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Original Research Article

Hepatitis E virus induced encephalopathy during pregnancy: a life threatening condition

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ABSTRACT

Background: Hepatitis E virus (HEV) infection during pregnancy has increased mortality up to 30% in the 3rd trimester.
Methods: A prospective study was conducted on the HEV positive pregnant patient with sign symptoms of encephalopathy admitted at the ICU of BRB hospital Ltd during the period of January 2018 to December 2018. During this period 26 patients were admitted. The serum of pregnant women was tested for HEV IgM by ELISA method and positive women were recruited for the study. Maternal variables such as gestational age, clinical progression, worsening of the disease, laboratory parameters, obstetric outcome, and fetal outcome were noted. All data were entered in SPSS 16 and analyzed. This study was ethically approved by the ethical review committee of BRB hospital Ltd.
Results: Among 26 HEV-positive patients, the mean age was 27.46 years. Among them 11 (42.3%) were primi and the rest were multigravida, 5 (19.2%) were in the first trimester, 9 (34.6%) were in the 2nd trimester and 12 (46.15%) were in the 3rd trimester of pregnancy.17 patients (65.4%) were housewives and 9 (34.6%) were service holders. Three patients (11.5%) were illiterate, 16 patients (61.5%) have completed primary level of education and 7 (26.9%) were completed higher level of education. Most of the patients were from middle-class families that are 18 patients (69.23%), 3 patients (11.5 %) were from poor social class, and the rest from upper social class is 5 (19.2%).
Conclusions: HEV infection during pregnancy has many serious fetomaternal complications including maternal and fetal death.

Keywords: HEV, Encephalopathy, Postpartum hemorrhage, Intrauterine fetal death

INTRODUCTION

Hepatitis E virus (HEV) is a small non-enveloped, positive-sense single-stranded RNA virus classified as member of Hepevirus structurally similar with the *Caliciviridae* and *Tombusviridae* virus families. It is a hepatotropic virus which cause minimum symptoms in healthy adults but may develop chronic hepatitis in immunocompromised patients.[1-3]

Globally around 20 million HEV infections occur every year and 70,000 died per year. Mortality is high in under-developed countries like Asia, Africa, and Latin America.[4] The HEV infection primarily occurs in young adults, usually mild and have self-limiting course. During pregnancy the mortality rate is high in the 2nd and 3rd trimesters.[5,6]

HEV is transmitted by the oro-fecal route.[7] Mother to fetal transmission of HEV is very well documented.[8]

HEV during pregnancy may cause fulminant hepatitic failure (FHF), in 2nd and 3rd trimester of pregnancy with a mortality up to 30%.[9,10] HEV infection spread to the area where sanitation system is poor.[11]

The severity of HEV infection in pregnant women is different in different region of the world. The incidence In Western Europe and North America is 1 in 20,000. Epidemics of Hepatitis E are occurring in Asia specially in India where the death rate is 1-2% which increases to 10-20% during pregnancy.[12]

METHODS

This study included HEV positive pregnant patient with sign symptoms of encephalopathy admitted in the ICU of BRB hospital during the period of January 2018 to December 2018. A prospective cross-sectional study was conducted among 26 patients who were admitted during this study period. The serum of the pregnant patient was confirmed for HEV IgM by ELISA method and positive pregnant patient were recruited.

Pregnant women with HELLP syndrome, haemolysis, acute fatty liver of pregnancy, biliary tract disorders and chronic liver disease which were the causes of jaundice were separated and excluded.

Consent taken from the relatives of the pregnant patients with HEV induced encephalopathy who were interviewed by a pre-tested standard questionnaire to collect data such as socio-demographic and causal factors. Maternal variables such as gestational age, clinical progression, worsening of the disease, laboratory findings and maternal outcomes were noted in detail. Fetal outcome also recorded.

Patients were monitored for complications of viral hepatitis like edema, ascites, paralytic ileus, nasal and gastrointestinal hemorrhage, coagulopathy, level of consciousness and altered sensorium. Fetal condition was observed by sonography and cardiotocography.

All data were entered in SPSS 16 and analyzed through it. Study was ethically approved by ethical review committee of BRB hospital Ltd.

RESULTS

In this study 26 patients were selected. Patient's age was in between 20-35 years, mean age 27.46 years. Among them 11 patients (42.3%) were primi and 15 patients (57.7%) were multigravida as shown below in the (Figure 1).

Five patients (19.2%) were admitted in first trimester of pregnancy, 9 (34.6%) were in second trimester of pregnancy and 12 (46.15%) were in third trimester of pregnancy as shown below in (Figure 2).

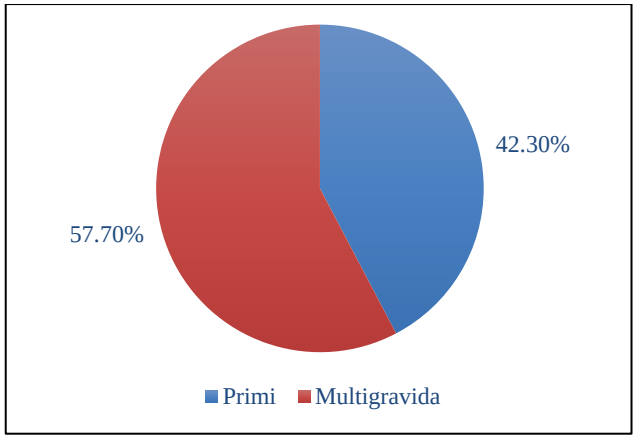

Figure 1: Parity.

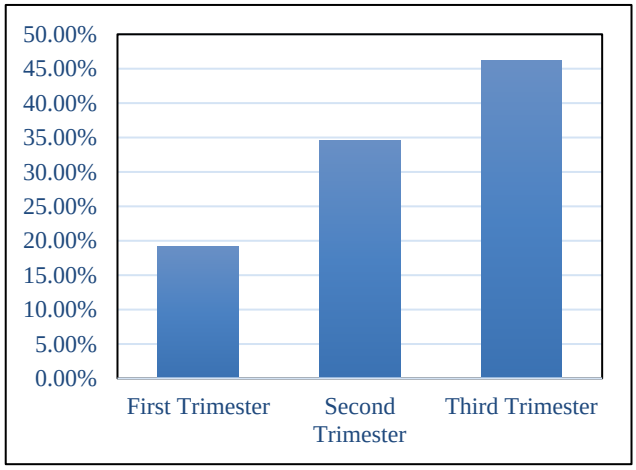

Figure 2: Gestational age.

Among 26 patients, 17 patients (65.4%) were housewife and 9 (34.6%) were service holder as shown below in (Figure 3).

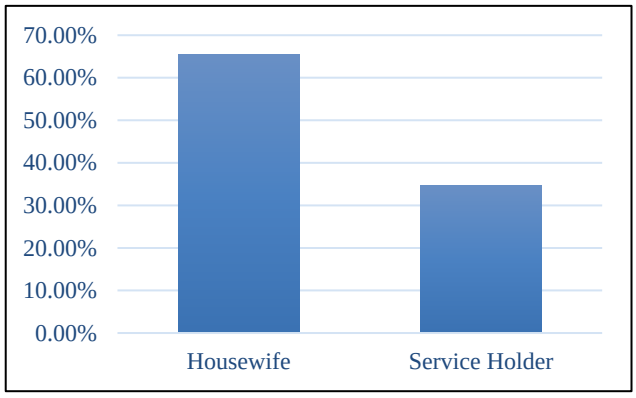

Figure 3: Profession.

Three patients (11.5%) were illiterate, 16 patients (61.5%) have completed primary level of education and 7 (26.9%) have completed secondary and higher level of education as shown in (Figure 4).

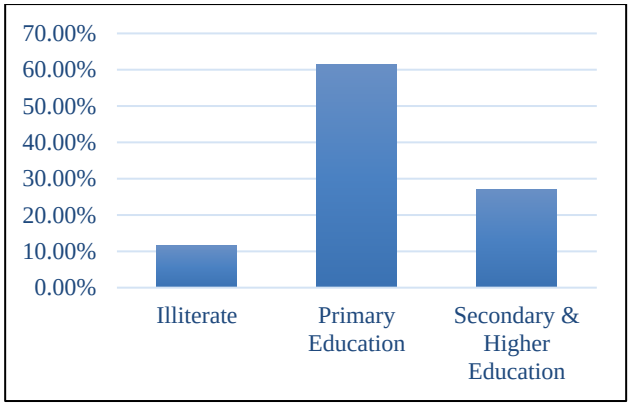

Figure 4: Academic level.

Most of the patients were from middle class family that is 18 patients (69.23%), 3 patients (11.5 %) were from poor social class and rest are from the upper social class that is 5 patients (19.2%) as shown below in (Figure 5).

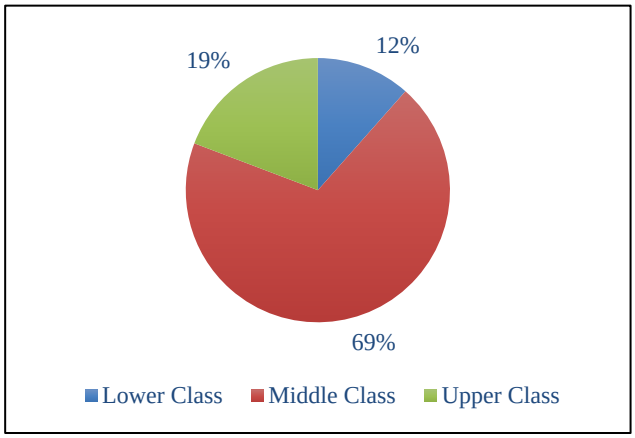

Figure 5: Family status.

From 26 patients, 15 (57.7%) patients gave history of taking street food within 2 weeks of disease. Six (23.7%) patients had poor sanitation system and lack of constant pure water supply; these people had their residence in the peripheral part of city. Rest of the patients had well-built sanitation system and constant pure water supply system (Figure 6).

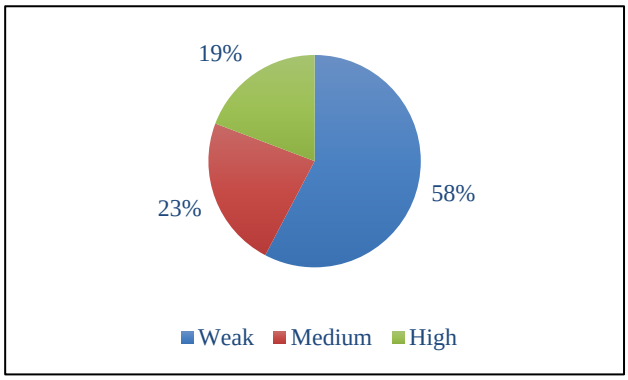

Figure 6: Food habit and sanitation system.

Among 26 patients 42.3% patients were in 20-25 yrs age, 34.6% patients were in 26-30 yrs age, 23.7% patients were in 30-35 yrs of age (Table 1).

Table 1: Age distribution.

Age (years)	Number	Percentage (%)	Mean
20-25	11	42.3	27.46
26-30	9	34.6	
31-35	6	23.7	
Total	26	100	

Among 26 patients, 7 (27%) patients had grade II encephalopathy, 16 (61.5%) patients developed grade III encephalopathy and 3 (11.5%) patients developed grade IV encephalopathy (Table 2).

Table 2: Grading of hepatic encephalopathy.

Grading of hepatic encephalopathy	Numbers	Percentage (%)
Grade I	0	0
Grade II	7	27
Grade III	16	61.5
Grade IV	3	11.5
Total	26	100

In this study we found mean hemoglobin level was 10.4 gm/dl, median leukocyte count was 10 cells×10^9/L, mean platelet count 245×10^9/L, mean serum Billirubin level 7.25 mg/dl, median SGPT 523 U/L, median prothrombin time (control 15s) was 19, median international normalized ratio 1.9, mean serum albumin level 30 g/l (Table 3).

Table 3: Laboratory findings.

Lab parameters	Reports
Mean hemoglobin level (gm/dl)	10.4
Median leaukocyte count (cells×10^9/L) (range)	10 (2.8-29)
Mean platelet count (cells×10^9/L)	245
Mean serum bilirubin level (mg/dl)	7.25
Median SGPT (U/L) (range)	523 (80-3700)
Median prothrombin time (control 15s) (range)	19 (15-53.5)
Median international normalized ratio (range)	1.9 (1-3.9)
Mean serum albumin	30

Among 26 patients 3 (11.5%) developed gastrointestinal hemorrhage, 1 (3.8%) ascites, 4 (15.5%) renal failure, 7 (26.92%) Coagulation defect, 18 (69.23%) need transfusion (blood and blood products), 3 (11.5%) ante partum hemorrhage, 11(42.3%) post-partum hemorrhage, 4(15.5%) mortality (Table 4).

Table 4: Maternal complications.

Maternal complications	Number (%)
Gastrointestinal hemorrhage	3 (11.5)
Ascites	1 (3.8)
Renal failure	4 (15.5)
Coagulation defect	7 (26.92)
Transfusion (blood and blood products)	18 (69.23)
Ante partum hemorrage	3 (11.5)
Post-partum hemorrage	11 (42.3)
Maternal mortality	4 (15.5)

This study showed 5 (19.2%) abortion, 4 (15.5%) IUFD, 7 (26.92%) live birth, 2 (7.6%) neonatal death, 8 (30.76%) continuation of pregnancy up to our study period (Table 5).

Table 5: Fetal outcome.

Fetal outcome	Number	Percentage (%)
Abortion	5	19.2
IUFD	4	15.5
Live birth	7	26.92
Neonatal death	2	7.6
Continuation of pregnancy	8	30.76
Total	26	100

DISCUSSION

In this study, the patients were young, i.e., mean age 27.46 years, which was higher in the different studies of hepatitis E infection during pregnancy.[7,12,14]

In our study most of the patient came with encephalopathy at their 3rd trimester of pregnancy. Yasmeen et al, Shrestha et al, Khruoo MS et al and Brohi et al showed that most of the patients came in 3rd trimester of pregnancy.[17-19]

This study showed level of mean serum albumin, median ALT, level of INR and level of prothrombin time were lower than the other studies done in South Asia and northern India.[14,15]

Patra et al in his study showed that the level of mean total bilirubin was 15, level of mean alanine transaminases was 90.5, level of mean prothrombin time was 58 and level of mean INR was 4.[7]

Another study showed mean total bilirubin levels was 10.54. The level of mean SGOT was 360 and SGPT levels was 471. The level of mean INR was 1.91.[16] Which was similar to our study.

In this study, medical complications such as coagulation failure found 26%, acute renal failure was 4%, GI bleeding was 11.5%. The patients were admitted in ICU and observed. Patra et al found that 79% of study population had coagulation failure and acute liver failure developed in 74% patients. Yadav`s found complications such as coagulation failure was 56%, 17% hepatic encephalopathy and 19% acute liver failure. Shrestha et al showed in her study that 24% cases were developed acute liver failure, 52% cases were developed coagulation failure and 8 % acute renal failure. Shinde et al showed that hepatic encephalopathy was commonly found during pregnancy with HEV infection.[7,16,17,20]

A study from Kumar et al has reported the incidence of Fulminant hepatic failure was 33%. Khuroos et al showed incidence of FHF was 55 %.[12,15] In our study FHF developed in 34.5% cases.

In this study four mother died who had features of FHF in 3rd trimester of pregnancy and 4 IUD were found. Maternal mortality was lower (15.5 %). The different study conducted in different region of India over the years showed maternal mortality range from 19-73%.[3,6,7,16,17,19]

In our study we found 42.3 % PPH, 11.5% APH and 15.5% IUD. Patra et al showed 23% APH, 58% IUD followed by 14% PPH and 9% PROM 7 Shrestha et al showed that PPH was 27% followed by 4% APH and 5% IUD.[17]

There was less PPH and less maternal mortality as patient was treated by fresh frozen plasma, reduced serum ammonia aggressively and kept prothrombin time below 17s prior induction and we used prophylactic intrauterine balloon by fluid filled condom in every patient after delivery.

CONCLUSION

Mortality is high among HEV induced pregnant patient with encephalopathy. In our study, we manage the patient and reduce mortality and morbidity by using FFP, by reducing serum ammonia aggressively. and by using a prophylactic condom catheter for preventing of postpartum hemorrhage. Early diagnosis and prompt management is the key for the reduction of maternal foetal mortality and morbidity. Further study is needed to assess the relationship between mortality and morbidity with HEV infection during pregnancy.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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