DOI: https://doi.org/10.53350/pjmhs211551341

ORIGINAL ARTICLE

Maternofetal Outcomes of Acute Hepatitis E in Pregnancy; A Cross Sectional Study

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ABSTRACT

Objective: To identify the maternofetal outcomes of Acute Hepatitis E in Pregnancy

Methods: A cross-sectional study was conducted at the Obstetrics and Gynecology Department of Services Institute of Medical Sciences, Lahore. It included 41 women with gestational age ≥32 weeks, singleton pregnancy, presenting with Hepatitis E infection. Their demographic and pregnancy-related characteristics were included. Maternal and fetal outcomes were assessed. Data was entered and analyzed using SPSS v.25.

Results: Mean age of the participatns was 27.12 ± 3.85 years; the mean gestational age was 31.00 ± 6.15 weeks. Thirty one patients (75.6%) were admitted through the emergency. Twenty four (58.5%) needed packed cell transfusion and 32 (78%) needed fresh frozen plasma transfusion. Eleven patients (26.8%) developed hepatic encephalopathy and all of them required intensive care admission. The maternal mortality rate was 4 (9.8%). Thirty eight (92.1%) pregnancies were viable at the time of arrival. The fetal mortality rate was 7 (17.1%).

Conclusion: HEV infections significantly contribute to materno-fetal morbidity and mortality. Screening for and monitoring HEV infection earlier during the pregnancy should be of primary public health importance. Improving awareness in women of childbearing age regarding HEV transmission and its adverse fetal effects should be prioritized.

Key words: Hepatitis E virus, Maternofetal Outcomes, pregnancy, Childbearing age

INTRODUCTION

Hepatitis E virus (HEV) comprises genetically diverse strains which are included in the Hepeviridaefamily. HEV has eight genotypes; of which the first four are the strains majorly associated with human infections. Genotypes 1 and 2 are transmitted through the feco-oral route and only infect humans. Genotype 3 and 4 are transmitted through undercooked pork/boar meat consumption and are zoonotic (1,2).

HEV-related hepatitis has an annual incidence of 20 million, according to figures from World Health Organization (WHO). In a recent report from WHO, there were 44,000 HEV-related deaths which accounted for 3.3% of all viral hepatitis-related mortalities (3). Commonly, HEV is known to cause a mild self limiting acute hepatitis in immunocompetent individuals – with non-specific signs and symptoms such as diarrhea, headache, jaundice, fatigue – and chronic hepatitis in immunosuppressed ones. It also has extrahepatic presentation including neurological, renal, and hematological manifestations (4). Studies have, additionally, reported a higher incidence of HEV during pregnancy; especially in developing countries. It has a mortality rate as high as 25% – 30%, particularly in the last trimester of pregnancy (1,5).

HEV infection complicating pregnancies has been seen in as many as 47.4% – 84.3%of women (6). These infections may range from mild asymptomatic to fulminant hepatitis which can cause mortality in up to 25% of women (7). Although the mechanism of fulminant HEV infectionduring pregnancy remains unclear, decreased ratio of CD4/CD8 and expression of progesterone receptors, and increased levels of stress hormones, interleukins, and viral load seem to be pertinent (8). Pregnancy-related HEV infectionis also associated with severe adverse maternal and fetal outcomes; particularly in developing countries. It may be due to viral variants, virulence, or host factors such as nutritional deficiencies and delay in healthcare reception (9).

Complications seen in pregnancy-related HEV infection include preterm labor, post-partum hemorrhage (PPH), and maternal and fetal mortality (10-12). Third trimester infections are more likely to progress to fulminant hepatitis and result in hepatic encephalopathy and acute liver failure. A multi-center study conducted across Pakistan in 2015 reported a 0.19% prevalence of HEV infectionduring pregnancy. It reported a maternal mortality rate in HEV-positive pregnant women as 14% and a fetal mortality rate of10% (10).

In the pregnant population, HEV infection is a significant complication; more severe than in general populations. However, scientific knowledge is limited – especially from developing and low resource countries. The existing information on maternal and fetal outcomes is contrasting. Hence, a cross-sectional study was conducted with pregnant women in Lahore to assess the adverse outcomes of HEV infection during pregnancy in mother and child.

METHODS

This was a cross-sectional study conducted at Obstetrics and Gynecology Department of Services Institute of Medical Sciences, Lahore from March 2019 to February 2020. A total of 41 cases were registered in the specified time duration. Pregnant females with gestational age ≥32 weeks (on dating scan), singleton pregnancypresenting with Hepatitis E (confirmed cases by IgM antibodies) were

included. Women who had any other liver-related issue or viral hepatitis, women with multiple gestations (assessed through USG), and fetal anomalies (assessed through USG) were excluded from the study. Ethical approval was taken from the Institutional review board of the hospital. Written and verbal informed consent was taken from each woman and the study procedure was explained.

In addition to laboratory information collected from the patient's files, they were screened for HEV IgM by taking 3 ml blood. Samples were sent to the main lab of the hospital where they were analyzed for HEV-specific IgM antibodies using indirect antibody capture, quantitative ELISA. Females were followed up until discharge and their outcomes (of both mother and fetus) along with delivery status were noted

Data entry and analysis were carried out by using the IBM Statistical Package for Social Science (SPSS) version-25. Quantitative variables were presented as mean with standard deviations while the qualitative variables were presented as frequency and percentage.

RESULTS

Based on the inclusion criteria, 41 registered pregnant females were included in the analysis. Their mean age was27.12±3.85 years and their mean gestational age was 31.00±6.15 weeks. As many as three-fourths (75%) women were admitted through an emergency with anorexia, nausea, and yellowish discoloration of eyes or skin as the most common signs at presentation. These women experienced this yellowish discoloration for a mean duration of 6.00±3.06 days.

Table 1: Characteristics of Study Population (n=41)

Patient characteristics	Frequency n (%)
Age in years, mean ± SD (range)	27.12±3.85 (19-34)
Duration of symptoms in days, mean ± SD (range)	6.00±3.06 (3-15)
Gestational age in weeks, mean ± SD (range)	31.00±6.15 (13-38)
Gravidity	
1-3	28 (68.3%)
4 or more	13 (31.7%)
Parity	
0	12 (29.3%)
1	13 (31.7%)
2 or more	16 (39.0%)
Route of admission	
Emergency	31 (75.6%)
Outpatient department	10 (24.4%)
Presenting signs and symptoms	
Anorexia	39 (95.1%)
Skin / Eye Discoloration	39 (95.1%)
Nausea	34 (82.9%)
Malaise	29 (70.7%)
Body Ache	22 (53.7%)
Fever	18 (43.9%)

Hematological Parameters of Study Population (n=41)				
	Mean	SD	Min	Max
Hb	10.33	1.69	7.2	13.9
TLC	13.86	10.49	6.5	76
Platelet	263.75	134.11	3.8	602
Bilirubin	8.80	4.46	2.5	18
ALT	1020.87	730.28	68	2580
AST	1067.12	1001.31	81	4754
PT	23.54	11.79	1.4	62
APTT	53.80	15.887	33	92

Table 2: Maternal Complications associated Hepatitis E infection (n=41)

Maternal complications	Frequency n (%)
Packed cell transfusion during / after delivery	
1-2	12 (29.3%)
3 or more	12 (29.3%)
Fresh frozen plasma transfusion during / after delivery	
1-2	10 (24.4%)
3 or more -4	22 (53.7%)
Intensive care unit admission	11 (26.8%)
Hepatic Encephalopathy	
Grade I	1 (2.4%)
Grade II	2 (4.9%)
Grade III	4 (9.8%)
Grade IV	4 (9.8%)
Induction of Labor	3 (7.3%)
Mode of Delivery	
Spontaneous / assisted / induced vaginal delivery	23 (56.1%)
Emergency Cesarean Section	18 (43.9%)
Maternal Death	4 (9.8%)

Fetal outcome in HEV infection pregnancies (n=41)	
Fetal status	Frequency n (%)
Alive on arrival	38 (92.1%)
Dead on arrival	3 (7.3%)
Fetal Death during / after delivery	4 (9.7%)
Total fetal deaths	7 (17.1%)

DISCUSSION

Hepatitis E infection is not an uncommon complication of pregnancy – especially in the last trimester. It is associated with significant morbidity and mortality, both for the mother and the baby. The prevalence data on HEV infection during pregnancy is conflicting, even in Pakistani literature. One study has reported a frequency of as low as 0.19% in pregnant females (10) as compared to 13.3% reported in another study with asymptomatic pregnant participants (13). In our study, multiparous and multigravida women were more common and anorexia, nausea, skin discoloration, and malaise were the common presentations.

In Javed et al., the mean age of HEV seropositive women was 29.2 ± 7.7 years which slightly more than the mean age in our study. Their mean gestational age was 33.46 ± 4.45 weeks which is also more than that reported in our study. Fifteen percent of women in their study were primigravida as compared to 29% in our study (10). In Asghar et al., the mean age of the women was 30.05 ± 4.94 years, mean gestational age was 35.73 ± 2.11 weeks, and 17% of women were primiparous (12). In Indian studies, the mean age of females and mean gestational age was even less (11, 14) and as many as 71% were primigravida (14).

Clinical presentation in our study sample was comparable to other reported studies. However, most of presenting complaints in our study were mild such as anorexia, nausea, and malaise as compared to other literature where women even presented with nasal bleed, bleeding gums, pruritus among other complaints (10, 14). Discolored sclera malaise was seen in all patients with 33% also presenting with vomiting, and 66% with anorexia (15). In our study,27% developed hepatic encephalopathy and all of them were shifted to ICU.In Javed et al., 14% developed hepatic encephalopathy (10). In Naru et al., 1%

developed hepatic encephalopathy (6), and in Yasmeen et al., 27% developed hepatic encephalopathy (15). Only 6% required ICU admission in Naru et al. (6) as compared to 60% in Yasmeen et al. (15) and 27% in our study. The differences in severity, complications, and outcomes have been attributed to underlying host factors such as immunocompetence and nutrition, along with viral load, genotype, and other virus-related factors (9).

The rate of maternal mortality in our study was 10% and that of fetal mortality was 17%; 10% of these were non-viable even at arrival to the hospital. This indicates a clear delay in seeking healthcare. In a recently published systematic review, the median case fatality rate for maternal, fetal, and neonatal deaths were 26%, 33%, and 8%, respectively (16). In another systematic review with 47 studies from Asia and Africa comprising of a sample of more than 3900 pregnant individuals, the case fatality risk for maternal outcomes was 21%, and that for fetal outcomes was 34%. Intrauterine fetal mortality (27%) was higher than neonatal mortality (4%) (17).

CONCLUSION

HEV infections represent an avoidable burden on antenatal healthcare. It has crucial impacts on maternal as well as fetal outcomes. Keeping in view late complications of HEV during pregnancy and high mortality in both the mother and the child, screening for and monitoring HEV infection earlier during the pregnancy should be of primary public health importance. Improving awareness in women of childbearing age regarding HEV transmission and its adverse effects on the fetus should be prioritized.

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