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Original Research Article

Acute viral Hepatitis E in antenatal women: a multicenter prospective study

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ABSTRACT

Background: Hepatitis E has poor prognosis in pregnancy and leads to 20-30% mortality in term cases. The Aim of the study was to observe the trend of maternal and perinatal outcome in acute viral hepatitis E.
Methods: A prospective study conducted in two high risk obstetric center of Jabalpur district in January 2015 to December 2017. The inclusion criteria were all antenatal women diagnosed with acute viral Hepatitis E entering to the Intensive care unit of any gestational age who later delivered in the same center. Other than acute hepatitis E all acute hepatitis cases and women missed in follow up in delivery were excluded from the study. The data collected on demographic, clinical and biochemical variables in excel sheet and descriptive analysis done by SPSS system.
Results: There were 72 antenatal women enrolled with mentioned criteria in study duration. Out of these only 67 were in follow up and alive till their delivery in the same set ups. Out of these 70.14% were Primigravida of median age 27 year. The mean gestational age at detection of hepatitis E was 30.3week. The maternal mortality observed was 17.9% (12/67) in the total study population. The high grade of mortality was significantly associated with high grade of disease. There were 19.4% (13/67) perinatal (mortality seen which included intrauterine (14.9%) and neonatal (4.4%).
Conclusions: The severity of Hepatitis and high grade of hepatic encephalopathy following poor primary care in the beginning of disease results in poor perinatal and maternal outcome.

Keywords: Acute viral hepatitis, Fulminant, Hepatitis E, Hepatic encephalopathy, Pregnancy

INTRODUCTION

Acute viral Hepatitis in pregnancy is one of the fulminant diseases may lead to severe morbidity and mortality for antenatal women and fetus. Hepatitis can be due to any of the Hepatitis viruses A, B, C, D, E or G with deranged liver function test (LFT), rise in serum aspartate aminotransferase (AST) along with clinical jaundice. In India viral Hepatitis is a major public health problem despite improving sanitation, health awareness and socio-economic conditions. Hepatitis E and A is among the hyper endemic diseases of India. Interestingly, when the virus infects pregnant women 20-30% mortality happens, and it has been implicated as an important etiological

agent for sporadic fulminant hepatic failure in developing countries.

The objective of the present study was to assess the trend of maternal and perinatal outcome in acute viral Hepatitis E in Ante natal cases (ANC'S).

METHODS

This was a prospective observational study carried out in two major high risk obstetric centers of district Jabalpur from January 2015 to December 2017.

Inclusion criteria

- All antenatal women diagnosed with acute viral Hepatitis E entering to the Intensive care unit of any gestational age with diagnosis of acute viral Hepatitis E
- All primarily enrolled cases with criteria 1 delivering in the same institute or alive till delivery.

Exclusion criteria

- The women diagnosed with acute viral Hepatitis (Hepatitis A, B, C, D, G) other than HEV infection, liver disease, HELLP syndrome (Hemolysis, Elevated Liver enzymes, and Low Platelet count) acute fatty liver of pregnancy
- Women enrolled primarily in the study but missed in their follow up at delivery
- Antenatal Hepatitis E infected who expired before delivery.

The data collected under demographic, biochemical, clinical and procedural variable and evaluated by descriptive analysis under SPSS version 17. The gestational age estimation was done by combined average age estimation from last menstrual period and ultrasonological findings.

RESULTS

There were 72 antenatal women enrolled with mentioned criteria in study duration. Out of these only 67 were in follow up and alive till their delivery in the same set ups. Two patients expired in antenatal period and three moved out to other center. Out of these 70.14% Primigravida presented to centre with median age 27 year. The mean gestational age at detection of Hepatitis E was 30.3 week. The multigravida in the study was 29.84% with median age 26.5 year. The highest admission with grade 0 HE (47.8%) and lowest in grade 3 and 4 (16.42%, 2.99% respectively) as referred case from nearby referral units. (Figure1).

Authors found most of the ANCs (50.75%) reported within three to seven days of detection of jaundice and among these large number of patients developed HE grade 0 while who were reported late to the centers developed grade 4 in 3% cases (Figure 2).

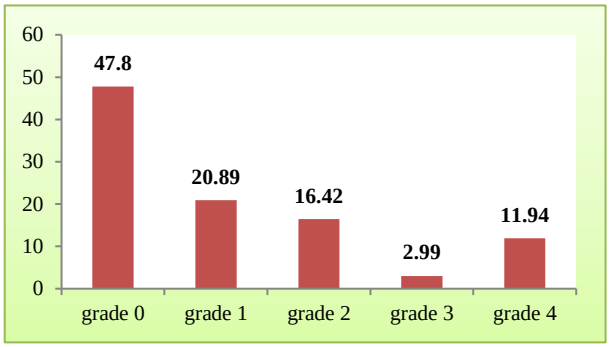

Figure 1: Grade wise distribution of hepatic encephalopathy (HE).

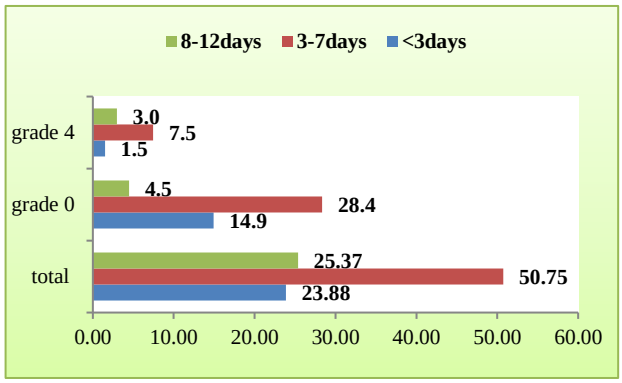

Figure 2: Duration of jaundice to development of HE.

The mean hemoglobin was 8.9 gm/dl, mean total leukocyte count was TLC 19150 cells/mm^3 and mean Platelet 172x109per liter (Table 1). Primarily the patients received with mean bilirubin of 11.1mg/dl and serum creatinine 1.1 mg/dl. Which reflects the overall population was with low grade HE at admission.

Table 1: The biochemical parameters during admission.

Biochemical parameter	Mean value
HB	8.94 gm/dl
TLC	19.15X10^3 cells/mm^3
Platelet	172X 10^9 per liter
Total bilirubin	11 mg/dl
AST	1305 IU/L
ALT	1191IU/L
Alkaline phosphates	291.15IU/L
Serum creatinine	1.1mg/dl

The severe morbidity was hepatic coma (11.94%) and disseminated intravascular coagulopathy (DIC) (7.46%) in the study population. Other morbidities were ARF (1.49%), thrombocytopenia (17.91%) and post-partum haemorrhage (8.96%) (Figure 3).

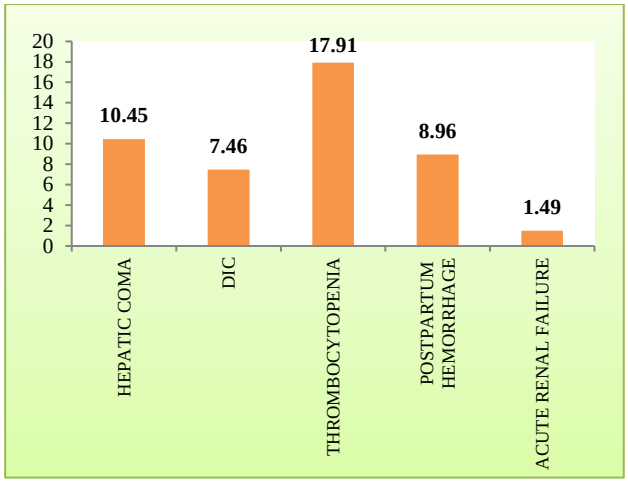

Figure 3: Morbidities in acute HEV infection.

All the women followed till delivery and their postnatal recovery in hospital. A total of 62.69 % vaginal birth took place which included 61.19% preterm delivery. LSCS was done in 35.82% cases only.

The maternal mortality observed was 17.9% (12/67) in the total study population. The mortality was significantly associated with high grade of disease. There were 19.4% (13/67) perinatal (mortality seen which included intrauterine (14.9%) and neonatal (4.4%) (Figure 4).

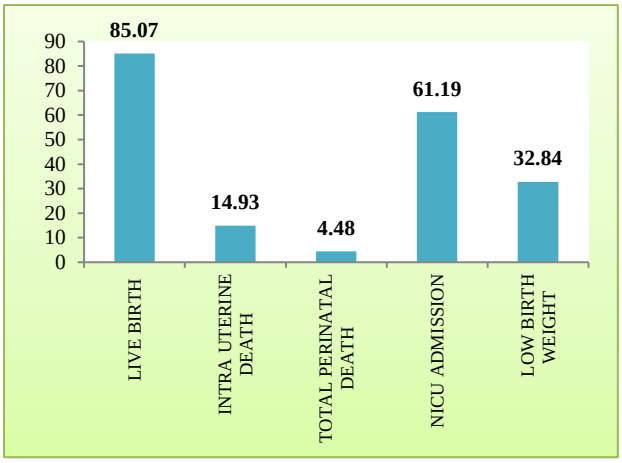

Figure 4: Perinatal outcome in acute HEV infected deliveries.

DISCUSSION

Hepatitis E virus is a water-borne pathogen transmitted by feco-oral route mostly due to contaminated water. Direct person-to-person transmission is uncommon. The incubation period ranges from 15 to 64 days with a mean of 6 weeks. The virus has a 50% rate of vertical transmission. It presents with typically unspecific, indistinguishable symptoms varying from

The age incidence varies from 21-40 year in various studies. The median age reported in previous studies was 24.1 and 23.85 similar to present study.[7] The gestational age at detection of acute HEV infection is also comparable to our study i.e. 27.5 week, 32.6 week by Wedemeyer et al and Shinde et al respectively.[7,8]

The most common clinical presentation was loss of appetite, nausea, vomiting Myalgia/arthralgia, fever, right upper quadrant pain, dark urine, light-colored stools, pruritus, diarrhea, altered sensorium and hematemesis/malena.

At the ICU admission most of the patients were in hepatic encephalopathy. Hepatic encephalopathy is a brain dysfunction caused by liver insufficiency and/or portosystemic shunt (PSS); it manifests as a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma. The impairment associated in neuropsychiatric status with HE can ranges widely from subtle, mild alteration of cognition and consciousness to coma, to severe neurodegeneration depending on the stage of the illness. The neuropsychiatric impairments associated with HE is largely reversible but complete regeneration and restoration of the brain functions may not be possible in the extreme cases of severe hepatocerebral degeneration.

The patients admitted in ICU were categorized according to the West Haven criteria (whc) classification of hepatic encephalopathy (Table 2) and we found the highest admission with grade 0 HE (47.8%) and lowest in grade 3 and 4 (16.42%, 2.99% respectively) as referred case from nearby referral units.

Amongst all HE Patients the duration of jaundice noticed by clinician to their first appearance taken as parameter for duration of Jaundice. The development of HE assessed from their admission grade.

The mean blood parameters on admission were taken as predictors for severity of disease (Table 3).

- The values compared with two previous studies and found comparable with no significant difference.
- Authors found most of the ANCs (50.75%) reported within three to seven days of detection of jaundice and among these large numbers of patients developed HE grade 0 while who were reported late to the centers developed grade 4 in 3% cases. It explains that duration of jaundice to development of HE grade matters if patient timely reports to the higher center. The shorter the duration of reporting to higher center the better the development of low grade HE.

There were most of patients with third trimester admission developed HE4 more frequently as compare to first trimester in previous studies. Since 29.85% cases hospitalized early after detection of Jaundice therefore got managed and the development of HE4 (8.9%) was less.

Table 2: West Haven Criteria (WHC) classification of hepatic encephalopathy.

WHC including MHE	ISHEN	Description	Suggested operative criteria	comment
Unimpaired		No encephalopathy at all, no history of HE	Tested and proved to be normal	
Minimal	Covert	Psychometric or neuropsychological alterations of tests exploring psychomotor speed/executive functions or neurophysiological alterations without clinical evidence of mental change	Abnormal results of established psychometric or neuropsychological tests without clinical manifestation	No universal criteria for diagnosis Local standards and expertise required
Grade I		Trivial lack of awareness Euphoria or anxiety Shortened attention span Impairment of addition or subtraction Altered sleep rhythm	Despite oriented in time and space, patient appears to have some cognitive/ behavioral decay with respect to his or her standard on clinical examination or to the caregivers	Clinical findings usually not reproducible
Grade II	Overt	Lethargy or apathy Disorientation for time Obvious personality change Inappropriate behavior Dyspraxia Asterixis	Disoriented for time (at least three of the followings are wrong: day of the month, day of the week, month, season, or year) ± the other mentioned symptoms	Clinical findings variable, but reproducible to some extent
Grade III		Somnolence to semistupor Responsive to stimuli Confused Gross disorientation Bizarre behavior	Disoriented also for space (at least three of the following wrongly reported: country, state [or region], city, or place) ± the other mentioned symptoms	Clinical findings reproducible to some extent
Grade IV		Coma	Does not respond even to painful stimuli	Comatose state usually reproducible
All conditions are required to be related to liver insufficiency and/or PSS.				

Table 3: Biochemical parameters comparison to other studies.

Lab parameters	Prasad et al	Banait et al	Present study
Mean hemoglobin level (g/l)	104	7.93	8.94
Median leukocyte count (cells × 10^9/l) (range)	11 (2.6-28)	13.2	19.4
Mean platelet count (cells × 10^9/l)	255	118	172
Mean serum bilirubin level (mg/dl)	7.85	11.5	9.5
Median SGPT (U/L)	580 (60-3800)	602	588
Median prothrombin time (control 15 s) (range)	18 (14-52.5)	8.0	19.0
Median international normalized ratio (range)	1.8 (1-3.9)		1.9
Mean serum albumin level (g/l)	32	29.0	30.0
Serum creatinine	-	1.2	1.3

There is a very high risk of preterm delivery in pregnant women with HEV infection, with poor neonatal survival rates. A total of 62.69 vaginal birth took place which included 61.19% preterm delivery.

The cause of preterm delivery was mostly oligohydramnios, PPROM, IUGR and fetal distress. This is comparable to other studies like Prasad et al, Sultana et al.[12,17]

Only 38.81% were full term deliveries. The incidence of cesarean was 35.82% in the study that too because of failed Induction, APH and Malpresentation.

Some studies quoted 4.54% to 14% LSCS for similar indication, which suggest due to the more number of grade 0 HE enrolled in present study at the end survived but with IUGR or oligohydramnios. There were 65% preterm delivery and 26.66 were delivered at term in past (80.85%) delivered preterm in Prasad et al.[12] There were 17.9% mortality in total study population, among it 33.33% were grade 4 HE. The interesting thing was the 25% mortality was in term patients who delivered and expired within 24-48 hours.

The previous studies informed that HEV infection in third trimester causes maternal mortality in up to 15% to 25% of cases by Ranger et al and 58% in acute HEV infection by Shinde et al.[8,15]

The severe morbidity was hepatic coma (11.94%), APH 12.5%, PPH 8.96% and DIC (7.46%) in the study population (Figure 3) The study by Khaskheli et al found in one cross sectional study hepatic coma in (36.36%) cases and disseminated intravascular coagulation in (63.63%) cases.[14]

Another study noticed that 21.66% DIC and APH in 20% cases, while Prasad et al quoted 7.40% PPH12.[12] Authors studied that there was more enrollment of severe grade HE as compares to present study. There were 19.4% (13/67) perinatal mortality seen which included intrauterine (14.9%) and neonatal (4.4%) death. The previous study of Sultana et al reported 26% perinatal mortality with 14 % in each group.[17] Present study result was comparable with the studies (Figure 4).[12]

Authors also study the morbidities of neonates by NICU admission rate, which was 61.19 % vs. 40.42% while 32.84% low birth weight as compare to 57 %, Prasad et al resulted in longer NICU stay.[12] The other parameters which were not significantly high in present study included respiratory distress syndrome in 16% vs 36%, asphyxia neonatorum in 37% versus 28% and jaundice in 22% versus 36%.[12]

CONCLUSION

The acute viral Hepatitis E diagnosed earlier in pregnancy results with better maternal and perinatal outcome with the advancement of gestational age the severity of disease increase and affects more to perinatal outcome as compare to maternal outcomes.

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REFERENCES

1. Aggarwal R, Krawczynski K. Hepatitis E: an overview and recent advances in clinical and laboratory research. J Gastroenterol Hepatol. 2000;15(1):9-20.
2. Acharya SK, Batra Y, Bhatkal B, Ojha B, Kaur K, Hazari S, Saraya A, Panda SK. Seroepidemiology of hepatitis A virus infection among school children in Delhi and north Indian patients with chronic liver disease: implications for HAV vaccination. J Gastroenterol Hepatol. 2003;18(7):822-7.
3. Kumar A, Beniwal M, Kar P, Sharma JB, Murthy NS. Hepatitis E in pregnancy. Int J Gynecol Obstet. 2004;85(3):240-4.
4. Nanda SK, Yalcinkaya K, Panigrahi AK, Acharya SK, Jameel S, Panda SK. Etiological role of hepatitis E virus in sporadic fulminant hepatitis. J Med Virol. 1994;42(2):133-7.
5. Khuroo MS. Viral hepatitis in international travellers: risks and prevention. Int J Antimicrobial Agents. 2003;21(2):143-52.
6. Wattré p. Hepatitis E virus. Ann Biol Clin (paris) 1994;52(7-8):507-13.
7. Wedemeyer H, Pischke S, Manns MP. Pathogenesis and treatment of hepatitis e virus infection. Gastroentrol. 2012; 142(6):1388-97.
8. Shinde NR, Patil TB, Deshpande AS, Gulhane RV, Patil MB, Bansod YV. Clinical profile, maternal and fetal outcomes of acute hepatitis e in pregnancy. Ann Medi Health Sci Res. 2014;4(8):133-9.
9. Practice guideline. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by AASLD and EASL. Vilstrup H, Amodio P, Bajaj J, Cordoba J, Ferenci P, Mullen KD et al. https://www.aasld.org.
10. Patra S, Kumar A, Trivedi SS, Puri M, Sarin SK. Maternal and fetal outcomes in pregnant women with acute hepatitis E virus infection. Ann Internal Med. 2007;147(1):28-33.
11. Krain LJ, Atwell JE, Nelson KE, Labrique AB. Fetal and neonatal health consequences of vertically transmitted hepatitis E virus infection. Am J Trop Med Hyg. 2014;90(2):365-70.
12. Prasad GS, Prasad S, Bhupali A, Patil AN, Parashar K. A Study of Hepatitis E in Pregnancy: Maternal and Fetal Outcome. J Obstet Gynecol India. 2016;66(1):18-23.
13. Yasmeen T, Hashmi HA, Taj A. Fetomaternal outcome with hepatitis e in pregnancy. J Coll Physicians Surg Pak. 2013;23(10):711-4.
14. Khaskheli MN, Baloch S, Sheeba A, Baloch S. Acute hepatitis E viral infection in pregnancy and maternal morbidity. J Coll Physicians Surg Pak. 2015;25(10):734-7.
15. Ranger-Rogez S, Alain S, Denis F. Hepatitis viruses: mother to child transmission. Pathologie biologie. 2002;50(9):568-75.

16. Nadar S, Shah MA, Jamil S, Habib H. Maternal and foetal outcome in pregnant ladies having acute hepatitis E. Gomal J Med Sci. 2015;13(1).
17. Sultana R, Humayun S. Fetomaternal outcome in acute hepatitis E. J Coll Physicians Surg Pak. 2014;24(2):127-30.
18. Banait VS, Sandur V, Parikh F, Murugesh M, Ranka P, Ramesh VS, et al. Outcome of acute liver failure due to acute hepatitis E in pregnant women. Indian J Gastroenterol: Official J Indian Soc Gastroenterol. 2007;26(1):6-10.

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