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Original Article

Predictors of mortality in a large cohort of patients with acute hepatitis in a Low Middle-Income Country

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Abstract

Background. *In developing countries, acute hepatitis poses a serious threat in terms of mortality and morbidity.* ***Objective:*** *The aim of our study was to assess the etiology, clinical, and biochemical profile of acute hepatitis patients and study the predictors of mortality.* ***Patient and Methods.*** *A retrospective study was conducted from records over 3 years in an infectious disease facility. The data on etiology, clinical presentation, complications, severity, and outcomes were collected. Univariate followed by multivariate analysis was done to derive the predictors of mortality.* ***Results.*** *A total of 2488 patients were included. Hepatitis E was the most common etiology (52.65%), followed by hepatitis A (22.18%) and hepatitis B (10.56%). The majority of patients with hepatitis C (68.9%) had cirrhosis. The overall mortality rate was 1.43% among patients with viral hepatitis. Altered sensorium, gastrointestinal bleeding, anemia, elevated bilirubin, low albumin, and presentation as acute liver failure (ALF) or acute on chronic liver failure (ACLF) were independent predictors of mortality. Among patients of autoimmune hepatitis (AIH), one-third had age>60 years and the majority (83.9%) had cirrhosis. Drug-induced liver injury (DILI) was the most prevalent etiology among non-viral causes. The most common offending drug was complementary medications. Patients with non-A/non-E hepatitis were older and had higher mortality than hepatitis A/E patients.* ***Conclusion.*** *Hepatitis E is still the most prevalent cause of acute hepatitis. ALF/ACLF presentation and related comorbidities, such as altered sensorium and GI bleeding, predict death.*

Introduction

Acute hepatitis (AH) is a major public health issue in Low Middle-Income countries (LMIC) like India. There is a significant under-reporting of instances of acute hepatitis. The precise global illness burden of acute hepatitis is unknown. Even though the majority of these individuals have viral hepatitis, autoimmune hepatitis (AIH) and drug-induced liver injury (DILI) are on the rise as a result of urbanization and greater knowledge of these conditions. Previous two-decade literature suggested that hepatitis A and hepatitis E were the most prevalent causes of acute hepatitis in pediatric and adult age groups in India, respectively[1-3]. However, a recent study has shown a rise in the incidence of hepatitis A in adolescents and adults, raising questions regarding adult immunization[4]. The majority of research so far has exclusively focused on viral hepatitis. The other prevalent causes, such as AIH and DILI, have been less studied. The yearly incidence rate for autoimmune hepatitis in the Asian population (1.31 per 100. 000) was comparable to that of the European (1.37 per 100. 000) and American (1.00 per 100,000) populations[5]. Apart from AIH, India has 2.7 million estimated tuberculosis patients and more than 50% of Hansen's disease burden worldwide as per the WHO report[6]. So, the prevalence of DILI secondary to anti-tubercular therapy is on the rise. Also, a subset of the population in India uses traditional medicines, such as Ayurveda, Unani, Siddha, and Homeopathy (AYUSH), in addition to conventional treatment. In a large study cohort conducted by Devarbhavi H et al, DILI accounted for 1.5% to 2.5% of hospitalizations among all admissions with the most common culprit being antitubercular (ATT) drugs[7]. Additionally, 10-15% of patients with acute hepatitis were diagnosed with non-A/non-E hepatitis since the etiology could not be determined despite proper evaluation[8,9]. There is a study on the prevalence of non-A/non-E hepatitis which did not have any mortality in outcome[10]. In this study, we analyzed the spectrum of acute hepatitis including non-viral causes, and studied the predictors of mortality.

Patient and Methods

This is single-center observational research at a specialized infectious disease center. We examined patients' discharge and death records over the previous three years (January 2017-December 2019). The study was approved by the Institutional Ethics Committee. Acute hepatitis was diagnosed with symptoms such as fatigue, abdominal pain, nausea, vomiting, loss of appetite, fever, and jaundice, as well as high serum aminotransferase (AST, ALT) levels for less than 6 months. Anicteric hepatitis was diagnosed as having acute hepatitis-like symptoms and a serum bilirubin level less than 3 mg/dl[11].

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Cirrhosis in patients was defined based on clinical, laboratory, or radiological findings. Acute on chronic liver failure (ACLF) was determined according to the definition of APASL, and acute liver failure (ALF) was defined according to the definition of AASLD[12]. Patients were categorized as

- Viral Hepatitis- Positive serology (IgM Hepatitis A, anti-HBsAg, IgM-anti HBc, anti HCV, anti-IgM HEV)
- Autoimmune Hepatitis (AIH)- International Autoimmune Hepatitis Group Criteria (Pre-liver biopsy score >10 and post-liver biopsy score >12)[13].
- Wilson Disease- Presence of Kayser-Fischner (KF) ring in the cornea, low serum ceruloplasmin (<20 mg/ml), and high 24-hour urinary copper (>40 mcg)
- Drug-Induced Liver Injury (DILI)- Appropriate history, Roussel Uclaf Causality Assessment Method (RUCAM) score) >6, and improvement of liver function tests after stopping the offending agent[14].
- Non-A Non-E Hepatitis- Exclusion of all other causes

Inclusion criteria

Adult patients of viral hepatitis (Age >18 years) with symptoms, signs and laboratory findings of hepatitis and cirrhosis were included.

Inclusion criteria

The following patients were excluded **(i)** Patients with alcoholic liver disease or a history of significant alcohol intake (Having more than four drinks on any one day or more than 14 drinks per week for men and having more than three drinks on any one day or more than seven drinks per week for women)[15]. **(ii)** Patients with sepsis-induced hepatitis. **(iii)** Patients with cholestasis liver disease (Primary biliary cholangitis and Primary sclerosing cholangitis) and extrahepatic biliary obstruction. **(iv)** Pregnant and lactating women. **(v)** Patients with non-alcoholic fatty liver disease. **(vi)** Patients with incomplete data.

Outcome

Each patient's detailed clinical history and all pertinent clinical data were collected. The main outcome of the study was to evaluate the etiology, clinical, and biochemical characteristics of acute hepatitis patients and to identify any potential predictors of mortality in these patients.

Statistical analysis

Data were analyzed using SPSS statistical software, v 22.0 (USA). Normally distributed data were expressed as mean ± standard deviation (SD). Nominal data were expressed as frequency and percentage. The student's t-test was used for comparing continuous data wherever appropriate. The chi-square test or Fisher's exact test was used for categorical variables. Univariate and multivariate Cox regression analyses were performed to determine the predictors of in-hospital mortality in patients with acute hepatitis. A p-value of <0.05 was considered significant.

Results

Etiological distribution of patients

A total of 13635 individual records underwent screening, and of them, 2488 were included. The majority of patients (66.1%) were males. The mean age of the group was 32.51 ± 12.23 years. Only 91 patients had multiple coexisting viral etiologies. The distribution of various etiologies of acute hepatitis across different age groupings is shown in **figure 1.** The majority of patients (92.56%; 2303 patients) had viral hepatitis, with hepatitis E (52.65%) being the most prevalent type. The other common etiologies included hepatitis A (22.18%) followed by hepatitis B (10.56%). In all age categories, hepatitis E accounted for the majority of cases. With advancing age, the prevalence of hepatitis A and hepatitis E declined, on the contrary, the prevalence of hepatitis B and hepatitis C increased with age. The prevalence of autoimmune hepatitis (AIH) was evenly distributed throughout all age categories. Non-A-non-E hepatitis and DILI were more common in the age group 18-30 years.

Viral hepatitis

Age distribution

The majority of cases of infectious hepatotropic viruses were in the age group of 18-30 years (59.79%), with a mean age of 26.31 ± 7.68 years for hepatitis A and 32.36 ± 11.44 years for hepatitis E. In contrast, individuals with hepatitis B and C had a mean age of 38.31 ± 13.15 years and 38.89 ± 13.76 years, respectively. The mean age of hepatitis A patients was lower than that of hepatitis E, hepatitis B, and hepatitis C patients ($p < 0.001$). Approximately 22.54% of adults were diagnosed with hepatitis A.

Seasonal distribution of cases.

During the monsoon and summer months, instances of infectious hepatotropic viruses tended to cluster, however, this was not statistically significant (p=0.738). The distribution of Hepatitis B and C was consistent throughout the year, **supplementary figure 1.**

Clinical characteristics and risk factors.

Jaundice was the most prevalent symptom (92.99%). Prodromal features were present in 74.8% and 85.9% of patients with Hepatitis E and Hepatitis A respectively. Anicteric hepatitis was observed in 52.2% of hepatitis C patients (p <0.005). Despite being one of the characteristic signs of cholestatic hepatitis, pruritus was present in 14.8%, 7.1%, and 29.9% of patients with hepatitis A, B, and E, respectively. Pruritus was more common in hepatitis E patients than in other groups (p= 0.04). In the hepatitis C group, prodromal symptoms such as nausea, vomiting, itching, and loose stools were less frequent (p<0.05). Patients with hepatitis B were statistically more likely to have a positive family history, a history of tattoos, blood transfusion, past surgery, and a history of high-risk behavior (p<0.05). Relapsing hepatitis A infection was seen in 42 patients (7.49%), **table 1** & **supplementary table 1**.

Laboratory findings, **table 2**.

When compared to the other groups, hepatitis C patients had significantly lower levels of hemoglobin, platelets, serum bilirubin, serum albumin, AST, and ALT levels. Patients with hepatitis A had substantially elevated levels of alkaline phosphatase. (p<0.005)

Underlying cirrhosis and mortality, **supplementary table 2**.

Cirrhosis was seen in the majority of hepatitis C patients (68.9%), which was statistically more prevalent than in other cohorts (p<0.005). Overall mortality was 1.43%, and the difference in mortality between groups was not statistically significant.

Predictors of mortality

Predictors of mortality in patients with acute viral hepatitis on the univariate analysis included advancing age, diabetes mellitus, addictions to alcohol and smoking, and presentation with altered sensorium, Gastrointestinal bleeding, ALF, and ACLF. The other predictors included anemia, raised leucocyte counts, high NLR ratio, raised AST, elevated bilirubin, low serum albumin, raised creatinine, and evidence of underlying cirrhosis. However, on multivariate regression analysis, altered sensorium, GI bleed, anemia, low albumin, and presentation in the form of ALF/ACLF, were independent predictors of mortality, **tables 3 and 4**.

Co-infection

90 patients had dual co-infections, whereas one patient had a triple infection (hepatitis A, hepatitis B, and hepatitis E). Hepatitis E and B co-infection was the most common one. However, the prognosis, clinical presentation, demographic distribution, and laboratory findings were all comparable to those of a single viral infection.

Autoimmune hepatitis.

51 individuals were diagnosed with AIH. 96.1% of the patients were females, and the mean age was 49.94 ± 16.58 years. Jaundice (98%) was the most common symptom. 26 (51%) patients had underlying cirrhosis at presentation. Five individuals had a history of jaundice in the past. 5 patients presented with acute severe AIH while 12 patients had ACLF. The overall mortality was 27.5%, with all patients suffering from either acute severe AIH or ACLF.

Drug-Induced Liver Injury (DILI).

The majority of DILI patients were in the 18-30 years age group. Complementary and herbal medicines (47.05%) were the most common offending agents. ATT (25.89%) were the second most common offending agents. Patterns of damage were hepatocellular in 34.13% of patients, cholestatic in 42.35% of patients, and mixed in 23.52% of patients with DILI. One patient presented with ACLF, while four individuals developed ALF. 11% of patients had underlying cirrhosis. The overall mortality rate of patients with acute hepatitis secondary to DILI was 2.4%.

Wilson disease

There were only 4 patients with Wilson disease presenting as acute hepatitis. The mean age of the patients was 29±12.6 years and all were females. Two patients had underlying cirrhosis. One died as a complication of cirrhosis.

***Non-A-E Hepatitis*, table 5**.

Despite extensive evaluation, the etiology of hepatitis in 45 individuals could not be determined, were classified as non-A/non-E hepatitis or cryptogenic hepatitis. Patients with non-A/non-E hepatitis were older than patients with hepatitis A/E. ($p<0.005$) The clinical symptoms profile of non-A/non-E hepatitis was similar to Hepatitis A/E. Hypertension and a history of smoking were more common in the non-A/non-E group ($p<0.05$). Neutrophils to lymphocyte ratio (NLR) and serum creatinine levels were on the higher side in the hepatitis non-A/non-E cohort ($p<0.005$). Serum transaminase levels were significantly higher in the hepatitis A/E group than in the non-A/non-E hepatitis cohort. Non-A/non-E hepatitis patients were more likely to have underlying chronic liver disease than hepatitis A/E patients ($p< 0.005$). Overall mortality was also higher in non-A/non-E hepatitis patients as compared to the hepatitis A/E cohort ($p=0.0028$).

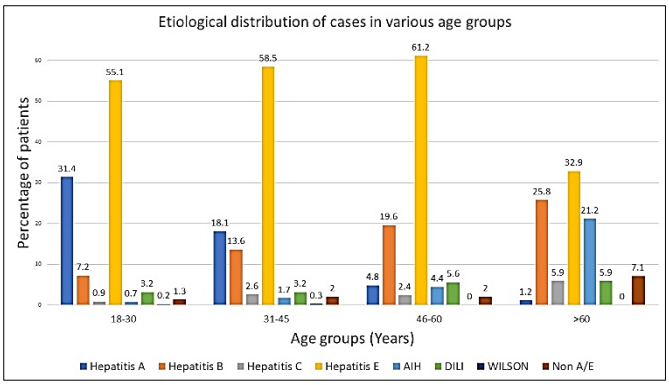
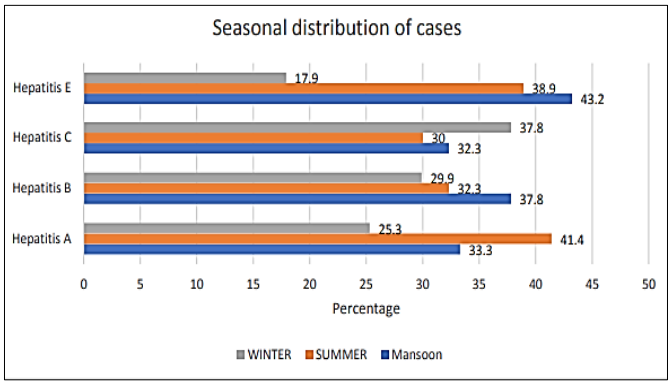


Figure 1. Etiology wise distribution of patients of acute hepatitis in various age groups



Supplementary figure 1. Seasonal distribution of viral hepatitis

Table 1: Clinical characteristic of viral hepatitis patients in the study.

Symptoms	Hepatitis A (n= 561)	Hepatitis B (n= 267)	Hepatitis C (n= 45)	Hepatitis E (n= 1339)	p- value
Age / years	26.31 ± 7.68	38.31± 3.15	38.89± 3.76	32.36 ± 11.44	<0.005
Jaundice (n, %)	530 (94.5)	219 (82)	22 (48.8)	1282 (95.7)	<0.005
Fever (n, %)	299 (53.3)	92 (34.5)	15 (33.3)	458 (34.2)	0.56
Nausea (n, %)	344 (61.3)	102 (38.2)	13 (28.9)	786 (58.7)	0.014
Vomiting (n, %)	205 (36.5)	86 (32.2)	11 (24.4)	537 (40.1)	0.016
Loss of appetite (n, %)	482 (85.9)	134 (50.1)	20 (44.4)	1002 (74.8)	0.08
Abdominal pain (n, %)	280 (49.9)	103 (38.6)	18 (40)	625 (46.7)	0.345
Myalgia (n, %)	10 (1.8)	12 (4.8)	1 (2.2)	13 (1.0)	0.55
Pruritus (n, %)	83 (14.8)	19 (7.1)	0 (0)	401 (29.9)	0.04
Diarrhea (n, %)	223 (39.7)	32(11.9)	5 (11.1)	655 (48.9)	0.03
Altered sensorium (n, %)	11 (2)	12 (4.5)	4 (8.9)	47 (3.5)	0.3

Supplementary table 1: Risk factors of viral hepatitis in the study cohort.

Risk Factor	Hepatitis A (n= 561)	Hepatitis B (n= 267)	Hepatitis C (n= 45)	Hepatitis E (n= 1339)	p- value
Family history (n, %)	29 (5.2)	39 (14.	0 (0)	59 (4.4)	<0.005
Tattooing (n, %)	8 (1.4)	92 (34.5)	9 (20)	26 (1.9)	<0.005
Blood transfusion (n, %)	13 (2.3)	48 (18)	2 (4.4)	22 (1.8)	<0.005
Previous Surgery (n, %)	13 (2.3)	42 (15.7)	6 (13.3)	62 (4.6)	<0.005

Table 2: Laboratory parameters of patients with viral hepatitis.

Parameters	Hepatitis A (n= 561)	Hepatitis B (n= 267)	Hepatitis C (n= 45)	Hepatitis E (n= 1339)	p- value
Hemoglobin (g/dl)	11.88 ± 2.18	11.99 ± 1.84	10.56 ± 2.41	12.75 ± 3.44	<0.005
Leucocyte (10^3/dl)	7960.38 ± 3282.12	8777.75 ± 3370.36	8305.56 ± 4591.92	8212.04 ± 4558.84	0.124
Neut/Lymph ratio	1.39 ± 0.99	1.38 ± 0.83	1.39 ± 0.65	1.77 ± 0.94	0.653
Platelets (10^3/dl)	258.1 ± 106.3	343.1 ± 198.6	188.4 ± 97.3	236.6 ± 389.1	<0.005
Bilirubin (mg/dl)	10.30 ±7.91	14.73 ± 10.87	4.39 ± 5.27	14.06 ± 8.65	<0.005
ALT (U/l)	1012.03 ± 924.33	797.88 ± 857.63)	112.69 ± 134.31	1138.91 ± 882.82	<0.005
AST (U/l)	655.18 ± 734.16	632.50± 609.23	129.24 ± 76.45	854.38 ± 783.28	<0.005
Alk Ph (U/l)	210.54 ± 129.63	128.83 ± 68.32	97.96 ± 38.67	160.98 ± 74.80	<0.005
Serum Protein (g/dl)	7.84 ± 3.38	7.89 ± 3.66	7.31 ± 0.72	7.72 ± 4.10	0.816
Serum Albumin (g/dl)	3.62 ± 0.45	3.29 ± 0.65	2.90 ± 0.57	3.63 ± 1.23	<0.005
INR	1.33 ± 0.50	1.42 ± 0.47	1.36 ± 0.37	1.38 ± 0.99	0.314
Creatinine (mg/dl)	0.80 ± 0.59	0.84 ± 0.80	0.81 ± 0.35	0.85 ± 0.38	0.541

Neut/Lymph ratio: *Neutrophils/ Lymphocyte ratio;* ***AST:*** *Aspartate transaminase;* ***ALT:*** *Alanine transaminase;* ***Alk ph:*** *Alkaline Phosphatase* ***INR:*** *International normalized ratio*

Table 3: Univariate analysis for predictors of mortality in patients with viral hepatitis.

Parameters	Survived (N= 2179)	Died (N=33)	p-value
Age / years	31.60 ± 11.40	36.85 ± 16.86	0.009
Gender: Male/Female	1502/677	21/12	0.515
Duration of symptoms/ days	9.80 ± 8.817	12.06 ± 10.95	0.146
Altered sensorium (n, %)	53 (2.43)	21 (63.64)	<0.005
Gastrointestinal bleeding (n, %)	7 (0.32)	3 (9.09)	<0.005
Oliguria (n, %)	28 (1.28)	1 (3.03)	0.382
Diabetes (n, %)	59 (2.71)	4 (12.12)	0.001
Hypertension (n, %)	48 (2.20)	1 (3.03)	0.749
Smoking (n, %)	55 (2.52)	3 (9.09)	0.019
Alcohol (n, %)	135 (6.19)	7 (21.21)	<0.005
ALF/ACLF (n, %)	52 (2.39)	20 (60.60)	<0.005

Underlying cirrhosis (n, %)	133 (6.10)	9 (27.27)	<0.005
Hemoglobin (g/dl)	12.41 ± 3.02	10.84 ± 2.64	0.003
Leucocyte count (10^3/dl)	8799.22 ± 4123.19	11806 ± 5858.32	<0.005
Platelets (10^3/dl)	238 ± 3.12	183 ± 0.70	0.30
Neutroph/ Lymph ratio	1.74 ± 1.11	2.94 ± 2.16	<0.005
Bilirubin (mg/dl)	12.90 ± 8.87	18.51 ± 12.94	<0.005
AST (U/l)	756.74 ± 744.63	1131.33 ± 1248.10	0.005
ALT (U/l)	1042.21 ± 890.39	1208.54±1345.22	0.291
Alkaline phosphatase (U/l)	168.43 ± 94.69	165.45 ± 109.90	0.858
Total protein (g/dl)	7.77 ± 4.52	7.07 ± 0.94	0.374
Albumin (g/dl)	4.21 ± 7.18	3.56 ± 0.54	<0.005
INR	1.50 ± 4.79	2.26 ± 0.75	0.363
Creatinine (mg/dl)	0.85 ± 0.48	1.32 ± 1.24	<0.005

ALF: *acute liver failure;* ***ACLF:*** *acute on chronic liver failure;* ***Neutroph/ Lymph ratio:*** *Neutrophils/ Lymphocyte ratio****: AST****, aspartate transaminase;* ***ALT:*** *alanine transaminase;* ***INR:*** *International normalized ratio*

Table 4: Multivariate analysis for predictors of mortality in patients with viral hepatitis

Parameters	Odds ratio (OR)	95% Confidence Interval		p-value
		Lower limit	*Upper limit*	
Age	0.998	0.962	1.035	0.920
Alcohol	1.146	0.288	4.557	0.847
Smoker	4.274	0.866	21.108	0.075
Altered sensorium	9.511	1.940	46.616	0.005
Gastrointestinal bleeding	16.566	2.086	131.398	0.008
Underlying cirrhosis	2.226	0.640	7.741	0.208
ALF/ACLF	10.364	2.171	49.469	0.003
Serum Albumin	0.827	0.708	0.966	0.016
AST	1.0	0.999	1.0	0.920
Hemoglobin	1.414	1.161	1.721	0.001
Leukocyte count	1.0	1.0	1.0	0.077
Serum Creatinine	0.772	0.499	1.192	0.243

Footnote: ***ALF****: Acute liver failure;* ***ACLF****: Acute on chronic liver failure;* ***AST****: Aspartate transaminase*

Table 5: Comparison of patient profile of non-A-non-E hepatitis to hepatitis A-E in various characteristics.

Features	Hepatitis A-E group (n=1900)	Non-A-non-E Hepatitis (n=45)	p- value
Age / years	30.57 ± 10.83	38.71 ± 14.48	<0.005
Gender: Male/Females	1306/593	26/19	0.459
Symptom/ days	9.42 ± 8.48	11.51 ± 8.98	0.103
Jaundice (n, %)	1812 (95.37)	40 (88.89%)	0.060
Fever (n, %)	757 (39.84)	14 (31.11)	0.49
Weakness (n, %)	742 (39.05)	20 (44.44)	0.537
Vomiting (n, %)	742 (39.05)	13 (28.89)	0.215
Abdominal pain (n, %)	905 (47.63)	23 (51.11)	0.875
Joint pain (n, %)	23 (1.21)	0 (0)	1.0
Altered sensorium (n, %)	58 (3.05)	4 (8.89)	0.06
Gastrointestinal bleeding (n, %)	6 (0.31)	0 (0)	1.0
Oliguria (n, %)	25 (1.31)	0 (0)	1.0
Past history of jaundice (n, %)	127 (6.68)	3 (6.67)	1.0
Family history (n, %)	88 (4.63)	0 (0)	0.265
Diabetes (n, %)	50 (2.63)	1 (2.22)	1.0
Hypertension (n, %)	33(1.73)	3 (6.67)	0.04
Alcohol (n, %)	102 (5.37)	1 (2.22)	0.513
Smoking (n, %)	36 (1.89)	4 (8.89)	0.012
Hemoglobin (g/dl)	12.49 ± 3.145	12.08 ± 2.02	0.384
Leucocyte count (/dl)	8842.47 ± 4259.83	9340 ± 4834.27	0.440
Neutroph/ Lymph ratio	1.66 ± 0.97	2.72 ± 2.58	<0.005
Platelets (lakhs/dl)	2.42 ± 3.31	1.99 ± .82	0.390

Bilirubin (mg/dl)	12.95 ± 8.61	11.69 ± 8.41	0.332
ALT (U/l)	1101.45 ± 896.90	461.18 ± 734.63	<0.005
AST (U/l)	795.57 ± 774.27	438.60 ± 623.15	0.002
Alkaline phosphatase (U/l)	175.61 ± 96.99	167.29 ± 94.24	0.569
Serum protein (g/dl)	7.76 ± 3.90	7.70 ± 0.69	0.091
Serum Albumin (g/dl)	3.63 ± 1.06	3.35 ± 0.57	0.083
INR	1.37 ± 0.87	1.46 ± 0.58	0.465
Creatinine (mg/dl)	0.84 ± 0.45	1.08 ± 0.62	<0.005
Underlying chronic liver disease (n, %)	8 (0.42)	9 (20)	<0.005
Mortality (n, %)	26 (1.37)	3 (6.67)	0.028

Neutroph/Lymph ratio: *neutrophils/ lymphocyte ratio;* ***AST:*** *aspartate transaminase;* ***ALT:*** *alanine transaminase;* ***INR:*** *international normalized ratio*

Discussion

In this large cohort of patients with acute hepatitis, the majority of patients were viral hepatitis (91.06 %). Hepatitis E was the most common etiology followed by hepatitis A and hepatitis B. Among non-viral causes, the common etiologies included DILI (3.36%), AIH (2.01%), and cryptogenic hepatitis (1.78%). Jaundice and prodromal symptoms were common in viral hepatitis except Hepatitis C. Similar to previous studies; individuals with acute viral hepatitis had a low fatality rate. Although hepatitis A is considered a disease of children, a significant proportion of adults (22.54%) were seen suffering from hepatitis A. The late peaking in instances of hepatitis A was likely due to improved sanitation and better food handling. Water logging, poor sewage disposal, and high contamination of the food chain, probably were responsible for the high prevalence of hepatitis A and E in monsoon and summer. Pruritus was seen in around 30% of participants with hepatitis E. Pruritus is common in individuals with cholestasis, which is a recognized consequence of hepatitis E, and has been recorded in 15–60 % of patients in various studies[16, 17]. Conversely, hepatitis C patients seldom experienced prodromal symptoms. Previous studies had shown that anicteric hepatitis (asymptomatic modest rise in transaminases) was common in persons with hepatitis C. In previous studies, only 15–30% of people with acute hepatitis C were symptomatic with mild symptoms[18]. Cirrhosis is a common consequence of hepatitis C infection. We found a majority of patients in the hepatitis C cohort (69%) had cirrhosis. Similar results were seen in another study, where cirrhosis was present in 56% of patients[19]. Reduced transaminase levels, platelet counts, albumin levels, and hemoglobin levels in hepatitis C could be explained by underlying cirrhosis. There was no statistically significant difference in mortality across virus subgroups. Altered sensorium, gastrointestinal bleeding, low hemoglobin levels, elevated bilirubin, low albumin, and presentation in the form of ALF/ACLF were the main predictors of mortality. Autoimmune hepatitis manifested itself in a variety of ways, ranging from acute hepatitis to decompensated cirrhosis. The demography of patients of AIH was similar to another large cohort study from North India[20]. Additionally, the majority of the patients of AIH (83.9%) already had cirrhosis. It was concordant to previous studies which showed AIH patients of Indian descent frequently had cirrhosis at presentation[21-23]. Although worldwide studies have shown that increasing age was independently associated with an estimated four-fold increased incidence of DILI[24,25]. In our study, the majority of patients with DILI belong to the younger age group. Increased use of health supplements and complementary medications in adolescents and young adults in India was probably responsible for the increased incidence of DILI in this group. Similar results were reported by the Indian DILIN network, with a mean age of 42 years as opposed to 49, 53, and 58 years from the United States, Spain, and Sweden[26]. In contrast to the Indian DILI network research, where anti-TB drugs were more prevalent, the most common offending drugs in our study were complementary and herbal medicines. The prevalence of chronic DILI varied widely, ranging from 5.7% to 39%[27]. A retrospective, multi-center study conducted in China[28], found that 13% of DILI cases were chronic. This was consistent with the numbers of chronic DILI in the US DILI Network (13.6%)[29]. We reported chronic DILI in 11% of patients. There were limited studies on non-A/non-E hepatitis. Often this entity is overlooked. We reported 45 cases of non-A/non-E hepatitis and compared them to the group with hepatitis A/E. Patients were older, which was consistent with the scantly published literature[8,10]. Smoking and hypertension were both significant risk factors for non-A/non-E hepatitis. However, these risk variables were not investigated in previous studies. The rise in transaminase level was lower in the non-A/non-E group than in the hepatitis A/E group and was similar to previous literature[8,10]. In the study by Alter et al, 32% of their patients had chronic hepatitis while we found chronic liver disease in 20% of the non-A/non-E hepatitis patients[8]. Our study had certain limitations. First, it was a single-center retrospective study. We included patients who required hospital attention. The true profile of patients with acute hepatitis would require a community-based approach. Thirdly, the liver biopsy was not available for all patients. Our inclusion of a diverse group of acute hepatitis patients with viral, drug-induced, autoimmune, non-A/non-E, and other types of acute hepatitis is another drawback of our study. This study, on the other hand, focuses on real-world scenarios.

Conclusion

This study has provided a comprehensive overview of the epidemiological and clinical profile of acute hepatitis. Hepatitis E continued to be the most common cause of acute hepatitis.

Gastrointestinal bleeding, anemia, low serum albumin, and presentation as ALF/ACLF were independent predictors of mortality in patients with acute hepatitis. Future research should look into non-viral hepatitis in a prospective design and determine its long-term outcomes.

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