Hepatitis E virus: Seroprevalence and associated factors in acute viral hepatitis during pregnancy

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ABSTRACT

Background: Acute viral hepatitis (AVH) is defined as those cases which have acute self-limited disease and a serum aspartate aminotransferase elevation of at least 5-fold or clinical jaundice or both. Hepatitis E virus (HEV) is the most common cause of acute hepatitis and common cause of jaundice in pregnant women. **Objective:** To study the seroprevalence and maternal mortality of HEV in AVH during pregnancy. **Materials and Methods:** 220 patients admitted in Tertiary Care Teaching Hospital, Ahmedabad, during August 2014 to July 2015 that presented with symptoms of AVH and satisfied the clinical, biochemical criteria for participation were included in this study and tested for anti-HEV immunoglobulin M (IgM) antibodies using enzyme-linked immunosorbent assay. **Results:** Out of the total 220 patients 63 (28.64%) were positive for anti-HEV IgM antibodies where patients 37 (58%) are belongs to age group 21-25 years and mean age was 23.80 ± 3.13 years. Majority of the patients were from lower socioeconomical class 130 (59.1%) and positivity in them 51 (81%). The maternal mortality was 22% and showed in the third trimester 31.03%, followed by second trimester 21.05% and first trimester 6.66%. **Conclusion:** Infection with HEV is an important cause of morbidity and mortality and representing a significance risk for pregnant women and indicates the need of appropriate strategies to reduce it.

KEY WORDS: Hepatitis E Virus; Acute Viral Hepatitis; Pregnancy; Seroprevalence; Maternal Mortality

INTRODUCTION

Acute viral hepatitis (AVH) is defined as those cases which have acute self-limited disease, and a serum aspartate aminotransferase elevation of at least five-fold or clinical jaundice or both. Acute liver failure is considered when the patient after having a typical acute hepatitis develops hepatic encephalopathy within 4 weeks. It is characterized by mental changes progressing from confusion to stupor and coma as a result of severe impairment of hepatic function, without any history of pre-existing liver disease.[1-3]

Hepatitis E virus (HEV) is the most common cause of acute hepatitis.[1] The commonly recognized cases occur after the contamination of water supplies such as after monsoon flooding, but sporadic, isolated cases occur.[4-6]

In India, viral hepatitis is a major public health problem. AVH continues to be a public health problem in India despite improving sanitation, health awareness, and socioeconomic conditions. AVH is also a serious health problem in lots of countries and is one of the most important infectious diseases to which man is prone. India is hyperendemic for hepatitis A and E.[7]

Viral hepatitis is the most common cause of jaundice in pregnant women. The incidence of hepatitis E varies greatly worldwide. In developed countries, the incidence is around 0.1%; whereas in developing countries, it can range from 3% to 20% or higher. There is no difference in the course of the disease in pregnant and non-pregnant women in developed

countries. However, in developing countries, there is a higher incidence of maternal mortality with fulminant hepatitis.[8]

The prevalence and etiology of viral hepatitis remain debatable in developing and developed countries. The exact prevalence of AVH and fulminant hepatic failure due to HEV in pregnancy is still a matter of conflict.

MATERIALS AND METHODS

The study was conducted on 220 patients admitted in Tertiary Care Hospital, Ahmedabad. These patients were presented with following signs and symptoms.

Criteria for Selection of Patient

A. Clinical
   - Patients with confirmed pregnancy
   - Fever, abdominal pain, yellow discoloration of sclera or urine, itching, altered sensorium, and other clinical symptoms such as nausea, vomiting diarrhea, pruritus, arthralgia, rash, myalgia, headache.
B. Biochemical
   - Serum alanine aminotransferase (serum glutamic pyruvic transaminase [SGPT]) - >35 IU/ml
   - Serum bilirubin: >2 mg/dl
   - Hepatitis B surface antigen: Non-reactive.

The blood sample (3-5 ml) was collected by venous puncture with disposable needle and syringe from each patient and was centrifuged at a speed of 3000 rpm for 20 min and separated serum was stored at −20°C until needed for analysis.

DS-EIA-Anti-HEV-M, an enzyme immunoassay kit (Company - DSI), was used for the detection of immunoglobulin M (IgM) antibodies to HEV in human serum. Microplates were precoated with HEV-specific synthetic antigens encoding for conservative and immunodominant derived from recombinant antigen of HEV. The coated strips were washed with working washing solution two times before the assay by the use of an automatic microplate washer. Following washing, the positive control, and negative control were added in duplicates and into the rest of the wells sample diluent and tested specimens were added. Then, the plate was incubated for 30 min in microplate incubator at $37.0 \pm 1.0°C$. After washing again, working solution of conjugate was added into each of the wells and incubated. Following this again, strips were washed, and substrate mixture was added into each well and incubated in a dark place. Then, stopping reagent was added to each well and read the optical density (OD) at 450/620-680 nm using a microplate reader. Reading the absorbance at 450 nm only is possible.

The presence or absence of antibodies to HEV is determined by the ratio of the OD of each sample to the calculated cutoff value (Cutoff = Average OD value of negative control + 0.200, where 0.200 is a coefficient defined by manufacturer during statistical processing for each lot). The sample was considered positive if the OD value is ≥ Cutoff.

RESULTS

220 patients admitted to Tertiary Care Teaching Hospital, Ahmedabad, during August 2014 to July 2015 that presented with symptoms of AVH and satisfied the clinical, biochemical criteria for participation were included in this study. The presence of anti-HEV IgM antibodies was evaluated among these patients.

Out of the total 220 patients, 63 (28.64%) were positive for anti-HEV IgM antibodies. The distribution of cases in relation to age, socioeconomical condition, clinical presentation, biochemical presentation, and the presence of Anti-HEV IgM antibodies was as follows (Table 1-4).

Maximum number of patients 37 (58%) belongs to age group 21-25 years and mean age of presentation was 23.80 ± 3.13 years.

The majority of the patients in this study were from lower socioeconomical class 130 (59.1%) and maximum positivity in lower socioeconomic class 51 (81%).

Mean bilirubin level was 7.93 mg/dl and mean SGPT was 881.45 U/L.

DISCUSSION

A present study out of 220 patients, 63 (28.64%) patients were positive for IgM antibodies HEV and mortality rate was 22%.

The prevalence of HEV in AVH during pregnancy in present study was 28.64%, while other studies held in the different region of India prevalence were Singh et al.[9] (37%), Sukla et al.[8] (18%). India is hyperendemic for hepatitis A and E.[7] The reasons for this geographical difference are not clear.[10,11] The maternal mortality of the present study was 22% which was similar with studies of Khuroo[12] (Saudi Arabia) 22.2% and Kumar et al.[13] (India) 24.7%. Other studies which were held in different region in India showed high mortality, for example, Sukla et al.[8] (33.3%), Patra et al.[14] (41%). The mortality was high in third trimester of pregnancy in according to Khuroo[12] (44.4%), Sukla et al.[8] (71.4%). Kumar et al.[13] and Begum et al.[15] also noted that mortality was high in 3rd and (2nd and 3rd) trimester of pregnancy. The present study also the high mortality in 3rd trimester was 31.03%. The high mortality rate in pregnancy has been thought to be secondary to the associated hormonal (estrogen and progesterone) changes during pregnancy and consequent immunological changes.[10,11]

Table 1: Age-wise distribution of total patients

Age (in years)	Number of positive patients	Number of negative patients	Total number of patients
18-20	9	29	38
21-25	37	68	105
26-30	13	57	70
≥31	2	5	7
Total	63	157	220

Table 2: Presenting symptoms of patients

Symptoms	Number of positive patients $N=63$	Number of negative patients $N=157$	Total number of patients $N=220$
Yellowish discoloration of sclera and/or urine	60	82	142
Abdominal pain	47	77	124
Fever	16	154	170
Itching	8	7	15
Altered sensorium	13	7	20

Table 3: Correlation of HEV and trimester of pregnancy and maternal outcome

Trimester of pregnancy	Number of positive patients $N=63$	Number of negative patients	Total number of patients	Maternal outcome	
				Discharge	Expired (%)
First	15	45	60	13	1 (6.66)
Second	19	63	82	14	4 (21.05)
Third	29	49	78	22	9 (31.03)
Total	63	157	220	49	14 (22)

HEV: Hepatitis E virus

Table 4: Distribution of patients according to serum bilirubin and SGPT

LFTs	Number of positive patient	Number of negative patients	Total
Serum bilirubin			
≥5 mg/dl	43	18	61
≥1.2-<5 mg/dl	20	139	159
Total	63	157	220
SGPT			
≥100 U/L	62	33	95
<100 U/L	1	124	125
Total	63	157	220

SGPT: Serum glutamic pyruvic transaminase, LFT: Liver function test

Hepatitis E occurs primarily in adults, with the highest rates of symptomatic disease being reported in young to middle-aged adults. In the present study, mean age of positive patients was 23.80 ± 3.13 years which was similar to Sukla et al.[8] 23.83 ± 2.5 and nearby the other studies, for example, Patra et al.[14] 24 ± 2.5, and Begum et al.[15] 21.92 ± 2.66. In the present study, the most common symptom was yellowish discoloration of urine and/or sclera was present in the majority (95.23%) of patients which was almost similar with studies Rasheeda et al.[16] (2008) (88.69%) and Patra et al.[14] (2007) (92.72%). Altered sensorium was found in 20.63%

of patients in the present study while it was quite higher in studies Rasheeda et al.[16] (2008), 36.52% and Patra et al.[14] (2007), 41.81% respectively. This difference may be due to early diagnosis and hospitalization of the patients at tertiary care hospital with proper indoor treatment.

In the present study, the elevated level of serum bilirubin (mean serum bilirubin 7.93 mg/dl) and the liver enzyme SGPT (mean SGPT 881.45 IU/L) were found in all the HEV-positive patients with acute infection among the pregnant women population. The reason could be inflammation of liver by HEV infection. Elevated level of liver function test is usually related to structural damage to the hepatocytes or this may reflect an improper function of hepatocytes. Similar results were reported by Rasheeda et al.[16] where serum bilirubin mean (7.24 mg/ml) and mean SGPT (856.54 IU/L). Government hospitals such as ours, catering mostly to people who are economically downtrodden and belonged lower socioeconomical class showed HEV infection (81%) maximally than the middle and upper class. These patients belong to the overcrowded area, which reflects the poor sanitation conditions and low standard of lifestyle - all these things contributes to the transmission of infection.

HEV infection is one of the predominant causes of pregnancy-related complications in the developing countries including

India and spread through the feco-oral route. Indian setting like low socioeconomic condition, overcrowding, and poor sanitation facilitates the spread of infection. Therefore, screening of HEV is necessary in high-risk patients such as pregnant women with suspected clinical and biochemical presentations although features are similar to other hepatitis virus.

CONCLUSION

Seroprevalence and maternal mortality of HEV during pregnancy in our study 28.64%, 22% respectively, suggest that HEV is an important cause of morbidity and mortality in our set up and representing a significance risk for pregnant women. It can be prevented by educating people regarding good personal hygiene, proper disposal of sanitary waste, and general food safety. In addition, indicate the need of appropriate strategies to reduce the severity of the disease in pregnant women.

It is also suggested that preventing HEV infection in this group should be a high priority for the vaccine program. Many different vaccines have been tested, but up to now, there is currently no FDA approved vaccine or Ig prophylaxis for the prevention of hepatitis E infection. Hence, further studies are needed to validate appropriate indication of vaccine and to develop a safe, fairly efficient vaccine to prevent the HEV infection.

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