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Original Research Article.

Hospital Based Study of Spectrum of Clinical Profile and Outcome of Acute Viral Hepatitis E Infection in Adults: Tip of the Iceberg!

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ABSTRACT

Introduction: Acute hepatitis E is an important cause of acute viral hepatitis (AVH) in adults throughout Asia. It is generally mild and self-limiting and resolves within six weeks. Pregnant women are at increased risk of complications and mortality. There was an outbreak of acute hepatitis E infection in Jamshedpur, Jharkhand due to the faecal contamination of drinking water supply. Hence, a study was undertaken with an aim to evaluate the clinical profile and outcomes of Hepatitis E viral infection in adult patients admitted in Tata Main Hospital (TMH), Jamshedpur.

Methods and Materials: A prospective study of 96 adult patients admitted in Tata Main Hospital with jaundice and was IgM anti-HEV positive from April to August 2018 was done. The data analysed included demographic profile, clinical presentation, biochemical parameters, and clinical outcomes.

Results: Most common age group affected was 21 to 30 years with male preponderance (M:F-1.6:1). Yellowish discoloration of eyes was the most common symptom (73.9%), followed by fever (42.7%). Hepatomegaly was most common finding on abdominal examination (22.9%). The average ALT and AST levels on presentation were 1894.7U/L (± 1357.3) and 1763.3U/L (± 1397.4) respectively. Most common ultrasound abdomen finding was edematous gall bladder wall (40.6%). Mean duration of hospital stay (LOS) was 6.35 ± 3.87 days. Overall mortality was 1.04%. 14.6% patients had complications. 4.2% women were pregnant and had uneventful outcome.

Conclusion: Acute viral hepatitis E is a self-limiting illness. All age groups are affected. Majority of cases are cured with supportive treatment. Mortality is low, despite complications.

Key words: Viral, Liver Enzymes, Jaundice, Hepatitis E.

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INTRODUCTION

Viral hepatitis is a cause for major health care problem in developing countries such as India and now poses threat comparable to the "big three" communicable diseases – HIV/AIDS, malaria and tuberculosis.[1] Hepatitis E virus (HEV) is responsible for both sporadic infections and epidemics of acute viral hepatitis (AVH) in India, Asia, Africa, the Middle East, and Central America.[2] Most of the outbreaks of waterborne hepatitis in India have been attributed to HEV and occur after contamination of water supplies after monsoon flooding.[2,3] HEV is predominantly enterically transmitted via the faecal-oral route like HAV infection.[3,4] In addition, transmission by blood transfusion, via allograft[5,6] and vertical transmission also have been reported, though rare.

It is uncommon in children younger than 10 years.[7] Infections arise in populations that are immune to HAV and affects young to middle-aged adults. It causes high mortality in pregnant women, to the tune of 20–30% as compared to 0.2–1% in general population.[4,8,9] Infection during pregnancy is also associated with increased risk of prematurity, abortion, low birth weight, perinatal mortality, and fulminant hepatitis.[7,9] It is an important cause of sporadic fulminant hepatic failure in developing countries.[4]

HEV is occasionally associated with HAV outbreaks in developing

countries in the form of dual infection.[10,11] Previously reported major HEV epidemics in India occurred in Delhi (1955) affecting 23,900 people, in Kanpur (2010) involving 79,091 people, and affecting 23,130 people in Nellore (2008).[1,12,13]

During an HEV epidemic, the secondary attack rate among the household contacts is estimated to be about 0.7–2% when compared to 50–75% for HAV.[1,14] Acute viral hepatitis E (HEV) is generally mild and self-limiting and resolves within six weeks, with no chronic sequelae.[4] However, chronic infection (persistent infection > 6 months) occurs in solid organ transplant (SOT) recipients infected with especially genotype 3 and can lead to cirrhosis in immunocompromised host.[1,6] HEV causing severe liver disease in individuals with underlying chronic liver disease, is termed as acute-on-chronic liver failure (ACLF). In a recent study (2016) by Shalimar et al from New Delhi, the prevalence of HEV related ACLF was 18.3%.[15] There occurred an outbreak of AVH due to Hepatitis E in Jamshedpur, Jharkhand this year, which started in April. Hence, a study was undertaken to explore the epidemiology, clinical features, biochemical parameters and outcome of this hepatitis. Also, limited data is available from this part of the country on the profile of acute hepatitis E infection.

AIMS

1. To evaluate the clinical profile and outcome of patients admitted with serologically confirmed HEV infection.
2. To assess their haematological and biochemical parameters which influence the prognosis.

METHODS AND MATERIALS

Inclusion Criteria

All adult cases (>12 years) of acute viral hepatitis (AVH) due to HEV infection (as evidenced by demonstrable anti IgM antibody to HEV in the serum).

AHV was defined as a person having an acute illness presenting with jaundice, dark urine, anorexia, malaise, extreme fatigue, right upper quadrant tenderness and either jaundice or serum alanine aminotransferase (ALT) > 2.5 times the upper limit of normal on at least two occasions during a week without any history of pre-existing liver disease ((United States Center for Disease Control and Prevention, 2012). Patients who developed encephalopathy after the onset of icterus were considered to have acute liver failure (Acharya et al., 2002).

Exclusion Criteria

1. Pre-existing liver disease due to any cause.
2. Other causes of acute viral hepatitis.

This was a prospective study involving patients of HEV infection admitted in the medical wards of Tata Main Hospital (TMH), Jamshedpur from 1st April to 31st August 2018. The data analysed included demographic profile, clinical presentation, biochemical parameters, haematological profile, treatment strategy and clinical outcomes (length of hospital stay, mortality and complications). History of travel, blood transfusion, food and water intake from outside sources, alcohol abuse and co-morbid conditions was also recorded. Clinical examination included general physical examination, vital parameters and systemic examination, with emphasis on presence of jaundice, presence of organomegaly, ascites, and presence of signs of hepatic encephalopathy.

Biochemical profile included liver function test- serum bilirubin (direct and indirect fraction), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline Phosphatase (ALP), serum proteins and renal function tests (blood urea and serum creatinine). Haematological parameters evaluated were complete blood count (CBC) and absolute platelet count in all patients, Prothrombin Test (PT), serum fibrinogen and Activated Partial Thromboplastin Time (APTT) in presence of bleeding manifestations. For viral profile, all the sera were screened for IgM antibody to HEV, HAV and HCV using commercially available IgM capture ELISA kit in accordance with the manufacturer's instructions. IgM antibodies to HEV were detected by ELISA kits manufactured by Dia.Pro (Diagnostic Bioprobes Sri), Milano, Italy. According to the manufacturer, the kit has diagnostic sensitivity of 100% and diagnostic specificity of 95%. Additionally they were also tested for hepatitis B surface antigen (HBsAg). Abdominal ultrasound was done in all cases. Chest x ray was done where there was an indication as decided by the treating clinician. Liver enzymes were repeated every 72 h till discharge. All patients were treated symptomatically with anti-emetics, proton pump inhibitors, intravenous fluids and multi-vitamins as needed while specific treatment was given for hepatic encephalopathy.

Criteria for discharge were symptomatic improvement and progressive decline in the level of both transaminases to < 1000 U/L or less than 25% of the baseline. Final outcome was recorded in the form of discharge or death. Patients were followed up at regular intervals for eight weeks for assessment of clinical and biochemical parameters. The study was approved by the institutional ethics committee and informed written consent was taken from the patients.

Statistical Analysis

Data was tabulated in Microsoft excel sheet and statistical analyses were performed using SPSS version 19.0/24. Results were analysed and presented as mean ± standard deviation (SD) for continuous variables. Frequency and percentage were given for categorical variables. Student's t test was used to compare categorical variables. A value of ≤ 0.05 was taken as significant.

RESULTS

Of the total of 96 admitted cases, 59 (61.45%) were males and 37 (38.54%) were females. The male to female ratio was 1.6:1. Their age ranged from 12 to 76 years with the average being 38.6 ± 15.8 years. The cases were classified according to their age groups into ≥12 – 20 years, 21– 30 years, 31– 40 years, 41–50 years, 51– 60 years, 61 – 70 years and > 70 years. Most common age group affected was 21-30 years (31.3%) followed by 41 – 50 years while only 8 (8.33%) patients were beyond 6th decade of life. The age and sex distribution of cases is shown in figure 1.

The geographical distribution of cases was as depicted in the figure 2. Maximum cases were from Kadma and Baridih areas.

The month-wise distribution of cases was as shown in the figure 3. Maximum number of cases were admitted in August (41.7%), followed by in May (19.7%).

The various co-morbid conditions seen along with HEV infection included diabetes mellitus (13.5%), hypertension (15.6%), hypothyroidism (2.1%), depression (1.04%), coronary artery disease (1.04%), thalassemia trait (1.04%), iron deficiency anaemia (1.04%), chronic pancreatitis (1.04%), old cerebrovascular disease (1.04%) and chronic alcoholism (2.1%).

The most common clinical symptom present was yellowish discoloration of eyes (jaundice) in 71 (73.9%) patients. Other

symptoms encountered were fever in 41 (42.7%), vomiting in 27 (28.1%), pain abdomen 28 patients (19.8%), nausea in 18 (18.9%) patients, and other symptoms in 51 (53%) patients.

Other symptoms included body aches (myalgia), itching, loss of appetite, loose stools and altered sensorium in 20 (20.8%), 10 (10.4%), 8 (8.3%), 5(5.2%) and 1 (1.04%) patients respectively as shown in figure 4. One patient (1.04%) did not have jaundice but had only nausea with body aches for one day. None of the patients had bleeding manifestations despite increase in PT (INR). Average duration of symptoms before admission to the hospital was 6.35 ± 3.87 days while the average duration of fever was 2.3 ± 1.2 days.

Leukopenia (leucocyte count < 4,500/cu mm) was seen in 4 patients (4.12%), while leucocytosis (leucocyte count > 11,000/cu mm) was observed in 11 (11.5%) patients. Rest of the patients (84.4%) had normal leucocyte count.

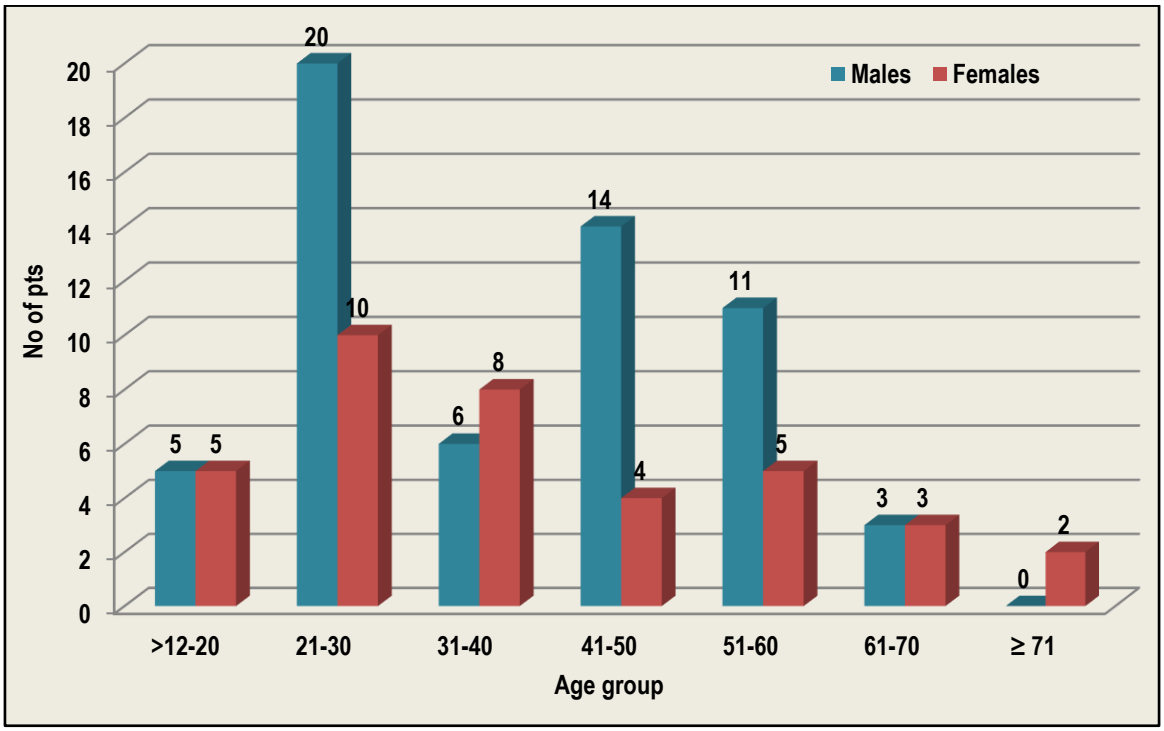

Figure 1: Age and gender wise distribution of cases (n = 96)

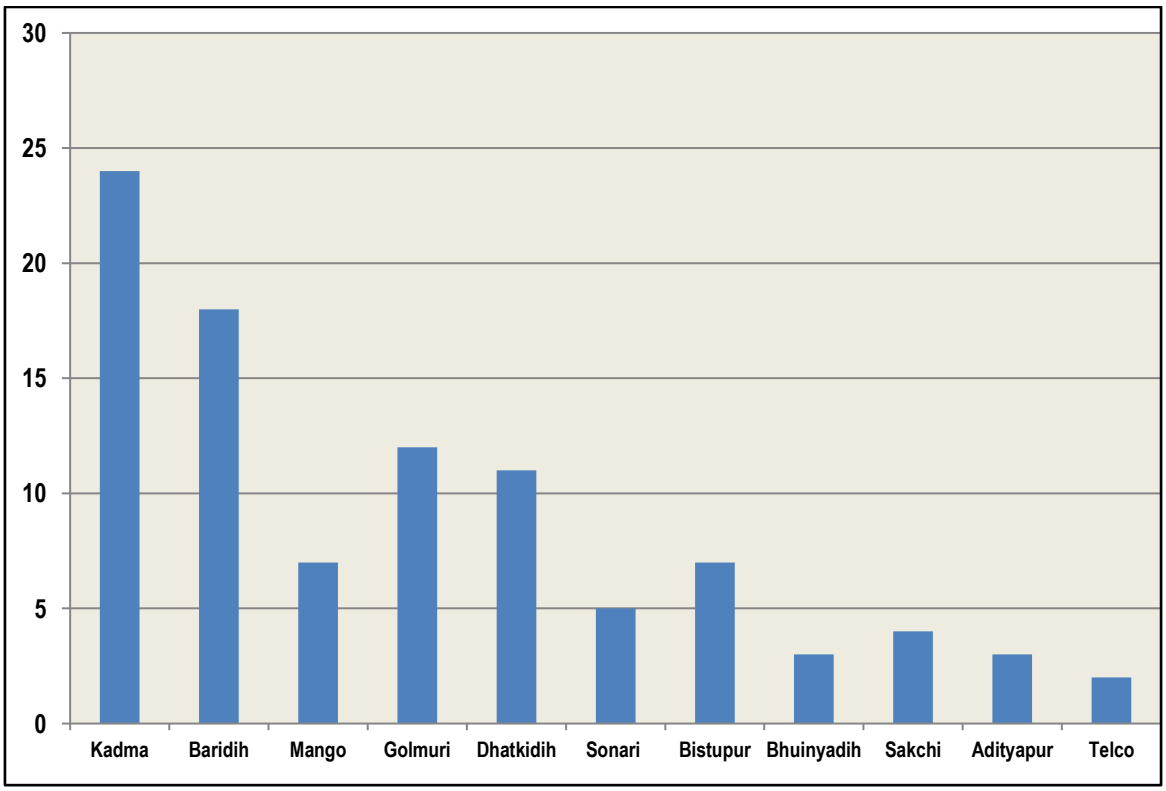

Figure 2: Geographical distribution of cases (n = 96)

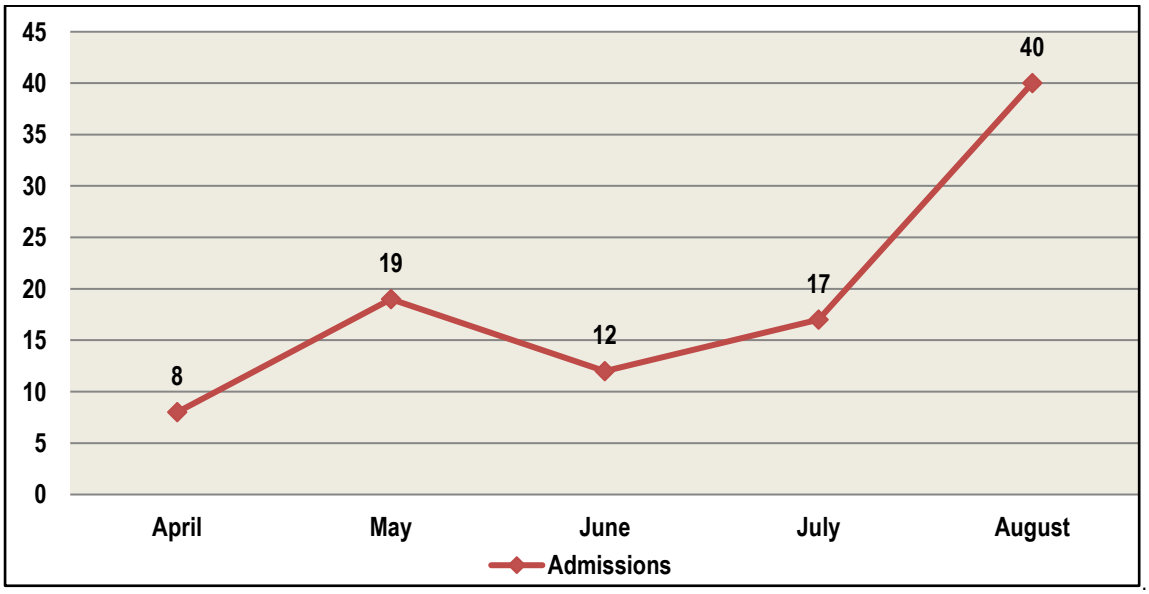

Figure 3: Month-wise distribution of cases (n = 96)

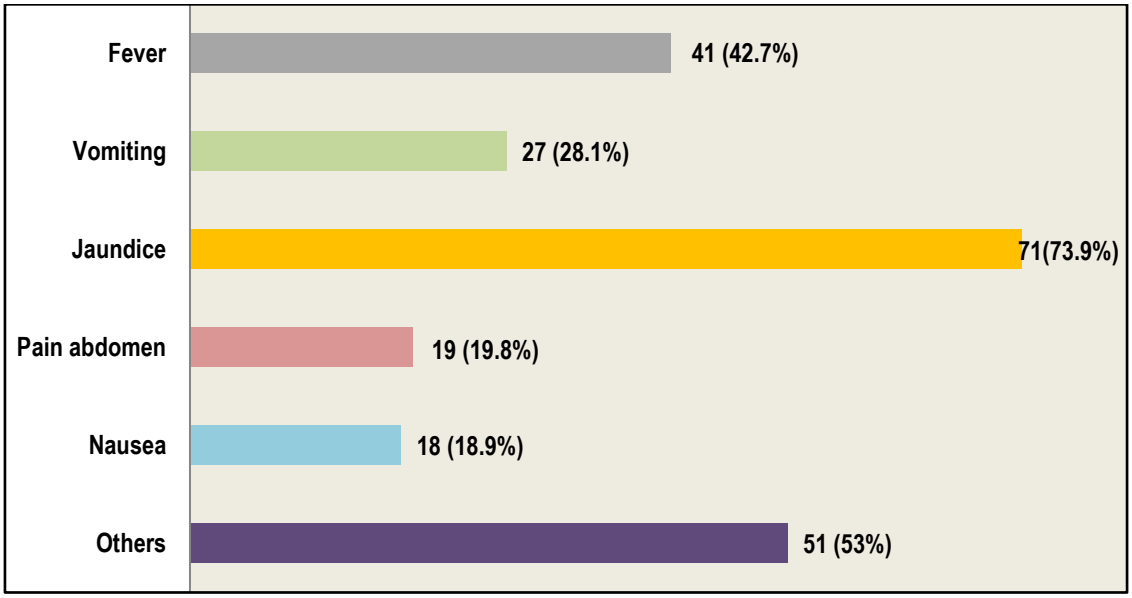

Figure 4: Distribution of symptoms (n = 96)

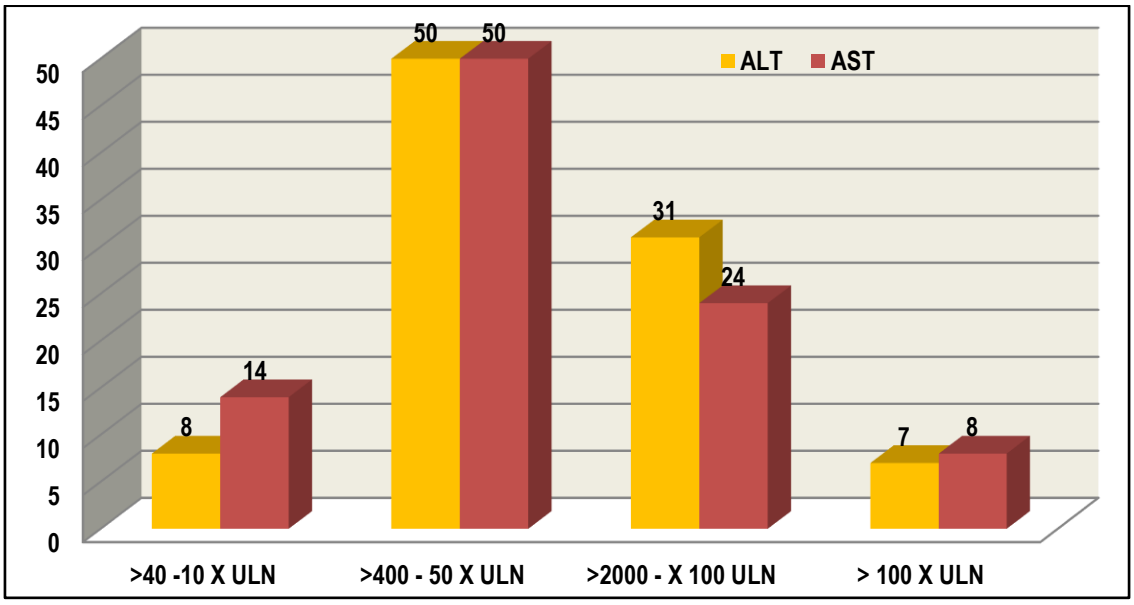

Figure 5: Severity of liver enzymes elevation (ALT & AST) n = 96

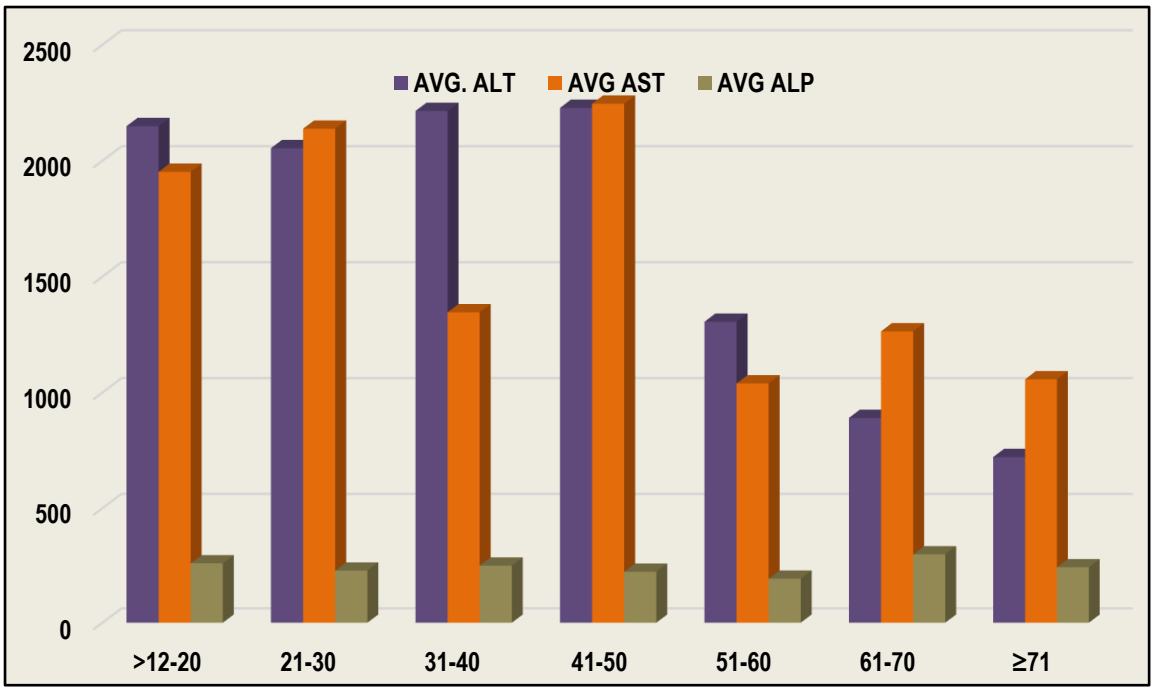

Figure 6: Pattern of liver enzymes elevation in various age groups (average levels)

Elevated total bilirubin was seen in all but one patient. Average total serum bilirubin and direct fraction were 9.9 mg/dl (± 8.9) and 6.7 mg/dl (± 5.5) respectively while the maximum level of total bilirubin and the direct fractions respectively were 73.5 mg/dl and 43.7 mg/dl. The total bilirubin level reached maximum within second week of onset of symptoms. One patient (1.04%) had anicteric hepatitis. Transaminitis (elevated liver enzymes) occurred in all the patients (100%) to a variable degree. While ALP was mildly elevated in most patients, ALT and AST were elevated up to more than 100 times the upper limit of the normal (figure 5) within first 2 weeks. The average ALT and AST levels on presentation were 1894.7U/L (± 1357.3) and 1763.3U/L (± 1397.4) respectively while the maximum ALT and AST levels were 8828.2 U/L and 8638.2 U/L respectively. The average ALP level on presentation was 230.6 KA units while maximum level seen was 850 KA units.

Depending upon the degree of elevation of liver enzymes, patients were classified as having mild (ALT/ and AST > 40 to 10 times ULN), moderate (ALT/ and AST > 10 to 50 times ULN), severe (ALT/ and AST > 50 to 100 times ULN) and very severe (ALT/ and AST > 100 times ULN) hepatitis. Accordingly, 8 (8.3%) had mild ALT elevation while 14 (14.6%) had mild AST elevation, 50 (52.1%) patients had moderate elevation of both ALT and AST, 31 (32.3%) patients had severe elevation of ALT, 24 (25%) patients had severe elevation of AST and 7 (7.3%) patients had very severe elevation of ALT while 8 (8.3%) patients had very severe elevation of AST (figure 5).

The ratio of average ALT/AST was 1.07. In the elderly age group (>60 years), ratio of ALT/AST was found to be < 1, that is AST was elevated more than the ALT while in the age group up to 60 years ALT/AST ratio was > 1 except in the age group of 21 to 30 years where AST level was higher than ALT level (figure 6). Enzyme levels started decreasing by the end of second week and laboratory profile of all survivors became normal by 6th to 8th week. None of patients showed cholestatic pattern of enzyme elevation during the course of illness. The average serum albumin level was 3.9 g/dl ± 0.1 and mean international normalized ratio (INR) was 1.13 ± 0.38 while the highest value observed was 3.35.

The average duration of symptoms, degree of elevation of liver enzymes, and INR in various age groups is as shown in the table 1. The degree of ALT and AST elevation was more in diabetic patients than in otherwise normal patients and those with other co-morbid conditions. The average ALT and AST levels in diabetics were 2152.4U/L and 2152.7U/L respectively while in non-diabetic patients were 1894.7U/L and 1763.3U/L respectively. Similarly the mean serum bilirubin level was higher (9.52 mg/dl) in diabetics than in hypertensive (8 mg/dl) patients. Also, the mean duration of hospital stay was higher in diabetics (7.05 days) than in other cases (5.26 days).

The various findings noted on ultrasound abdomen were thickened and edematous wall of gall bladder in 39 patients (40.6%), increased periportal hyper echogenicity in 24 patients (25%), hypoechoic liver pattern in 19 patients (19.8%), mild hepatomegaly with normal echogenicity in 22 patients (22.9%), enhanced echotexture of liver in 4 patients (4.2%), splenomegaly in 6 patients (6.3%), fatty liver in 2 (2.1%), mild to moderate ascites in 4 patients (4.2%), cholelithiasis in 3 patients (3.1%) and normal in 16 patients (16.7%). Thus, the most common abnormality found on ultrasound abdomen was thickened and edematous wall of gall bladder (Figure 7).

Outcomes

The overall mean length of stay (LOS) was 6.5 ± 2.91 days (maximum was 15.2 days). Complications were seen in 14 (14.6%) patients, of which 3 (3.12%) patients had hepatic coagulopathy. 5 (5.2%) patients had thrombocytopenia (platelets < 1,00,000/ cu mm). The lowest platelet count seen was 56,000/cu mm. However, none of these patients had bleeding manifestations. One (1.04%) patient each had fulminant hepatic failure with hepatic encephalopathy, reversible acute kidney injury (AKI), and acute hemolytic anemia. Four (4.1%) patients had mild to moderate ascites. The overall mortality was 1 (1.04%) and was related to the development of fulminant hepatic failure (FHF).

Table 1: Average duration of symptoms, degree of elevation of liver enzymes, and INR in various age groups

Age group (yrs) (no)	Symptoms duration (days) (Avg ± SD)	Total bilirubin (Avg ± SD) (mg/dl)	Direct bilirubin (mg/dl)	ALT (Avg ± SD) (U/L)	AST (Avg ± SD) (U/L)	ALP (Avg ± SD) (U/L)	PT (INR) (Avg ± SD)
14-20 (n=10)	5.74±3.8	9.5±8.95	8.9±5.6	2149±1355.1	1952.1±1420.9	259.4±122.3	1.08 ±0.37
21-30 (n=30)	5.33±3.9	13.3±9.3	8.6±5.8	2053.9±1183.9	2138.1±1190.9	227.5±135.5	1.3±0.4
31-40 (n=14)	6.35±3.7	9.7±8.5	6.7±5.4	2214.4±1351.5	1346.3±1402.1	249.4±132.4	1.06±0.4
41-50 (n=18)	7.8±3.8	8.65±8.8	6.11±5.5	2227.6±1342.3	2245.8±1433.7	222.6±119.9	1.13±0.37
51-60 (n=16)	7.1±3.9	6.72±6.2	4.6±4.2	1305.3±1369.5	1039.5±1400.9	192.2±131.8	0.89±0.4
61-70 (n=6)	5.62±3.7	8.52±8.8	5.94±5.3	890.8±1346.1	1264.2±1444.3	298.7±119.7	0.97±0.3
≥ 71 (n=2)	6.5±3.6	4.9±8.6	3.74±5.4	721.9±1367.4	1057.2±1403.7	242.1±133.1	1.02±0.3

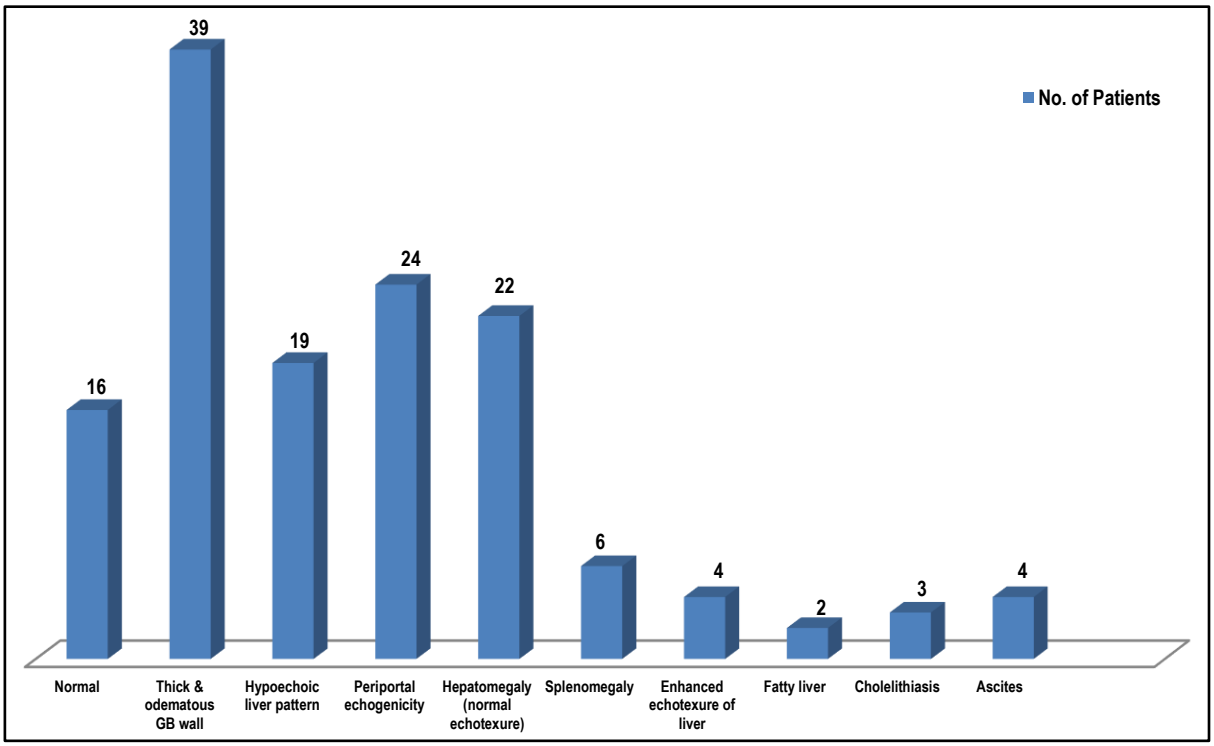

Figure 7: Profile of ultrasound abdomen findings (n=96)

DISCUSSION

Hepatitis E virus (HEV) is a hepatotropic, positive-sense, single-stranded RNA virus with 7.5 kb genome, belonging to the family hepeviridae.[2] HEV has 4 genotypes of which genotypes 1 and 2 exclusively infect humans whereas genotypes 3 and 4 also infect several other mammalian species. It is a major cause of acute epidemic and sporadic viral hepatitis in several developing countries.[1,2] The infection is transmitted predominantly by the fecal–oral route, usually through contaminated drinking water supplies. The incubation period is 2–9 weeks (mean 40 days).

Hepatitis E was first recognised during an epidemic of hepatitis in Kashmir valley in 1978.[16] According to Panda SK et al, hepatitis E is widespread in developing countries, accounting for 30 to 70 per cent of all sporadic cases of acute viral hepatitis.[17] In a study from Rajasthan, on acute sporadic viral hepatitis by Chandra NS et al, of 736 patients, HEV infection was found in 49.7% of patients.[18] Khuroo et al noted that in India, 92% (23/25) of patients with epidemic non-A non-B hepatitis had acute HEV infection.[19] Globally, there are approximately 20 million cases of hepatitis E infection every year.

Study on the prevalence of HEV infection during acute sporadic hepatitis in West Bengal by Chandra et al[18] and from Ranchi by Kumar M et al[20] showed figures of 34.4% and 11.2% respectively. In Jamshedpur, there were only 8 admissions in TMH due to HEV

infection in 2017. The present outbreak in Jamshedpur involved more than 400 residents since July in Dhatkidih, as per the National Centre for Disease Control (NCDC) report and was caused by faecal contamination of drinking water supply while establishing illegal water connections. Similarly, the largest waterborne Hepatitis E outbreak in India, in Kanpur city in 1991 was traced to the faecal contamination of drinking water supplied from the Ganges river.[13] Our study showed male preponderance with male to female ratio being 1.6:1, which is in accordance with other studies done in North India (Punjab), China, Taiwan, Ahmedabad and Bangladesh.[3,4,20,23] The male preponderance can be explained by the fact that males get exposed more due to their outdoor activities. However, gender ratio was found to be 1:1 in an epidemic outbreak in Africa.[24] In our study, the youngest patient was of 13 years age and the oldest patient was a 71-year-old female. Thus, all age groups were susceptible to hepatitis E infection, which was comparable to the study by Khuroo et al.[19] The mean age of patients was 38.6 ± 15.8 years whereas a lower mean age (28.8 years) was seen in a study done in Kanpur by Naik SR et al.[13] In yet another study by Murthy et al[2], the mean age of patients was 45.59 ± 14.4 years, probably as they had not included patients under 18 years of age. 21 to 30 years was the commonest age group affected in our study. This trend is a hallmark of HEV epidemiology and has been reported by other Indian authors like Modi et al in a one year study from Ahmedabad.[4]

Analysis of the clinical profile showed, yellowish discoloration of eyes was the most common symptom (73.9%) and icterus (98.9%) was commonest sign at presentation. It was not found only in 1 (1.04%) patient. Fever was the next common symptom and was associated with chills in 20 patients (20.8%). It varied from low to high grade. Gastrointestinal symptoms like nausea, vomiting and appetite variably preceded or followed the development of fever. Among the non-specific symptoms, asthenia was very prominent. It was present during the febrile period and up to 1 week after fever disappeared. Hepatomegaly was the most common finding on abdominal examination and was seen in 22 (22.9%) patients, while splenomegaly was seen in 6 (6.3%) patients respectively. Hepatomegaly was mild, measuring approximately 2 to 3 cm below the right costal margin except in one patient (1.04%) who was alcoholic and had grade 2 fatty liver and had liver enlargement of 4 to 5 cm below the right costal margin. Splenomegaly was mild in all cases. Of the 4 cases, ascites was clinically detectable in 1(1.04%) patient while the rest showed mild ascites on ultrasound. In a study by Murthy et al[4], hepatomegaly was found in 60.3% patients, whereas ascites and splenomegaly were seen in 6.9% and 5.2% patients, respectively.

In our study, varying degrees of elevation of serum bilirubin was seen. Maximum value observed was 78.3 mg/dl. Such high serum bilirubin value has not been hitherto reported in literature. His bilirubin at 2 weeks was 36.4 mg/dl. Subsequently, he was lost to follow-up. Seven patients (7.3%) had elevation of serum bilirubin to more than 20 mg/dl. In a study by Modi et al, the maximum value of bilirubin noted was 32 mg/dl. In our study, the mean bilirubin was 9.9 ± 8.9 mg/dl while in a study by Murthy et al from Mysore, the mean bilirubin in patients who were discharged was 11.33 ± 7.26 mg/dl while it was 20.3 ± 5.08 mg/dl among the patients who died.

Transaminitis was seen in all patients (100%) from mild to very severe degree. The degree of elevation of ALT and AST were out of proportion to that of ALP. ALT/AST ratio of <1 was seen in elderly patients (> 60 years) and in the age group 21 to 30 years. However, the average ALT/AST ratio was 1.07. All patients had "hepatocellular" pattern of liver injury (due to viral replication in the hepatocytes). None of the patients had "cholestatic" or "mixed" pattern of liver enzyme elevation. Similar observations were made in a study by Murthy et al[2], who noted an approximately 20-fold increase in mean ALT and AST values, whereas mean ALP elevation was by just 1-fold. Serum ALT was elevated more than AST (mean SGPT/SGOT = 1.148). Modi et al[4] in their study, noted 43% of the patients had ALT elevation in the range of 500 to 1,000U/L while only 20% had ALT > 1,000U/L. In a study on acute sporadic hepatitis by Chandra NS et al[19] from West Bengal, the mean ALT value was 877.1 ± 600.4 U/L and that of AST was 1051.7 ± 660.7 U/L. The mean ALP values were 1223 ± 706.9 U/ which were much higher than in our and other studies. The LOS was not determined by the degree of severity of elevation of the liver enzymes (P=0.66). It was comparable in both groups, that is the group with mild to moderate elevation and the group with severe to very severe elevation of liver enzymes (6.5 days vs 6.34 days).

Search for other published studies revealed that the degree of liver enzyme elevation except ALP was maximum in our series. 38 patients (39.6%) had ALT > 100 times ULN and 32 patients (33.3%) had AST >100 times ULN. ALT elevation > 1,000U/L is found in hepatocellular injury due to viruses, toxins and ischemic insult. Thus, in our study, we saw elevation of both the liver enzymes (ALT and AST). The elevation of liver enzymes was monophasic and the levels returned to normal within 8 weeks irrespective of the initial level of rise. Average time required for transaminases levels to reduce by 50% was 6.4 ± 1.2 days. All patients except one had clinical and biochemical recovery from illness.

Ultrasound of abdomen revealed collapsed gall bladder with wall edema as the most common (40.7%) finding followed by increased periportal echogenicity in 25% of the patients. Gall bladder sludge was found in 2.08% of the patients. In a two year study of ultrasound findings in acute viral hepatitis E by Sudhamshu KC et al[25], gall bladder wall edema was found in 85% of HEV infection. Gall bladder sludge was detected in 37% of the cases. Gall bladder findings were common in all type of hepatitis and were more common in patients with higher level of liver enzymes. Similar finding was also noted in our study. The average ALT level and AST level was 1,956.4U/L and 1,820.2 U/L respectively in patients with thickened and edematous gall bladder. The proposed mechanisms include decreased bile production and excretion due to hepatocyte injury[26], direct injury to and inflammation of the mucosal and muscular layers of the gallbladder by hepatitis virus contained in bile juice[27], inflammatory reaction in the tissues surrounding the liver, including the gallbladder wall[28] and lymphatic obstruction by the virus. Hepatomegaly, splenomegaly and ascites were found in 55%, 34% and 5% respectively in their study. Ascites was mild (3.12%) to moderate (1.04%). In a study by Sudhamshu KC et al, thicker the gall bladder, more elevated were the liver enzymes. Similar observation was made in our study as shown in the table 2. However, the observation did not reach statistical significance.

Table 2: Comparison of parameters in those with gall bladder wall edema with those who had normal gall bladder on ultrasound (n=96)

Parameters	Gall bladder wall edema	No GB wall abnormality	95% CI	P value
LOS* (yrs) (Avg ± SD)	6.6 ± 3.2	6.2 ± 2.9	-1.6 to 0.8	0.5
ALT (U/L) (Avg ± SD)**	2030.7 ± 1351.9	1840.9 ± 1356.7	- 748.7 to 369.1	0.5
AST^ (U/L) (Avg ± SD)	1965.9 ± 1399.8	1683.7 ± 1394.4	- 849.9 to 303.5	0.34

LOS*– Length of stay, ALT **– Alanine aminotransferase, AST^ – Aspartate aminotransferase, Avg – average, SD – standard deviation, CI – confidence interval

Table 3: Comparison of parameters in diabetics and non-diabetics (n=96)

Parameters	Diabetics (Avg ± SD)	Non-diabetics (Avg ± SD)	95%CI	P value
Age (Yrs)	53.2 ± 15.5	36.4 ± 15.5	-25.9 to -7.6	**0.004**
LOS *(days)	7.1 ± 2.7	6.4 ± 2.9	- 2.35 to 1.05	0.45
Serum Bilirubin (mg/dl)	9.5 ± 9.4	9.9 ± 8.4	- 4.8 to 5.6	0.88
ALT (U/L)**	2152.4 ± 1386.1	1862.6 ± 1350.2	-1092.1 to 512.6	0.47
AST^ (U/L)	2152.7 ± 1467.3	1708.7 ± 1390.1	-1273.2 to 328.6	0.29

LOS* – Length of stay, ALT **– Alanine aminotransferase, AST ^– Aspartate aminotransferase, Avg – average, SD – standard deviation, CI – confidence interval

Outcomes: The average length of stay (LOS) was 6.5 ± 2.91 days (maximum being 15.2 days). It was higher in diabetics (7.05 days) and in patients who had leucocytosis (7.9 days) at presentation. Complications were observed in 14 (14.6%) patients. Mild thrombocytopenia was seen in 5.2% of patients. Spontaneous recovery was observed in all. The mechanism of severe thrombocytopenia is believed to be immune-mediated, and platelet-associated antibodies.[29] HEV infection associated with severe thrombocytopenia has been cited in six case reports[30-33] and one case series by Fourquet E.[34] Patients' platelet count ranged from 1,000/cu mm to 21,000/cu mm. Hence, it is prudent to perform HEV testing in patients with severe thrombocytopenia associated with elevated liver enzymes.

Acute kidney injury (AKI) is noted in both acute and chronic HEV infection, in immunocompetent and immunocompromised patients. The mechanism of AKI is uncertain. It is related to glomerular damage, acute tubular necrosis (ATN), cryoglobulinemia (as in chronic HEV infection) and is reversible.[29] In our case, renal failure occurred in 1 (1.04%) patient and was non-oliguric and renal function returned to normal within one week of supportive treatment. Renal failure was observed in 9% of the cases in a study by Modi et al.[4] Hepatic coagulopathy was the commonest complication observed in 39% of their patients, while it was found in only 3.12% of our patients. One patient needed 4 units of fresh frozen plasma for correction of coagulopathy. None of these patients had bleed. Three cases of auto-immune hemolytic anemia (AIHA) associated with HEV infection have been reported earlier.[35,36] These cases developed sudden and rapid drop in hemoglobin level during the course of illness and were diagnosed after excluding other causes of anemia and hemolysis. Our patient had hemoglobin of 11.2 g/dl on admission but dropped to 3.2g/dl on ninth day. He had no overt bleed. His direct Coomb's test (DCT) was positive. He ultimately went into sepsis, hepatic encephalopathy, multi-organ dysfunction syndrome (MODS) and expired leading to an overall mortality of 1.04%. He had mild elevation (less than 5 times) of liver enzymes suggestive of massive hepatic necrosis leading to fulminant hepatic failure and was admitted after 20 days of onset of symptoms. The overall mortality in a study by Murthy et al, involving 290 patients from Mysore, Southern India, was 3.45%. It was higher among alcoholics (12.5%) probably, because alcohol causes decompensation in acute viral hepatitis E infection. The mortality was 7% in a study by Modi et al from Ahmedabad and was strongly associated with FHF which developed in 17% of the cases. Fulminant hepatitis occurred in 10.3% of the patients in a study by Murthy et al.[2]

We had 4 (4.2%) pregnant patients of which 3 were in the second trimester and one was third trimester (9 months). Though HEV infection runs a virulent course in pregnant females, in our study all had uneventful recovery and maternal mortality was zero. Patient in the last trimester delivered healthy baby of 3.2 kg. Delivery outcomes are awaited for rest of the patients. In the study by Modi et al, 12 women were pregnant. Intrauterine deaths (IUD) occurred in 66% and maternal mortality in 33%. Similar findings have been reported by Patra et al[9] and Tandon et al.[37]

Patients with diabetes mellitus were found to have a higher mean duration of hospital stay in a study by Murthy et al. However, in our study, though the mean LOS, ALT and AST levels were higher in diabetics, this difference was not found to be statistically significant (table 3). The mean age of patients with diabetes mellitus (53.2 ± 15.5) with acute hepatitis was more than non-diabetics (36.4 ± 15.5) and this was statistically significant.

CONCLUSION

Acute viral hepatitis E is a self-limiting illness. Outbreaks occur due to faecal contamination of drinking water supply. All age groups are susceptible to infection. Most common symptom is yellow discoloration of eyes. Transaminitis could be mild to

severe. Serum alanine transaminase (ALT) to serum aspartate transaminase (AST) ratio (mean ALT/AST >1) was found in younger age group while AST/ALT >1 was found in the elderly age group. Length of hospital stay was more in diabetics and in those with leucocytosis. Mortality is low despite complications.

DRAWBACKS

Genotyping of the virus could not be done.

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