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Acute hepatitis in children: A wide clinical spectrum

Vijay Ganesh [1] and Poornima Modi [2,*]

[1] *Department of Paediatrics Base Hospital, J45P+3M5, Hospital Road, Delhi Cantonment, New Delhi- 110010, India.*
[2] *Department of Paediatrics, Army College of Medical Sciences, J45Q+FF4, near Base Hospital Brar Square, Delhi Cantonment, New Delhi- 110010, India.*

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Abstract

Introduction: Acute hepatitis remains an important health problem in children. viral hepatitis particularly hepatitis A remains the most common cause. Nevertheless, other causes such as non A non B hepatitis and mixed infections like enteric fever are other causes particularly in developing countries like India. The spectrum of acute hepatitis is also varied with many atypical presentations in the form of fever along with icterus as presenting features. Use of lab parameters as prognostic markers for development of acute liver failure (ALF) needs further exploration as it can be used to identify patients who need better monitoring and may be the potential candidates for liver transplantation. In our study we have tried to find a possible association between liver enzyme values and number of children who develop ALF.

Methods: Children between 1 and 15 years of age who presented with features of acute hepatitis were enrolled in the study after taking informed consent from their parents. Data was collected about their epidemiological and clinical characteristics in a predesigned study performa. Quantitative data were described as means and standard deviations and qualitative data were computed into frequency (No) and percentages (%). Chi-square ($\chi 2$) test was used to determine the statistical difference between the categorical variables, while means were compared using student's t test. For all statistical analyses, p value < 0.05 was adopted as level of significance.

Results: We enrolled 68 patients of acute hepatitis. Most of them were males (78%) and majority were in 6 to 10 years age category. The most common clinical presentation was with abdominal pain followed by fever and icterus. Liver enzymes were raised to the tune of 10 to 20 times in the second week of illness. Serum bilirubin mean value was 5.3. Serum bilirubin values remained almost constant over 3 weeks period while liver enzymes showed a decline. 26% patients presented with ALF. Also, liver enzyme values in the second week showed a positive association with development of ALF with higher values associated with a higher chance of development of ALF.

Conclusion: Hepatitis A was the most important cause of acute hepatitis in children and albeit early, a significant proportion of them develop features of ALF. Regular monitoring of liver enzymes can serve as a prognostic marker for development of ALF. It requires larger level studies to use liver enzymes as prognostic markers of ALF in paediatric patients.

Keywords: Hepatitis; Acute liver failure; Bilirubin; Liver enzymes; Transplantation

1. Introduction

Acute hepatitis in children is an alarming public health problem with a lot of morbidity and mortality. Timely recognition of the cause of acute hepatitis can prevent lots of deaths by recognizing the treatable causes of hepatitis in children.

* Corresponding author: Poornima Modi

Historically, hepatitis A infection has been known to be a major cause of acute inflammation of liver (1,2). Prevalence of acute hepatitis A has been reported to the tune of 39% and 49% among hospitalized children in U.K and India respectively in various studies (3,4). Apart from hepatitis A, hepatitis E is also a major cause of acute hepatitis especially in developing countries (5,6). Apart from hepatotropic viruses, other viruses include Cytomegalovirus (CMV), Epstein Barr virus (EBV) , Herpes virus, adenovirus etc (7). Acute hepatitis can also be part of systemic bacterial infections like enteric fever, leptospirosis, scrub typhus, brucellosis and others. Autoimmune hepatitis (AIH) is yet another cause of pediatric acute hepatitis (8). In addition to these causes, there is a recent surge in cases of acute hepatitis with a relatively fulminant presentation and no identifiable cause, termed as indeterminate acute hepatitis (9). This upsurge of indeterminate cases of acute hepatitis in children started from April 2022 with 10 cases reported in U.K and a rising incidence thereafter from other countries (10). We wish to review the cases of acute hepatitis presenting to our hospital with the aim of discerning any common etiologies and clinical course.

Hepatitis A infection usually presents as fever, malaise, anorexia, vomiting, joint pains followed by onset of jaundice. Onset of jaundice usually marks the subsidence of prodromal features (11,12). Hepatitis A infection can have varied presentation. Although, most infections are subclinical, rarely it has been known to cause fulminant hepatitis and sometimes death. However, chronic hepatitis has not been shown to be associated with hepatitis A infection even in immunocompromised children (13,14). Hepatitis A infection is usually diagnosed by the presence of anti HAV IgM antibodies which appear after around 4 weeks of infection and remain positive for an year (15). Hepatitis A infection causes a rise in liver enzymes due to acute liver injury which take 4 to 6 weeks to normalize.

Coinfection of hepatitis A with enteric fever is also seen in our study. Previously, there have been few reports from India where coinfection of hepatitis A and enteric fever has been shown with the latest being from Vellore in south India in 2019 (16,17). The common route of transmission which is feco-oral for both hepatitis A and salmonella infection is one of the hypothesis. Another, theory suggests that gall bladder inflammation which is seen in hepatitis A causes persistence of *Salmonella typhi* leading to a carrier state (18,19).

2. Material and methods

A prospective observational study was conducted in the inpatient ward of paediatric department of Base Hospital, Delhi Cantonment from august to October 2024**.** A total of 68 children between 1 and 15 years of age presenting with jaundice of less than or equal to 7 days duration as primary complaints were included in the study. Children with previously diagnosed liver disease, children with comorbidities like cerebral palsy, cystic fibrosis, those with history of chronic drug use like anti tubercular therapy were excluded from the study.

Study definitions used during the study were:

Acute Hepatitis : defined as acute onset jaundice within 7 days

Acute liver failure is defined as: Duration of less than 8 weeks with no evidence of chronic liver disease and presence of hepatic based coagulopathy defined as prothrombin (PT)> 15sec or international normalised ratio (INR) >1.5 not corrected by vitamin K in the presence of clinical hepatic encephalopathy or a PT >20 sec or INR >2 regardless of the presence of clinical hepatic encephalopathy

The data was collected in a pre-designed study proforma after taking an informed consent from the parents. history about clinical symptoms and epidemiological characteristics such as travel history, history of jaundice in the sibling and drinking water was collected. Clinical features suggestive of acute liver failure were also collected. Details of lab investigations including liver function tests, etiology work up and PT INR values were recorded.

The collected data was numerically coded and entered in Microsoft excel 2007 and then transferred to Windows Statistical Package of Social Sciences (SPSS) software (version 21). Quantitative data was described as means and standard deviations and qualitative data was computed into frequency (No) and percentages (%). Chi-square ($\chi 2$) test was used to determine the statistical difference between the categorical variables, while means were compared using student's t test. For all statistical analyses, p value < 0.05 was adopted as level of significance

3. Results

Among the 68 children who presented with acute hepatitis, 78% were males. As per the age distribution, 49% children were between 6 to 10 years age category (table1, figure1). Among the clinical presentation, abdominal pain was present

in all patients with a mean duration of 4.3 days. Other presenting complaints included fever and icterus present in 95% and 94% of the children respectively. Altered sleep pattern which is an early marker of acute liver failure was present in 42% cases of hepatitis. History of intake of outside food was present in 23% cases, 27% children had history of travel and 25% children had history of similar complaints in the siblings (table2). Among the lab parameters, mean serum bilirubin values remained almost constant from 5.3 to 5.9 over 3 weeks of illness (table 3). SGOT values showed a steady decline from 1660 to 653 mean value over 3 weeks duration (table4) . SGPT values also showed a steady decline from 1900 to 950 over 3 weeks duration (table5).

Table 1 Gender and age Distribution

Gender	Frequency	Percentage
Male	53	78%
Female	15	22%
Age group		
≤5	18	26%
6 to 10	33	49%
>10	17	25%

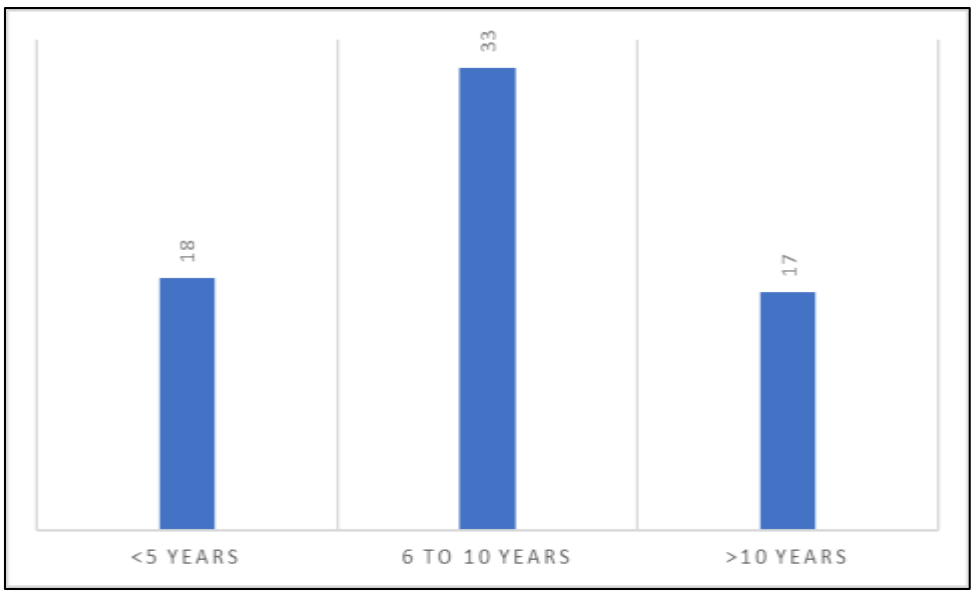

Figure 1 Age wise distribution of cases

Table 2 Distribution of patient history

History	Yes	No
Abdominal pain	68	0
Fever	65	3
Icterus	64	4
Altered sleep	29	41
Outside food intake	16	52
Travel history	19	49
Siblings	17	51

Table 3 Distribution of Total Bilirubin among study group

Total Bilirubin	1st week	2nd week	3rd week
Minimum	1.800	2.900	2.000
Maximum	14.00	11.10	9.800
Mean	5.350	5.871	5.932

Table 4 Distribution of SGOT among study group

SGOT	1st week	2nd week	3rd week
Minimum	284.0	116.0	85.00
Maximum	6780	3345	3700
Mean	1663	1169	653.2

Table 5 Distribution of SGPT among study group

SGPT	1st week	2nd week	3rd week
Minimum	356.0	285.0	112.0
Maximum	5990	4863	3127
Mean	1931	1583	950.6

Table 6 Statistical correlation of ALF positive and negative cases with lab parameters

Tests	Week	ALF +ve	ALF -ve	95.00% CI of diff.	Adjusted P Value
Total bilirubin	1st week	6.429	5.070	-647.6 to 650.3	>0.9999
	2nd week	6.886	5.607	-647.7 to 650.2	>0.9999
	3rd week	6.721	5.728	-647.9 to 649.9	>0.9999
SGOT	1st week	2306	1497	160.6 to 1458	0.0042
	2nd week	2160	911.5	599.5 to 1897	<0.0001
	3rd week	1152	523.9	-21.02 to 1277	0.0599
SGPT	1st week	2379	1815	-85.02 to 1213	0.1302
	2nd week	2402	1370	382.6 to 1680	<0.0001
	3rd week	1533	799.7	83.97 to 1382	0.0140
PT/INR	PT/INR	1.907	1.443	-648.5 to 649.4	>0.9999

Acute liver failure (ALF) was present in 26% children with acute hepatitis that is 18 patients. Out of the total children presenting or developing ALF during the course of disease, 33 % had deranged prothrombin time international normalised ratio of more than or equal to 2.0. Altered sleeping pattern was present in 72% children with ALF while 22% had both micrographia and altered sleeping pattern. Liver enzyme values showed a significant correlation with ALF . SGOT values above 2000 in the second week of illness showed a high probability of developing ALF with a p value of 0.0001. Similarly , SGPT values more than 2000 in second week had a higher probability of going in ALF with a p value of 0.0001 (table 6). Etiology work up in our study showed 100% cases were positive for hepatitis A antibody IgM and 6 children (8.8%) had combined infection with hepatitis A and enteric fever having a positive blood culture for *Salmonella typhi*

4. Discussion

The gender distribution of acute hepatitis in our study showed that males were almost four times more affected than females which is in contrast to other studies which show almost an equal ratio (11,12). Age distribution of cases is in line with other studies previously done. Clinical presentations were also in sync with other studies except that in our study abdominal pain was present in 100% patients as compared to other studies where it was 70 to 80% (11,20). We found a significant elevation of liver enzymes upto 100 times in hepatitis A which is noticed in other studies from India also (21,11). Our study showed a significant association between liver enzyme values in the second week and the probability of developing acute liver failure. There are not many studies in the past that have explored the association of liver enzymes with development of ALF. All the previous studies have been performed mostly in severe ALF patients requiring liver transplantation and in those patients the trend of liver enzymes has been towards the decline in non survivors of ALF (22). Our study found hepatitis A IgM antibodies in all cases of acute hepatitis. Although, hepatitis A remains the most common cause of acute hepatitis, values this high have not been found in past studies (11,20). The proportion of children with ALF was also high in our study as contrast to other studies where in the percentage of ALF is around 3 to 5% (12, 22). However, there was 100% survival rate in our study.

5. Conclusion

Our study shows that hepatitis A remains the most important cause of acute hepatitis. The presenting features include abdominal pain, fever and icterus most commonly. ALF , although of minor degree is present in a substantial number of children presenting with acute hepatitis but majority had good prognosis. Liver enzyme values showed a significant association with the development of ALF with higher values associated with a greater probability of developing ALF. The role of Liver enzymes values as a prognostic marker for development of ALF can be further explored. The limitations of the study include that a very limited section of population was studied and therefore the results may not be generalisable to a larger population.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

Ethical approval was taken from the institutional ethics committee prior to the start of study

Statement of informed consent

Informed consent was taken from the parents of children participating in the study as to the use of medical records for research and publication purpose while maintaining the anonymity of the participants.

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