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Etiology and Prognostic factors of Acute Liver Failure in Children and Adolescents; A Single Centre Experience From Northernmost India'

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Abstract

Introduction: Acute Liver Failure is a life-threatening condition characterised by jaundice, encephalopathy and coagulopathy leading to multiorgan failure in a patient with no prior history of liver disease. There is paucity of epidemiological and prognostic factors in Acute Liver Failure in children from the region of Jammu and Kashmir. This study was done to find out etiology, prognostic factors and short term outcome of acute liver failure in children admitted to pediatric intensive care unit.

Materials & Methods: This study was a hospital based prospective observational study conducted at children's hospital of Government Medical College Srinagar Kashmir. Fifty-one consecutive patients of ALF in the age group of 1 to 18 years admitted in pediatric ICU were studied for etiology and prognostic factors. Prognostic factors were studied by dividing the patients into two groups: those who expired and those who improved & were discharged from the hospital.

Results: Infections were the most common cause of ALF (76.5%) followed by indeterminate (9.8%), autoimmune (5.9%), drug induced (3.9%), Wilson's disease & HLH (2% each). Among infections, Hepatitis A (66.7% o) was the most common cause of Acute Liver Failure in children. Out of total 51 patients, 34 (66.7%) patients expired while 17 (33.3%) patients were discharged from the hospital. The characteristics of patients who expired and those who were discharged from the hospital were analysed. Presence of hepatic encephalopathy at admission (p value = 0.016), increasing grade of hepatic encephalopathy (p value < 0.05), higher serum bilirubin at admission (p value < 0.05)), higher peak bilirubin levels (p value < 0.05), higher peak INR (p value < 0.05) and low RBS at admission (p value < 0.05) were found to be strong predictors of mortality.

Conclusions: Hepatitis A is the most common cause of Acute Liver Failure in children. Presence of hepatic encephalopathy at admission, increasing grade of hepatic encephalopathy, higher serum bilirubin at admission, higher peak bilirubin levels, higher peak INR, low RBS at admission are associated with increased risk of mortality.

Keywords: Acute Liver Failure, Hepatic encephalopathy, Prognostic factors, Outcome

Introduction

Hepatitis A is the most common cause of Acute Liver Failure in children and adolescents in the Kashmir, northernmost India.

Hepatic encephalopathy at admission, increasing grade of hepatic encephalopathy, higher serum bilirubin at admission, higher peak bilirubin levels, higher peak INR, low RBS at admission are associated with increased risk of mortality.

Acute liver failure (ALF) is a rapidly progressive, potentially fatal syndrome caused by a large variety of insults. The etiology of ALF varies according to the age of patient and development of the country [1-3]. In developing countries, hepatitis A is the most significant etiological agent causing acute liver failure (ALF) in children [4-5]. In developed countries metabolic liver diseases is the most common cause of ALF in children under 3 years and in older than 3 years, acetaminophen intoxication is the main cause [6]. However, the cause of ALF still remains undetermined in a large proportion of children.[7]Five studies published between 1996 and 2007 studies from India (Chandigarh, Vellore, Delhi, Kolkata and Pune) enrolling 215 children showed acute viral hepatitis to be the commonest cause, either alone or in combination (overall 61-95%: hepatitis A 10-54%; hepatitis E 3-27%; hepatitis B 8-17%, multiple viruses 11-30%- (commonest being hepatitis A+E), drugs 6-8% cases and unestablished etiology in 6-22% patients[8-15].Kings college criteria hold good for paracetamol related ALF. Factor V concentration <25% and INR> 4 are the best predictors of mortality without liver transplant [19]. Determining the prognosis of ALF is vital when considering the patient for transplant so as to identify those patients who are unlikely to survive without liver transplant. There is lack of data on etiology and prognostic factors of acute liver failure in children, from the region of Jammu and Kashmir. Therefore, we tried to explore the epidemiology, prognosis and outcome of acute liver failure in PICU setting where significant mortality is due to this disease**.**

Materials And Methods

The study was conducted at Pediatric Intensive Care Unit (PICU) of Department of Pediatrics in G. B. Pant Hospital, an associated hospital of Government Medical College Srinagar, after obtaining institutional ethical clearance and consent from guardians. The study was a hospital based prospective observational study conducted from November 2017 to October 2019. All children older than one year and ≤ 18 years of age were included and liver failure was defined as

1. Absence of a previously known history of chronic liver disease,
2. Biochemical evidence of acute liver injury, and
3. Hepatic-based coagulopathy defined as PT ≥ 15s or INR ≥ 1.5 not corrected by vitamin K in the presence of encephlopathy or PT ≥ 20s or INR ≥ 2 regardless of the presence or absence of clinical HE [12].

Grading of Hepatic Encephalopathy was done using the standard criteria. [21]

Patients younger than 1 year were excluded as they have different clinical characteristics and aetiology.

After detailed history and physical examination, all the patients were subjected to haematological and biochemical investigations. The investigations included complete blood count (CBC), arterial blood gas (ABG), serum electrolytes, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), total and conjugated bilirubin, prothrombin time (INR), blood group, direct coombs test (DCT), blood and urine cultures, chest X-ray, lactate, blood ammonia and urine for reducing substances. All the patients were tested for viral markers for hepatitis: IgM anti-hepatitis A virus, IgM anti-hepatitis E virus, hepatitis B virus surface antigen, IgM anti-hepatitis B core antibody. Positive blood cultures were taken as diagnostic of enteric fever [22].

Wilson's disease profile was done in patients with alkaline phosphatase/bilirubin ratio <4.0, AST/ALT ratio > 2.2 +/- evidence of Coombs negative hemolysis. This included ophthalmological examination for KF rings, 24-hour urinary copper estimation and serum ceruloplasmin. Investigations for autoimmune hepatitis were sent in the following: female sex, age> 6 years, positive family history, raised immunoglobulin G levels and positive direct Coombs test. This included anti-nuclear antibody (>1:40), liver kidney microsomal antibody, smooth muscle antibody (>1:20) and Ig G levels. HLH was diagnosed by having 5 of the following 8 signs or symptoms: fever, splenomegaly, cytopenia (affecting ≥2 cell lineages; hemoglobin ≤9g/dl, platelets <100,000/microlitre, neutrophils <1,000/microlitre), hypertriglyceridemia (265 mg/dl) and/or hypofibrinogenemia (≤150mg/dl), hemophagocytosis in the bone marrow, spleen, or lymph nodes without evidence of malignancy, low or absent natural killer cell cytotoxicity, hyperferritinemia (≥500 ng/ml) and elevated soluble CD25 (interleukin-2Rα chain;

Volume 5, Issue 6; November-December 2022; Page No 753-762

≥2,400 U/Ml). Young adults and adolescents with history of drug intake and abnormal renal function, drug levels (valproate) were done. In cases where no positive viral markers, no history of toxin or drug exposure, and no metabolic cause were detected, the etiology of PALF was classified as indeterminate [22,23].

All the patients were managed according to the standard ICU protocols [12].

Cases were divided into two groups according to the final outcome: first group included those patients who expired while the other group comprised of those who improved or discharged. The following clinical and laboratory parameters were assessed: age, HE at admission, grade of HE at admission, interval between onset of prodromal symptoms and HE, pH, blood sugar at admission, bilirubin level at admission, peak bilirubin levels, INR at admission and peak INR [24].

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 23.0. Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Continuous variables were compared using student independent t-test. Chi-square test and/or Fisher's exact test was used to analyse the relationship between categorical variables.

Results

During the study period 51 children with Acute Liver Failure were admitted out of which 27 (52.9%) were males and 24 (47.1%) were females. The mean age of the study population was 7.0 ± 3.3 years. Most of the patients were from rural than urban areas as shown in Figure 1.

The etiologies of PALF included infectious (76.5%, n=39), indeterminate (9.8%, n=5), autoimmune (5.9%, n=3), drug induced (3.9%, n=2). Wilson's disease (2%, n=1) and HLH (2%, n=1). Among infections the most common etiology was found to be Hepatitis A virus (66.7%, n=34) followed by Hepatitis E virus (2%, n=1) and Enteric Fever (7.8%, n=4) as shown in Figure 2 and figure 3.

The most common clinical findings (figure 4) during presentation were jaundice (100.0%, n=51) followed by anorexia (90.2%, n=46), vomiting (84.3%, n=43), fever (76.5%, n=39), abdominal pain (64.7%, n=-33), hepatic encephalopathy (54.9%, n=28), ascites (33.3%, n=17), bleeding (19.6%, n=10), edema (5.9%, n=3).. Hepatic encephalopathy was present in 54.9% (n=28) patients at admission of which grade I HE was seen in 29.4% (15/51), grade II HE in 9.8% (5/51), grade III HE in 11.8% (6/51) and grade IV HE in 3.9% (2/51). The laboratory parameters of study subjects are shown in Table 1.

Out of total 51 cases of ALF, 34 patients died giving a mortality of 66.7%. Outcome across gender was found to be statistically insignificant (p value= 0.569). Age specific mortality rate was highest in 6-10 years' age group. However, comparison of the mean ages of expired and discharged group showed that difference in age group was statistically insignificant (p value=0.294).

HE was present in 28 patients at admission out of which 23 expired and 5 were discharged from the hospital. Presence of HE at admission was found to be statistically significant (p value =0.016). Among the patients who had HE at admission, grade I HE was seen in 15 patients, out of which 10 patients expired and 5 patients were discharged while grade II/III/IV HE was present in 13 patients all of which expired. On comparing the grades of HE (grade I vs grade II/III/IV) between the expired and discharged groups, the results were found to be statistically significant (p value<0.05). The interval between the onset of prodromal symptoms and HE was found to be ≤7 days in 9 patients out of which 6 patients expired while the interval between the onset of prodromal symptoms and HE was found to be >7 days in 19 patients out of which 17 patients expired showing no statistical significance (p value=0.29).

Bleeding manifestations were present in 23 cases, out which 14 (27.4%) expired and 9 were discharged. Comparison of bleeding manifestations between expired and discharge groups showed that the results were not statistically significant (p value=0.553). Thus, bleeding was not a significant predictor of mortality.

Total serum bilirubin (table 1 lab parameters) of the patients at admission was 13.93±5.85 and peak bilirubin of the patients was 20.96±7.20. Patients

Volume 5, Issue 6; November-December 2022; Page No 753-762

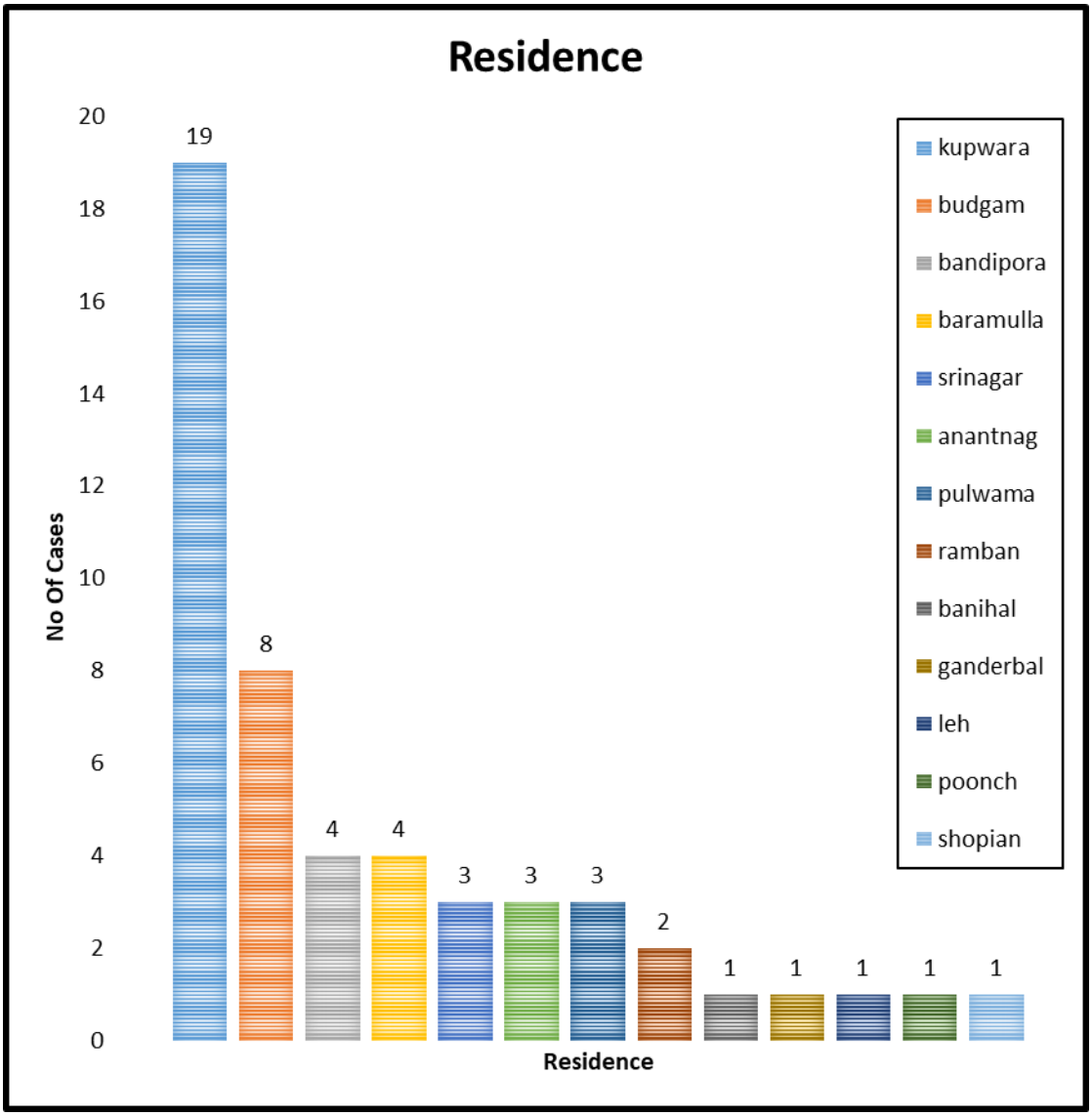
who expired had higher mean bilirubin level at admission as compared to the patients who were discharged (15.91±5.39 vs 9.96±4.68, p value<0.0001) and the peak bilirubin level of the patients who expired was also significantly higher as compared to the patients who were discharged (23.73±6.16 vs 15.41±5.88, p value<0.0001).

INR of the patients at admission was 2.27±0.61. INR of the patients who expired was not significantly different as compared to the INR of the patients who were discharged (2.37±0.66 vs 2.05±0.45, p value=0.079). Thus, INR at admission was not a significant predictor of mortality in our study. Peak INR of the patients was found to be 3.74±1.07. Peak INR of the patients who expired was significantly higher as compared to the patients who were discharged (4.20±0.96 vs 2.82±0.54, p value<0.0001).

Random blood sugar (RBS mg/dl) of the patients at admission was 98.20±39.82. expired patients had significantly lower RBS (87.12±40.43) than the patients who were discharged (120.35±28.28, p value=0.004).

pH of the patients at admission was 7.37±0.14. pH of the patients who expired was not significantly different from the patients who were discharged (7.37±0.16 vs 7.38±0.07, p value=0.783), therefore, pH of the patients was not a significant predictor of mortality in our study.

Figure 1: Distribution of study subjects according to residence (district)



Volume 5, Issue 6; November-December 2022; Page No 753-762

Figure 2: Etiology of ALF in study subjects

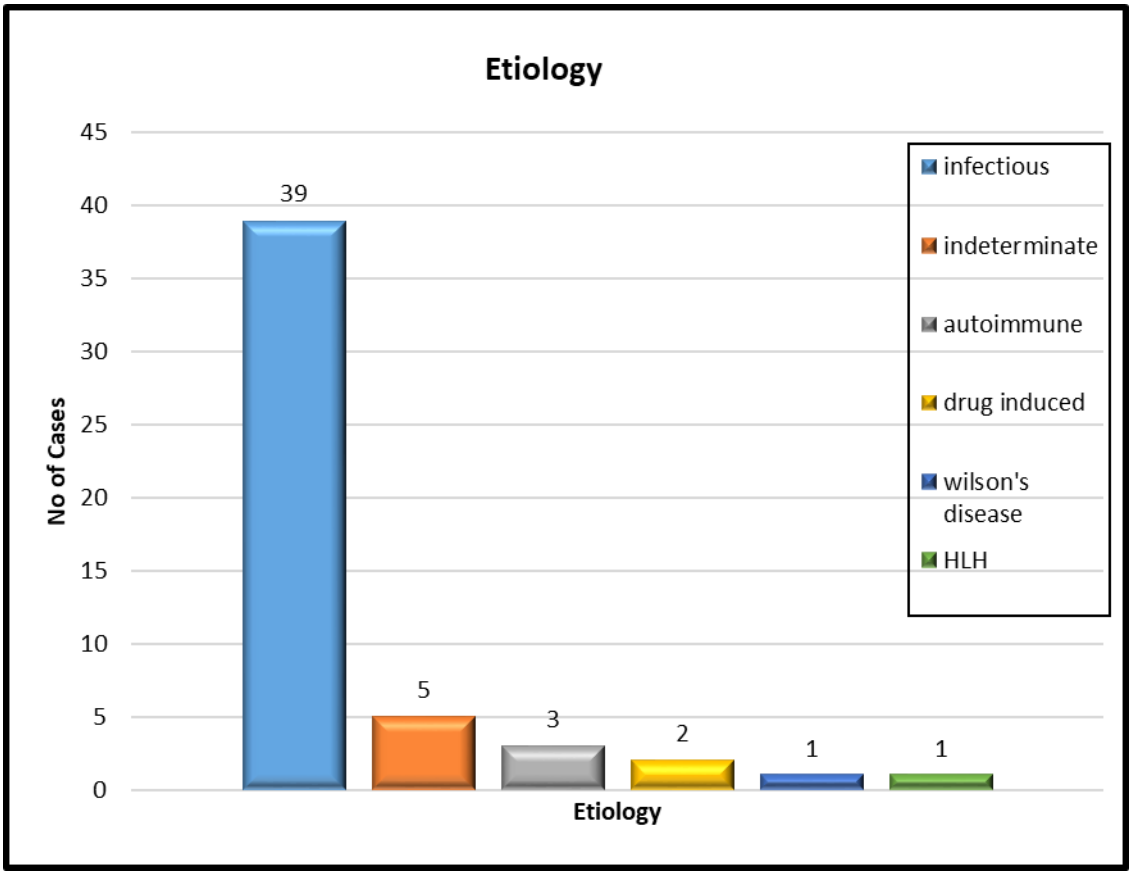
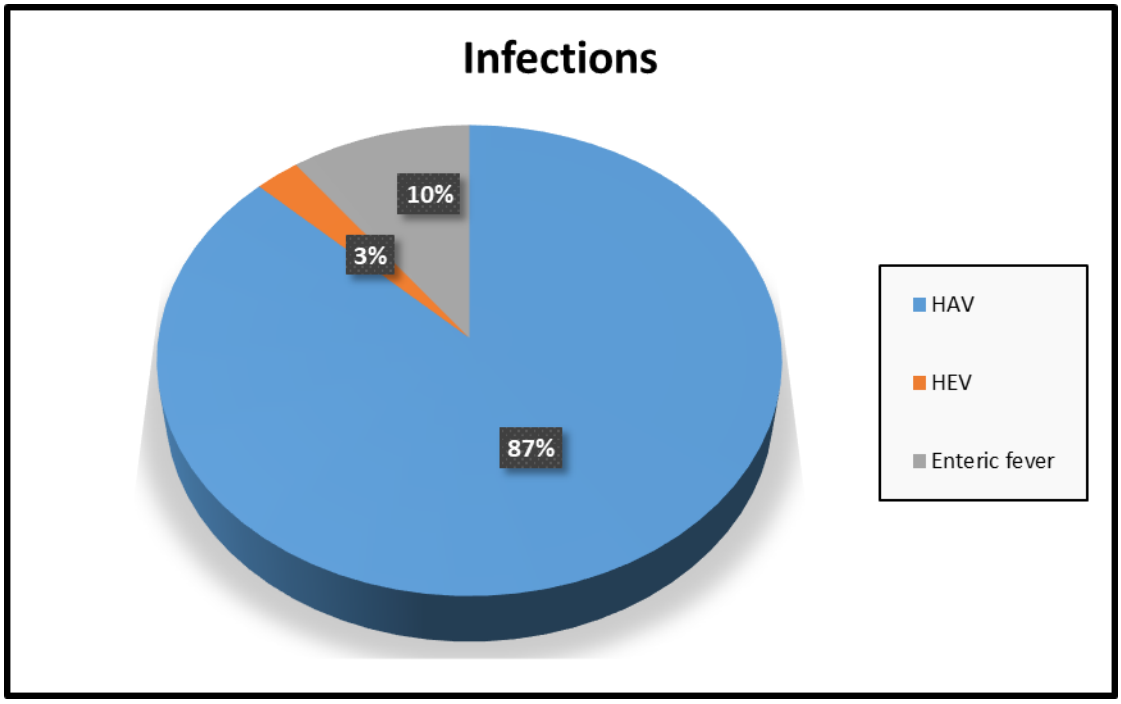


Figure 3: Distribution of infectious causes of ALF in study subjects



Volume 5, Issue 6; November-December 2022; Page No 753-762

Figure 4: Clinical presentation in study subjects

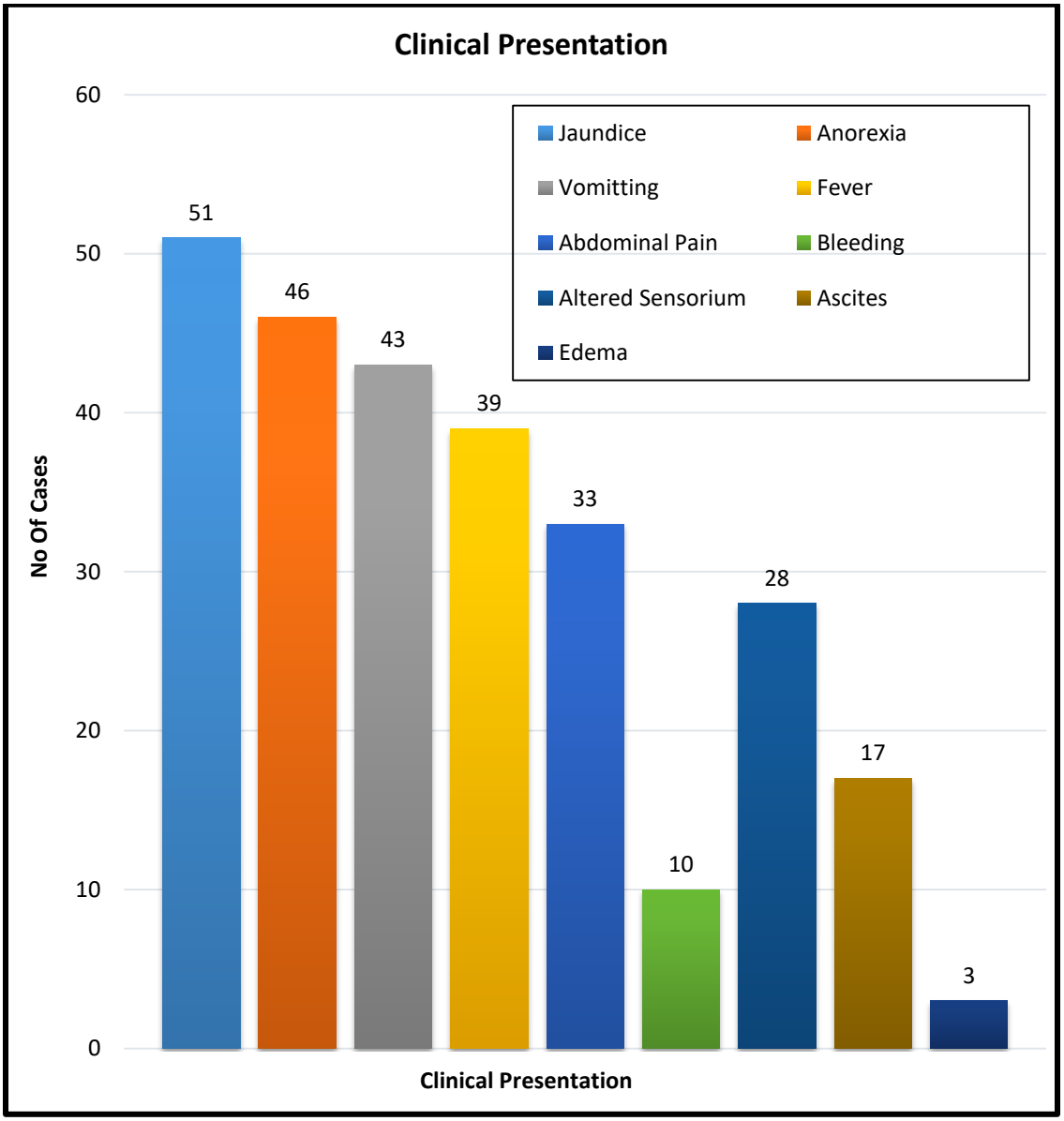


Table 1: Laboratory Parameters in study subjects

	Minimum	Maximum	Mean	Std. Deviation
Total Bilirubin at Admission (mg/dl)	3.2	26.6	13.929	5.8509
Peak Bilirubin (mg/dl)	4.7	36.7	20.961	7.1976
INR at Admission	1.2	4.5	2.267	.6147
Peak INR	1.6	5.5	3.737	1.0660

Volume 5, Issue 6; November-December 2022; Page No 753-762

BSR at Admission (mg/dl)	32.0	187.0	98.196	39.8161
pH	7.10	7.65	7.3747	.13829

Discussion

Our study comprised a total of 51 patients out of which 27 (52.9%) were males and 24 (47.1%) were females, (approximately 1:1). The mean age of the study subjects in our study was 7.0±3.3 years, the highest number of patients being in the age group of 6 to 10 years comprising 30 patients which was 58.8% of the total study population. The male; female ratio and age group demographics was similar to other studies [25,26]. Although study cases presented from all the parts of the Kashmir valley, majority of the patients were from rural than urban regions. This could be attributed to poor access of people to safe drinking water facilities, rivers and springs as source of drinking water, unhygienic practices, poor sanitation and low socioeconomic standards. The most common clinical presentation of our study cases was jaundice which was present in all cases (100%) followed by anorexia (90.2%), vomiting (84.3%), fever (76.5%), abdominal pain (64.7%), hepatic encephalopathy (54.9%), bleeding in 45.1% cases, ascites (33.3%) and edema (5.9%) consistent with other studies [14,25,27]. Poddar U et al [14] stated that prodromal symptoms (fever, anorexia, vomiting) were present in 95.5% cases. Hepatic encephalopathy (HE) was present in 55% of study subjects at admission, consistent with study by Ciocca M et al [26] (58%) and Bravo LC et al [28] (46.2%). The interval between the prodrome and onset of HE was found to be ≤ 7 days in 32.1% and >7 days in 67.9%. This was comparable to a study conducted by Ciocca M et al [26] which interval between prodrome and onset of HE was <7days in 21.8% of the patients and >7days in 78.2% of the patients.

Infection is the most common cause of ALF in developing world[11,24,26,29].In our study we found that infections were the most common cause of ALF in children (76.5%) of the total study population followed by indeterminate (9.8%), autoimmune (5.9%) , drug(valproic acid) induced (3.9%), Wilson's disease (2%) and HLH (2%).In infectious etiology, the most common cause was found to be Hepatitis A virus comprising 34 cases (66.7%) of the total patients followed by Enteric fever (7.8%, n=4) and Hepatitis E virus (2%, n=1). The results were consistent with the study conducted by Ciocca M et al [26], Kaur S et al [24] and Poddar U et al [14]. The short-term outcome in terms of mortality during hospital stay was studied. Out of total 51 patients admitted with ALF, 34 patients (66.7%) died during hospital stay. However, mortality in studies by Kaur S et al [24] was 44.2%, Ozcay F et al [25] 31.9% and Silverio CE et al [30] 41.9%. The higher mortality in our study could be attributed to late referral, small study group and one among many tertiary care centres available.

In our study, we found that age was not related to the poor prognosis (p value=0.089). Age specific mortality rate was also found to be insignificant predictor of mortality (p value=0.294). These findings correlate well with the studies conducted by Kaur S et al[24], Ozcay F et al [25], Ciocca M et al[26] , Lee WS et al[27]and Poddar B et al[29]**.** Gender of patients was also found to be insignificant predictor of mortality (p value=0.569), which is in agreement with the other studies [24,25,29]**.**

In our study we found that out of total 28 patients who presented with HE at admission, 23(45.1%) patients expired while 5 patients were discharged. Comparison of HE at admission between the expired and discharge groups showed the results to be statistically significant (p value=0.016). This is in accordance with other studies that hepatic encephalopathy at admission is the strong predictor of mortality [24,25,26] . We observed in our study that grade I HE was present in 15 patients out of which 10 cases (19.6%) expired and 5 cases were discharged. Grade II/III/IV HE was observed in 13 patients all of which expired. Comparison of grade I HE and grade II/III/IV HE between expired and discharge group showed the results were statistically significant (p value<0.05). Various studies have shown that higher grades of hepatic encephalopathy are associated with higher mortality [24,25,26,27] . Interval between onset of

Volume 5, Issue 6; November-December 2022; Page No 753-762

prodromal symptoms and HE is the significant predictor of mortality [24]. The interval between onset of prodromal symptoms and HE (at admission) in our study was ≤7 days in 17 patients out of which 9 patients expired and 8 patients were discharged. While the interval was >7days in 11 patients out of which 9 patients expired and 2 were discharged. Comparison of interval between onset of prodrome and HE between expired and discharge groups showed that the results were not statistically significant (p value=0.29). Gastrointestinal haemorrhage may occur in up to 70% of pediatric ALF patients [16]. Bleeding manifestations were present in 23 cases in our study, out of which 14 (27.4%) expired and 9 were discharged. Comparison of bleeding manifestations between expired and discharge groups showed that the results were not statistically significant (p value=0.553).. Total serum bilirubin of the patients at admission was 13.93±5.85 and peak bilirubin of the patients was 20.96±7.20. We observed the patients who expired had higher mean bilirubin level at admission as compared to the patients who were discharged (15.91±5.39 vs 9.96±4.68, p value<0.0001) and the peak bilirubin level of the patients who expired was also significantly higher as compared to the patients who were discharged (23.73±6.16 vs 15.41±5.88, p value<0.0001). High serum bilirubin at admission and higher peaks of serum bilirubin are associated with high mortality [24,25,26] .In our study the peak INR of the patients was 3.74±1.07. Peak INR of the patients who expired was significantly higher as compared to the patients who were discharged (4.20±0.96 vs 2.82±0.54, p value<0.0001). Higher peaks of INR are associated with higher mortality. [25,26,27]. Low random blood sugar(RBS) at admission is associated with high mortality and poor outcome in ALF [24,31]. In our study the RBS (mg/dl) of the patients at admission was 98.20±39.82. RBS (mg/dl) of the patients who expired was significantly lower (87.12±40.43) than the patients who were discharged (120.35±28.28, p value=0.004). Although deranged pH is strong predictor of mortality [17,24], in our study the pH of the patients at admission was 7.37±0.14 and the pH of the patients who expired was not significantly different from the patients who were discharged (7.37±0.16 vs 7.38±0.07, p value=0.783).

The limitations of this study are small sample size as it was the one of the many tertiary care centres in this region yet first study of this kind from the northernmost India.

In conclusion, pediatric ALF is a life-threatening condition, hepatitis A being the most common cause. Higher HE grade at admission, higher peak INR, low RBS at admission, higher total bilirubin at admission and higher peak bilirubin levels were found to be strong predictors of mortality. These factors need identification at an early stage to make early referral to transplant centre. Improving sanitary conditions, providing safe drinking water facilities, creating awareness about hygienic practices like hand washing, drinking boiled water and providing hepatitis A immunization through national immunization program may help prevent hepatitis A related acute liver failure.

References

1. Acharya SK, Dasarathy S, Kumar TL, Sushma S, Presanna U, Tandon A, et al. Fulminant hepatitis in a tropical population: clinical course, cause and early predictors of outcome. Hepatology 1996; 23: 1448-55.
2. Ostapowicz J, Lee WM. Acute hepatic failure: a western perspective. J Gastroenterol Hepatol. 2000;15;480-8.
3. Dhiman RK, Seth AK, Jain S, Chawla YK, Dilawari JB. Prognostic evaluation of early indicators in fulminant hepatic failure by multivariate analysis. Dig Dis Sci. 1998;43:1311-6.
4. Ciocca M, Ramonet M, Cuarterolo M, López S, Cernadas C, Alvarez F. Prognostic factors in paediatric acute liver failure. Arch Dis Child 2008; 93: 4851.
5. Shah U, Habib Z, Kleinman RE. Liver failure attributable to hepatitis A virus infection in a developing country. Pediatrics 2000; 105: 436-8.
6. Squires RH Jr, Shneider BL, Bucuvalas J, et al. Acute liver failure in children: the first 348 patients in the pediatric acute liver failure study group. J Pediatr 2006;148:652–658.
7. Dhawan A. Etiology and prognosis of acute liver failure in children Liver Transpl 2008; 14: 80-4.

Volume 5, Issue 6; November-December 2022; Page No 753-762

8. Wilson DC, Phillips MJ, Cox DW, Roberts EA. Severe hepatic Wilson's disease in preschool-aged children. J Pediatr 2000; 137: 719-22.
9. Arora NK, Mathur P, Ahuja A, Oberoi A. Acute liver failure. Indian J Pediatr. 2003; 70:73-9.
10. Arora NK, Nanda SK, Gulati S, Ansari IH, Chawla MK, Gupta SD, et al. Acute viral hepatitis types E, A, and B singly and in combination in acute liver failure in children in north India. J Med Virol. 1996;48:215-21.
11. Bendre SV, Bavdekar AR, Bhave SA, Pandit AN, Chitambar SD, Arankalle VA. Fulminant hepatic failure: etiology, viral markers and outcome. Indian Pediatr. 1999; 36:1107-12.
12. Bhatia V, Lodha R. Intensive care management of children with acute liver failure. Indian J Pediatr. 2010;77:1288-95.
13. Bhowmick K, Mammen A, Moses PD, Agarwal I, Mathew L, Kang G. Hepatitis A in pediatric acute liver failure in southern India. Indian J Gastroenterol. 2005;24:34.
14. Poddar U, Thapa BR, Prasad A, Sharma AK, Singh K. Natural history and risk factors in fulminant hepatic failure. Arch Dis Child. 2002; 87:54-6.
15. Samanta T, Ganguly S. Aetiology, clinical profile and prognostic indicators for children with acute liver failure admitted in a teaching hospital in Kolkata. Trop Gastroenterol. 2007;28:135-9.
16. Alonso E, Squires R, Whitington P. Acute Liver Failure in Children. In: Suchy FJ, Sokol RJ, Balistreri WF, editors. Liver Disease in Children. 3rd ed. Cambridge: Cambridge University Press; 2007. p.71–96.
17. O'Grady JG, Alexander GJ, Hayllar KM, Williams R. Early indicators of prognosis in fulminant hepatic failure. Gastroenterology. 1989;97:439-45.
18. Bernuau J, Goudeau A, Poynard T, Dubois F, Lesage G, Yvonnet B, et al. Multivariate analysis of prognostic factors in fulminant hepatitis B. Hepatology. 1986; 6:648-51.
19. Shanmugam NP, Dhawan A. Selection criteria for liver transplantation in paediatric acute liver failure: the saga continues. Pediatr Transplant. 2011;15:5-6.
20. Dhawan A, Taylor RM, Cheeseman P, De Silva P, Katsiyiannakis L, Mieli-Vergani G. Wilson's disease in children: 37-year experience and revised King's score for liver transplantation. Liver Transpl. 2005;11:441-8.
21. Squires Jr. RH. Acute liver failure in children. Seminars in Liver disease June 2008; doi:10.1055/9-2008-10/3115.
22. Pediatric Gastroenterology Chapter of Indian Academy of Pediatrics; Bhatia V, Bavdekar A, Yachha SK; Indian Academy of Pediatrics. Management of acute liver failure in infants and children: consensus statement of the pediatric gastroenterology chapter, Indian academy of pediatrics. Indian academy of pediatrics. Indian Pediatr. 2013; 50(5): 477-82.
23. Kliegman and Nelson (21st edition).2020; p.2712.
24. Kaur S, Kumar P, Kumar V, Sarin SK, Kumar A. Etiology and prognostic factors of acute liver failure in children. Indian Pediatr. 2013; 50(7):677-9.
25. zçay F, Karadag-Oncel F, Baris S, Canan O, Moray G, Haberal M. Etiologies, outcomes, and prognostic factors Oof pediatric acute liver failure: A single center's experience in Turkey. Turk J Gastroenterol 2016; 27: 450-7.
26. Ciocca M, Ramonet M, Cuarterolo M, Lopez S, Cernadas C, Alvarez F. Prognostic factors in paediatric acute liver failure. Arch Dis Child 2008;93:48–51.
27. Lee WS, McKiernan P, Kelly DA. Etiology, Outcome and Prognostic Indicators of Childhood Fulminant Hepatic Failure in the United Kingdom. Journal of Pediatric Gastroenterology and Nutrition 40:575–581.
28. Bravo LC, Gregorio GV, Shafi F, Bock HL, Boudville I, Liu Y, et al. Etiology, incidence and outcomes of acute hepatic failure in 0–18 year old Filipino children. Southeast Asian J Trop Med Public Health. 2012 May;43(3):764–72.
29. Poddar B, Saigal S, Kumar A, Singh RK, Azim A, Gurjar M, Baronia A. Factors associated with

Volume 5, Issue 6; November-December 2022; Page No 753-762

outcome in acute liver failure in an intensive care unit. Indian J Gastroenterol 2013;32(3):172–178.

30. Silverio CE, Smithen-Romany CY, Hondal NI, Diaz HO, Castellanos MI, Sosa O. Acute Liver Failure in Cuban Children. MEDICC Rev. 2015; 17(1): 48-52.

31. Srivastava KL, Mittal A, Kumar A, Gupta S, Natu SM, Kumar R et al. Predictors of outcome in fulminant hepatic failure in children. Indian J Gastroenterol 1998; 17: 43-45.

Volume 5, Issue 6; November-December 2022; Page No 753-762