Original Research Article

Study of hepatitis E infection during pregnancy

Reka Sindhura[1], Akurathi Krishna Rao[2*]

[1]IIIrd Year PG, [2]Professor & HOD, Department of Obstetrics and Gynaecology, Katuri Medical College and Hospital, Guntur, Andhra Pradesh.
Email: dr.rekasindhura@gmail.com

Abstract

Background: Hepatitis E infection during pregnancy and in the third trimester, especially with genotype 1, is associated with more severe infection and might lead to fulminant hepatic failure and maternal death in up to 15% to 20% of cases. The various maternal complications associated with viral hepatitis are preterm labour, obstetric haemorrhage, fulminant hepatitis, hepatic encephalopathy, renal failure, DIC and death. The various foetal complications are intrauterine death, prematurity and risk of vertically transmitting the hepatitis infection5. Hepatitis E during pregnancy is also associated with prematurity, low birth weight and an increased risk of perinatal mortality6. We planned present study to evaluate maternal and fetal outcome in cases of hepatitis E infection during pregnancy. **Material and Methods:** Study design was prospective observational type, conducted in department of obstetrics and gynaecology, Katuri Medical College and Hospital, Guntur. All pregnant women presenting at any gestational age with icterus were systematically assessed for hepatitis virus infection by serologic analysis and patients with Anti-HEV IgM-positive test were included. **Results:** After applying inclusion and exclusion criteria, total 66 patients were included in present study. Most patients were less than 25 years age group (56 %), primigravida (62 %) and HEV diagnosed in third trimester (55 %) or postpartum (24 %). Most patients with HEV delivered, but 10 remain undelivered. Most patients delivered pre-term (55 %), vaginally (82 %). Common maternal complications were post-partum haemorrhage (29%), fulminant hepatic failure (24%), hepatic encephalopathy (14%), DIC (8%), thrombocytopenia (18%), acute renal failure (3%). Maternal mortality was 27%. Foetal outcome was normal in 29 % babies. We noted 17% intrauterine death and 18% early neonatal death (18%) in our study. **Conclusion:** Hepatitis E infection during third trimester is associated with severe maternal and neonatal mortality and morbidity. Early diagnosis and proper treatment can reduce morbidity and mortality. While disease burden can be lessened by ensuring better sanitation and provision of clean drinking water for pregnant women.

Key Word: hepatitis E virus, viral hepatitis, jaundice in pregnancy.

[*]**Address for Correspondence:**
Dr. Akurathi Krishna Rao, Professor & HOD, Department of obstetrics and Gynaecology, Katuri Medical College and Hospital, Guntur.
Email: chandavathupadma@gmail.com

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INTRODUCTION

Hepatitis E virus (HEV) is a major cause of enterically transmitted non A non B hepatitis in many developing countries and most importantly, high mortality rates have been reported for HEV related infection during pregnancy[1]. Hepatitis E virus (HEV) is a hepatotropic single-stranded RNA virus causing acute viral hepatitis worldwide. Each year more than 20 million estimated cases of HEV infection occur globally, resulting into more than 55, 000 deaths[2]. Outbreaks of HEV infection of up to several hundred to several thousand persons have been reported frequently in the Indian subcontinent, China, south-east and central Asia[3]. Hepatitis E infection during pregnancy and in the third trimester, especially with genotype 1, is associated with more severe infection and might lead to fulminant hepatic failure and maternal death in up to 15% to 20% of cases. Although the mechanism of liver injury is not yet clear, it is possible that interplay of hormonal and immunologic changes during pregnancy, along with a high viral load of HEV, renders the woman more vulnerable. Immunologic changes during pregnancy promote the maintenance of the fetus in the maternal environment by suppression of T cell–mediated immunity, rendering pregnant women more susceptible to viral infections like HEV infection. During pregnancy, levels of progesterone, estrogen, and human chorionic gonadotropin increase as pregnancy advances. These hormones play a considerable role in

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altering immune regulation and increasing viral replications[4]. The various maternal complications associated with viral hepatitis are preterm labour, obstetric haemorrhage, fulminant hepatitis, hepatic encephalopathy, renal failure, DIC and death. The various foetal complications are intrauterine death, prematurity and risk of vertically transmitting the hepatitis infection[5]. Hepatitis E during pregnancy is also associated with prematurity, low birth weight and an increased risk of perinatal mortality[6]. We planned present study to evaluate maternal and fetal outcome in cases of hepatitis E infection during pregnancy.

MATERIAL AND METHODS

Study design was prospective observational type, conducted in department of obstetrics and gynaecology, Katuri Medical College and Hospital, Guntur.. Study period was 1 year (from June 2018 to June 2019). Institutional ethical committee approval was taken for present study.

All pregnant women presenting at any gestational age with icterus were systematically assessed for hepatitis virus infection by liver function tests and serologic analysis.

Inclusion Criteria

1. The serum was analyzed for IgM Anti-HEV by Rapid Immuno chromatographic Assay, and only patients with Anti-HEV IgM-positive test were included.
2. Patients delivered in our hospital, in immediate post-partum period diagnosed Anti-HEV IgM-positive test were included.

Exclusion Criteria

1. Patients with clinical evidence of jaundice due to other causes, e.g., HELLP syndrome, Hemolysis, Acute Fatty Liver of Pregnancy, Biliary tract disorders, Drug induced hepatitis, chronic liver disease, etc.
2. Post-partum patients with Anti-HEV IgM-positive test who were delivered outside.

Written informed consent was obtained from patients or from relatives for participation in present study. All patients were managed by a team of obstetricians, physicians, intensivists, and neonatologists. On admission demographic details, previous records were noted. Patients were observed for viral hepatitis symptoms such as fever, edema, ascites, paralytic ileus, nasal and gastrointestinal hemorrhage, level of consciousness, and altered sensorium. Maternal features such as gestational age at the time of first detection of infection, clinical progression of the disease, worsening or otherwise of laboratory parameters, and obstetric outcomes were noted in detail. Fetal well-being was monitored by ultrasonography and CTG. Further evaluation was done on an individualized basis. Treatment included received antibiotics, parenteral nutrition, and ventilator support, transfusion of blood and blood products as deemed necessary. All these patients were admitted and were studied regarding pregnancy status, mode of termination, and complications encountered. The decision for termination of pregnancy was taken on an individualized basis. Labor monitoring was conducted as per protocol. Data was entered in Microsoft excel sheet and analysed. Statistical analysis was done using descriptive statistics.

RESULTS

After applying inclusion and exclusion criteria, total 66 patients were included in present study. Most patients were less than 25 years age group (56 %), primigravida (62 %) and HEV diagnosed in third trimester (55 %) or postpartum (24 %).

Table 1: Characteristics of pregnant women

Maternal characteristic	No. of patients	percentage
Age Groups		
<25 years	37	56%
26-30 years	18	27%
31-35 years	9	14%
35 years	2	3%
Gravida		
1	41	62%
2	19	29%
3 or more	6	9%
HEV diagnosed during		
First trimester	3	5%
Second trimester	11	17%
Third trimester	36	55%
Postpartum	16	24%

Most patients with HEV delivered, but 10 remain undelivered. Most patients delivered pre-term (55 %), vaginally (82 %). Common maternal complications were post-partum haemorrhage (29%), fulminant hepatic failure (24%),hepatic

encephalopathy (14%), DIC (8%), thrombocytopenia (18%), acute renal failure (3%). Maternal mortality was 27%. Foetal outcome was normal in 29 % babies. We noted 17% intrauterine death and 18% early neonatal death (18%) in our study.

Table 2: Obstetrics, maternal and foetal outcome among study participants

Characteristic	No. of patients	Percentage
Mode of delivery		
vaginal	46	82%
LSCS	8	14%
instrumental	2	4%
Undelivered	10	15%
Time of delivery		
Full term	25	45%
Preterm	31	55%
Maternal morbidity		
fulminant hepatic failure	16	24%
Hepatic Encephalopathy	9	14%
DIC	5	8%
Thrombocytopenia	12	18%
Post-partum haemorrhage	19	29%
Acute renal failure	2	3%
Maternal mortality	18	27%
Foetal outcome		
Normal	19	29%
IUD	11	17%
NICU admission required	26	39%
Low birth weight (less than 2500 grams)	37	56%
early neonatal death	12	18%

DISCUSSION

Pregnancy with jaundice is considered as a high-risk pregnancy. Viral hepatitis is the most common cause of jaundice in pregnant women, acute viral hepatitis is commonly caused by HAV and HEV. Hepatitis E outbreaks are characteristically associated with a high disease attack rate among pregnant women. Further, affected pregnant women are more likely to develop fulminant hepatitis. In our study 56% of patients were below 25 years of age and 62 % were primigravida. Mean age of our patients was 23.55±3.9 yrs. Kumar *et al*[8] in his study with acute viral hepatitis in pregnancy noted mean age of patients as 24.13±3.6 yrs. Most patients were diagnosed in third trimester (55 %) or postpartum (24 %). Mishra *et al*[9] reported majority (60%) of the hepatitis E infection among Indian pregnant women in below 25 years of age. They also reported higher severity of HEV infection among primigravida and in third trimester of pregnancy. WHO also stated that in regions with high disease endemicity like India, symptomatic infection is most common in young adults (aged 15–40 years) and pregnant women, case fatality rates as high as 20–25% has been reported in their third trimester[10]. Most common mode of delivery was vaginal delivery (82 %) which is common finding in most of the studies in similar settings. 45 % preterm deliveries were noted in present study. Mishra *et al* and Jaiswal *et al* also reported approximately one third of the pregnant women with hepatitis E viral infection to deliver prematurely[9,11]. However Patra *et al* in their study had reported a higher preterm delivery rate in patients with HEV infection[12]. We noted 27 % maternal mortality in present study. Maternal death among different studies in India has been reported upto 15%- 20% of women with hepatitis E viral infection[12,13]. Patra *et al*. in New Delhi reported 15-20% maternal mortality rate in pregnant patients with HEV[12]. Banait *et al* 54% maternal mortality in HEV in pregnancy which is much higher than our study results[14]. We noted 17% intrauterine deaths and 18% early neonatal mortality. Increased neonatal mortality and morbidity is due to preterm babies. Patra el al reported stillbirth in 54% of cases while Mishra *et al* reported perinatal mortality of 24%[9,12]. Patra *et al*[12] stated that HEV infection might be responsible for 2400 to 3000 stillbirths each year in developing countries, with many additional fetal deaths linked to antenatal maternal deaths. Various immunologic and hormonal changes during pregnancy impair cellular immunity by triggering adapter protein (ORF3 of HEV), which could facilitate viral replication and lead to release of cytokines and liver cell apoptosis causing significantly higher morbidity and mortality[15]. Hepatitis E infection is usually self-limiting with overall mortality rate in FHF is 1–3%. Pregnant women are a special risk category. Pregnant women with acute hepatitis E infection have an

approximately 15% risk of FHF. The mortality rate is high, ranging from 5% to 25% in different studies. HEV infection causes mortality in up to 25% of pregnant women in the third trimester of pregnancy. Treatment is supportive only. The management should focus on treating the symptoms. The number of HAV and HEV cases and outbreaks can be prevented by improving sanitation and the quality of water. There is a need to provide intensive training to water and sanitation staff on how to prevent and contain HAV and HEV outbreaks. However, early diagnosis by high suspicion can definitely improve fetal and maternal outcome.

CONCLUSION

Hepatitis E infection during third trimester is associated with severe maternal and neonatal mortality and morbidity. Early diagnosis and proper treatment can reduce morbidity and mortality. While disease burden can be lessened by ensuring better sanitation and provision of clean drinking water for pregnant women.

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