of the five viruses known to cause viral hepatitis, A and E are water borne agents, the infection being usually acquired by drinking fecally contaminated water.[1] Pakistan is a developing country with generally low socioeconomic and poor hygienic conditions.[2] Hepatitis E is also an enterically transmitted infection and occurs in epidemics in South East Asia and other developing countries. Infection occurs in epidemics during summer months and rainy seasons. It is self limiting illness having good prognosis except in pregnant women where mortality can reach upto 20%.[3]

Person-to-person transmission from patient with epidemic and sporadic Hepatitis E is uncommon for unknown.[4] Transmision of HEV from mother to fetus and through transfusion of HEV infected blood has been shown to occur.[5] The disease was first recognized in the Indian subcontinent in 1950. Pregnancy is associated with high levels of steroids hormones. These steroid hormones may promote viral replication. It also has a direct inhibition on hepatic cells, which may predispose to hepatic dysfunction and failure when exposed to infectious pathogens. Steroid hormones are immuno-suppressive. These immunological changes include down regulation of p65 component of NFkB with a predominant Th2 bias in the T-cell response along with host susceptibility factors, mediated by HLA expression.[6]

Viral hepatitis in pregnancy has been a subject of continuing interest and controversy as both the incidence and severity in pregnancy vary widely around the world. In Western Europe and North America, the incidence is as low as one in 20,000 whereas in the Middle East, Africa and India, the reported incidence is around 3.0%. Fulminant hepatic failure is also more common in pregnancy than in non-pregnant women with hepatitis.[8] Reason for the difference in the outcome of HEV in different geographical areas remain unclear,[7] but could be the result of early childhood HEV exposures, producing long lasting immunity and or modify subsequent responses to exposure to the virus. Alternatively, the predominant HEV genotype(s) in some geographical location could be less virulent than those in others.[9]

This study was conducted to determine the frequency of Hepatitis E in pregnancy, its clinical presentation, maternal morbidity, mortality and perinatal outcome.

METHODOLOGY

After approval by institutional ethical committee, this study was carried out on the pregnant women admitted at Liaquat National Hospital, Karachi, from May 2008 to April 2010. All pregnant women admitted at Liaquat National Hospital, Karachi, either booked or unbooked with serologically proven HEV alone or in combination

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with other viral types were included in the study. All patients having hepatitis i.e. A, B, C other than HEV were excluded.

Diagnosis was made on clinical presentation i.e. jaundice, vomiting, loss of appetite, altered sensorium, baseline investigations i.e. complete blood count and liver function tests, prothrombin time, APTT and serological tests including anti-HEV, anti-HAV, anti-HCV and HbsAg. All these patients were followed during their hospital stay regarding pregnancy status, either continued or terminated, mode of termination, either induced or spontaneous onset of labour, any complication including obstetrical, medical and surgical were noted, maternal and fetal morbidity was recorded and maternal mortality and perinatal mortality rate were calculated. Data was analyzed on Statistical Package for Social Sciences (SPSS) version 12 and expressed as descriptive statistics.

RESULTS

Thirty patients were admitted in hospital during the study period, with mean age of 29.71 ± 5.3 years. Patients presented at different gestational ages with maximum during 3rd trimester and postpartum period as mentioned in Table I. Termination of pregnancy was done according to the gestational age (Table I). All patients presented with yellowish discolouration of sclera and generalized weakness; 33.3% patients presented with altered sensorium and vomiting each, 66.6% with loss of appetite, 16.6% with upper abdominal pain, 10% with preterm labour pains and 3.33% with generalized itching. Different maternal mortalities were noted and 18 patients (60%) required ICU care, 8 patients expired with maternal mortality rate of 29.3% and rest were discharged home safely, while perinatal mortality rate was 30.3 per 1000 live births. All these patients were serologically proven Hepatitis E, while 03 were anti-HCV RNA positive and 02 were HbsAg positive along with anti-HEV. Haemoglobin of these patients was between 6 – 12 g/dl with mean value of 9.33 ± 1.5 g/dl. Platelets ranged between 30 – 306 x 10^9/L with mean of 157 ± 82.4 x 10^9/L. Prothrombin time was between 10 – 93 seconds with mean volume of 28.57 ± 24.9 seconds, APTT ranged between 22 – 120 seconds with mean volume of 44.67 ± 24.3 seconds. Serum bilirubin of these patients varied between 1 - 49 mg/dL with mean of 13.83 ± 11.62 mg/dL, SGPT ranged 24 – 1933 IU/L with mean value of 602 IU/L. Maximum derangement of haematological and biochemical tests was noted in patients who presented during third trimester and postpartum.

Table I: Patients' age and gestational age.

Class interval	Frequency	Percentages
Age of patients in years		
22-27	12	40.00%
28-33	11	36.67%
34-40	7	23.33%
Total	30	100.00%
Gestational age (weeks)		
0-12	2	6.67%
13-26	3	10.00%
27-40	15	50.00%
Postpartum	10	33.33%
Total	30	100.00%

Table II: Fetomaternal outcome.

Morbidity	Frequency	Percentages
Maternal morbidity		
Postpartum haemorrhage	9	30.00%
DIC	7	23.33%
Hepatic-encephalopathy	8	26.67%
DIC-APH	1	3.33%
Maternal outcome		
Recovered	22	73.33%
Maternal Mortalities	8	26.67%
Total	30	100.00%
Mode of termination of pregnancy		
Induction of labour (followed by SVD)	3	10.00%
Preterm SVD	19	63.33%
Lower segment c/section	3	10.00%
Hysterotomy	1	3.33%
D and E	1	3.33%
Conservative management	3	10.00%
Total	30	100.00%
Fetal outcome		
Alive / healthy	17	56.67%
Intrauterine deaths	4	13.33%
Neonatal deaths	5	16.67%
ERPC done	1	3.33%
Conservative management	3	10.00%
Total	30	100.00%

DISCUSSION

Hepatitis E virus (HEV), is a single stranded RNA virus of the hepeviridae family, is an emerging infectious disease of global importance.[10] It is a public health problem in several countries of the world where safe drinking water is a problem. HEV infection occurs most frequently in rainy season. The disease affects mainly young adults in the age of 15 – 40 years which is in accordance with this study as 70% patients were between the age of 22 – 30 years and 30% were between 31 – 40 years. The course of disease during epidemics has increased incidence and severity in pregnant women.[11]

Kumar *et al*. observed that two-third of the pregnant women with HEV had preterm deliveries,[12] which is consistent with our results as 20 patients (66.6%) had preterm deliveries between 25 – 35 weeks of gestation. Better maternal outcome was noted in those patients whose pregnancy was terminated earlier irrespective of gestational age.

Fifty percent patients presented during the third trimester and maximum morbidities were noted in this group, which is consistent with the study of Jaiswal *et al*. where 50 and 51% HEV infected pregnant females developed fulminant hepatic failure during second and third trimester respectively in comparison to 16.66% females developing during first trimester. This shows increasing incidence of fulminant hepatic failure with increasing gestational age.[13]

Begum *et al*. proved that prevalence of HEV was found to be much higher in third trimester of pregnancy, 30.3% compared with 25.0% in second trimester.[14] This is consistent with the study as 33.3% patients presented in third trimester and 20% in second trimester. It is a potential disaster for mother and child.

HEV infection during pregnancy is fulminant and fatal especially if it occurs in third trimester. The mortality in the second trimester is around 20% and reaches upto 45% in the third trimester[11] which is consistent with the present study in which maternal mortality was 29.3% and 30.3% perinatal mortality rate and all mortalities noted were between third trimester and postpartum period.

Kumar *et al*. reported that the mortality rate among HEV positive pregnant women was 26.9%. Vertical transmission was observed in 33.3% and had severe forms of hepatitis in third trimester of pregnancy, hepatitis E in pregnancy is associated with high rates of preterm labour and mortality.[12] Begum *et al*. reported 22.2% fatality rate with maximum severity during 3rd trimester 44.4% which is comparable with this study.[14]

Patra *et al*. in New Delhi reported 15-20% maternal mortality rate in pregnant patients with HEV.[15] Nassim *et al*. reported 30% mortality rate as compared to 1% in general population.[16] Banait *et al*. in Mumbai reported 69% perinatal mortality and 54% maternal mortality in HEV in pregnancy which is much higher than our results.[17] Beniwal *et al*. reported mortality rate in the range of 30.0 – 45.0% and may be as high as 70.0%.[18] Saeedi *et al*. reported 20% mortality rate in pregnant patients with HEV.[3] Aliya *et al*. in Pakistan reported 14 – 25% mortality rate and 30% perinatal mortality rate in patients with HEV in pregnancy, especially during 3rd trimester.[1] Ahmed reported 25% maternal mortality rate and 17.8% intrauterine deaths in pregnant HEV positive mothers.[19] Shukla reported 33.3% maternal mortality rate in patients with hepatitis E in pregnancy.[20]

The main limitation of this study was its small sample size.

CONCLUSION

Acute hepatitis E in pregnant women had high mortality rate, especially in those who present with higher grades of encephalopathy. Better maternal outcome was noted in those patients who were terminated earlier irrespective of gestational age.

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