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Original Research Article

Etiology of hepatitis in children

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ABSTRACT

Background: Hepatitis (plural hepatitides) is inflammation of the liver and characterized by the presence of inflammatory cells in the tissue of the organ. Although infectious hepatitis, autoimmune hepatitis and metabolic diseases are the cause but in majority of the cases etiology remain obscure. Worldwide, the overall frequency of pediatric liver disease is 1:8,000. According to a study in U.S, it amounts to almost 15,000 hospital admissions per year. Objective of present study was to study and determine etiologies of the hepatitis in non-neonatal age group and find out the commonest etiological cause, along with to study clinical course of acute hepatitis and average time for recovery from the illness

Methods: A prospective study of 100 children presented with the clinical jaundice between the age group of 1 month to 18 years were evaluated using inclusion criteria utilizing clinical proforma, complete history, clinical examination and blood investigations, in the pediatric out-patient, in-patient and emergency department at Moolchand Medcity, New Delhi from August 2008 to August 2010.

Results: Hepatitis A was positive in 88 children (88%) which was the highest in frequency, followed by Typhoid in 5 of children (5%), while Hepatitis E (3%), B (2%) and dengue 1(1%) were the least in the incidence respectively. Two patients had fulminant hepatitis and both were positive for Hepatitis A, of which one was referred for liver transplant. Period for clinical recovery was found to be 12-24 days (19.87±3.489) and for biochemical recovery was range from 23- 59 days (36.71±5.9437) while all 99 (99%) patients were recovered from the illness in 99 % of cases.

Conclusions: Hepatitis A is the most common cause of acute hepatitis. Clinical recovery occurred in 2 to 3 weeks, followed by biochemical recovery in 3 to 8 weeks respectively.

Keywords: Etiology of hepatitis, Infective hepatitis, Pediatric liver disease

INTRODUCTION

Hepatitis (plural hepatitides) is the inflammation of the liver and characterized by the presence of inflammatory cells in the tissue of the organ.[1] Hepatitis continues to be a major public health problem worldwide especially in developing countries like India. The common causes for hepatitis in children are hepatitis A, hepatitis B, hepatitis C, hepatitis D, autoimmune hepatitis and metabolic disorders like Wilson's disease and α-1 antitrypsin deficiency. In majority of the patients the etiology remains uncertain. Autoimmune hepatitis was found to the commonest cause in the western literature while infections are among the lowest3; the biggest chunk is

however idiopathic. The scenario is likely to be different in the tropical and subtropical countries like India because of high prevalence of infection.

Childhood hepatitis constitutes a significant population of hospital admissions in India. Worldwide, the overall frequency of pediatric liver disease is 1:8,000. According to a study in U.S, it amounts to almost 15,000 hospital admissions per year.[2] Over the last few years, pediatrics has witnessed a gradual but a definite change in the pattern of the liver diseases. For instance, Indian childhood cirrhosis (ICC) which earlier accounted for about 50% of all chronic liver diseases and almost 5% of all pediatric admissions, has today become a rare entity, with only occasional case reported annually even from large medical centers.[4] Certain liver diseases, which have a subtle presentation but run an indolent course, only to present later in life as a serious and even life threatening disease e.g. α-1 antitrypsin deficiency, cystic fibrosis, metabolic liver diseases, etc. Some of these diseases are completely preventable if diagnosed early e.g. metabolic liver diseases like galactosemia. However, a delay in diagnosis can prove fatal or may result in significant morbidity e.g. failure to thrive, neurological abnormality, involvement of other organs due to underlying disease and chronic liver disease.

Despite the above-mentioned facts, a search into the literature reveals only a few such studies highlighting the currently prevailing spectrum of the pediatric liver diseases. Taking all these factors into consideration, we decided to do a study to understand the current etiology of the hepatitis in children attending outpatient and inpatient departments in our hospital.

Understandably, pediatric liver disease adds substantially distress in the parents and also to the economic burden of the country taking into consideration the costs involved in hospitalization and the long-term follow-up required thereafter in most of the cases.

METHODS

The study was conducted in the Department of Pediatrics, Moolchand Medcity, New Delhi over a period of 2 years from August 2008 to August -2010. Patients were recruited from out-patient, emergency room and in patient wards. Hundred children (age group 1 month to 18 years) presenting with jaundice and who fulfilled the inclusion criteria were included in the study after taking informed consent and the approval from ethical committee for post graduate studies, Moolchand Medcity, New Delhi.

Inclusion criteria

All children who were presented with clinical jaundice, in the form of yellowish discoloration on sclera between age group 1 month and 18 years.

Exclusion criteria

- All children below 1 month and above 18 years presents with the jaundice.
- Children presenting with the deranged liver profile without jaundice.

A detailed history and physical examination was done and findings were recorded in the clinical proforma. Serological markers for hepatitis were done in all patients. Patients with negative viral serological markers were further investigated for other infective causes of hepatitis (typhoid, dengue, malaria). Patients in which infective cause were not found were further investigated for the non-infective causes. All cases were followed up clinically and biochemically till recovery. Data was analyzed using standard statistical software SPSS. For statistical analysis Chi-square test was used for analyzing qualitative data. $P<0.05$ was considered as statistically significant.

The investigations analyzed during the study includes heamogram, peripheral smear, liver function test (SGOT, SGPT, Sr. Bilirubin- Total, direct, Indirect, Alkaline phosphatase), blood urea nitrogen, sr. creatinine, Hepatitis viral serological markers (Anti HAVIgM, anti HEVIgM, HbsAg, AntiHCV in patient presenting with history of blood transfusion). The other infectious causes for hepatitis were evaluated by doing Widal test, dengue serology, malaria smear and rapid diagnostic test in respective cases then finally work up for autoimmune hepatitis was done wherever required. Severity of the disease was assessed by associated multi-organ dysfunction manifested by cardiac, renal, neurological, hematological and respiratory derangements.

Those children presenting with altered sensorium, reduced urine output, persistent vomiting, very poor oral intake and bleeds were admitted in the hospital and in these patients PT/aPTT was done. All children were stated on multivitamins and low fat diet; ursodeoxycholic acid (udilive) and cholestyramine were included in treatment if child had pruritus. All patients were followed up in OPD to see trend of SGOT (normal range between 15-55 IU/L) and SGPT (normal range between 5-45 IU/L) and sr. bilirubin, till values were normalized. Total duration of illness was calculated, with time required for clinical recovery of symptoms and biochemical recovery determined by normalization of liver enzymes.

RESULTS

Out of 100 children presenting with jaundice 88 (88%) children were found to have Anti HAV IgM positive which was highest in frequency followed by typhoid which was found in 5 (5%) children. Next in frequency was hepatitis E which was found in 3 (3%) children, Hepatitis B in 2 (2%) children and lowest with dengue fever which was 1% while in 1% of children diagnosis was undetermined.

Table 1: Etiological profile.

	Frequency	Percentage
Dengue Fever	1	1.0
HAV	88	88.0
HBV	2	2.0
HEV	3	3.0
Undetermined	1	1.0
Typhoid	5	5.0
Total	100	100.0

Out of total 100 children 88 those diagnosed with hepatitis A 12 (13.63%) were below 5 years, 33 (37.5%) were between 6-9 years of age group, 28 (34.81%) were from 10-13 years of age group and 15 (17%) children were from more than 14 years of age group. Those 2-patient diagnosed with Hepatitis B were from age group 6-9 years (100%).

Three out of 100 patient diagnosed with Hepatitis E, 2 (66.66%) were from age group 6-9 year and 1 (33.33%) patient was from 10-13 years of age. Of 5 patients diagnosed with typhoid fever, 3 (60%) were from age group 10-13 years of age group and 1 (20%) each from age group 6-9 years and more than 14 years age.

Table 2: The age wise distribution of etiological factors is given.

		Diagnosis						Total
		Dengue fever	HAV	HBV	HEV	Undetermined	Typhoid	
Age group	≤5 yrs	0	12	0	0	0	0	12
	6-9 yrs	0	33	2	2	1	1	39
	10-13 yrs	1	28	0	1	0	3	33
	≥ 14 yrs	0	15	0	0	0	1	16
Total		1	88	2	3	1	5	100

Table 3: Clinical profile.

	Total	HAV (n=88)	HBV (n=2)	HEV (n=3)	Typhoid (n=5)	Dengue Fever (n=1)
Yellow discoloration of eyes	99	87	2	3	5	1
Vomiting	93	81	2	3	5	1
Fever	89	77	2	3	5	1
Loose Motion	13	12	0	1	0	0
swelling on face and feet	1	1	0	0	0	0
Decreased urine output	1	1	0	0	0	0
High colored urine	68	62	0	2	3	1
Itching	5	5	0	0	0	0
Weakness	65	57	1	2	5	0
Malaise	58	53	0	3	1	1
pain in abdomen	54	48	2	1	3	0
Anorexia	77	70	2	1	3	1
Abdomen distension	1	1	0	0	0	0
Bleeding tendencies	0	0	0	0	0	0
Icterus	100	88	2	3	5	1
Pruritus mark	5	5	0	0	0	0
palmer erythema	0	0	0	0	0	0
spider nevi	0	0	0	0	0	0
Ascites	2	1	0	0	0	1
Facial puffiness	1	1	0	0	0	0
Pedal edema	0	0	0	0	0	0
Hepatomegaly	78	69	1	2	5	1
Rt. hypochondriac tenderness	73	65	2	0	5	1
Splenomegaly	31	27	1	0	3	0
Dilated veins	0	0	0	0	0	0

Patient diagnosed with dengue fever fall in 10-13 year age category. A patient in whom etiologic agent could not be determined was in less than 5 years age group.

Table 4: Duration of various symptoms.

	Duration of symptoms (days) Range (mean±SD)
Yellow discoloration of eyes	12-24 (19.87±3.489)
Vomiting	1-4 (2±0.707)
Fever	1-8 (3.76±1.1616)
High colored urine	2-6 (4.43±0.908)
Itching	10-16 (13.2±2.387)
Weakness	6-12 (7.99±1.345)
Pain in abdomen	1-6 (3.48±1.145)
Anorexia	2-8 (4.78±1.438)

The average prodromal period before presentation of patients was noted and found to be in range of 2- 14 days with mean of 6-24 and standard deviation of 2.252. Icterus took longest time for recovery ranging from 12-24 days while itching was second annoying symptom last for about 10-16 days, while all other symptoms gets subsided in approximately 6-8 days. Vomiting had shortest duration lasting for 1-4 days (mean 2±0.707).

Of the 100 patients, two (2%) patients had severe hepatitis both were positive for Hepatitis A, of which one (1%) patient was referred for the liver transplantation.

Biochemical and clinical recovery, in the form of resolution of the clinical symptoms and normalization of biochemical parameters respectively, was observed in remaining 99 patients. Period for clinical recovery was found to be 12-24 days (19.87±3.489) and for biochemical recovery was range from 23- 59 days (36.71±5.9437) while all 99 (99%) patients were recovered from the illness.

Table 5: Outcome.

Etiology	Total cases	Recovered	Mortality	Referred for liver transplantation
HAV	88	87	0	1
HEV	3	3	0	0
HBV	2	2	0	0
Typhoid	5	5	0	0
Dengue fever	1	1	0	0
Undetermined	1	1	0	0

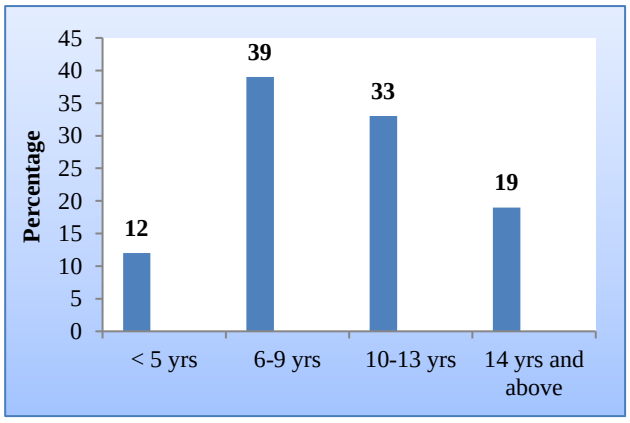

Figure 1: Age wise distribution of the patients diagnosed as hepatitis.

Most of the patients with hepatitis were between age group 6-9 years (39%), followed by age group 10-13 years (33%) and age group >14 years (16%) while least were seen in age group less than 5 years (12%). Thus, mean age of presentation was 9.5 yrs.

There were 59 (59%) males and 41 (41%) females out of 100 patients with hepatitis.

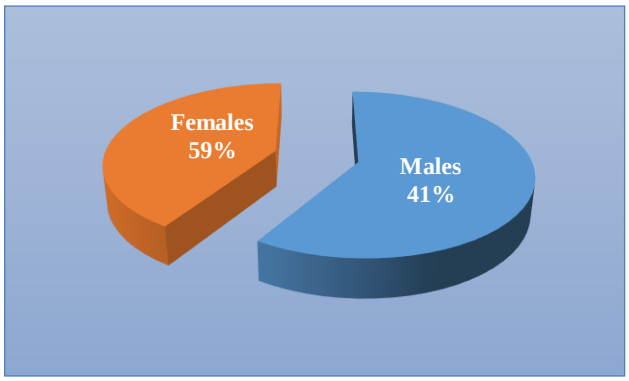

Figure 2: Sex distribution.

DISCUSSION

In present study of 100 children with acute hepatitis, hepatitis A was found to be the most common cause of sporadic childhood acute hepatitis (88%). These findings are higher than the earlier studies in north Indian children by Tondon BN et al and a study by Thapa BR et al in which Hepatitis A was found 67% and 78% respectively.[5,6] Typhoid fever was found to be the second most important cause of hepatitis with the incidence of

5%. In the literature, it has been mentioned that typhoid hepatitis is an important cause of morbidity in patient with typhoid fever.[7,8] Typhoid hepatitis is often mild to moderate nature with abnormal liver function tests. Biochemical alteration of hepatic enzymes has been reported in 24-87% of cases in various adult series.[9] Present study established an important role of these agents in childhood acute hepatitis. Hepatitis E (5%) was found to be the third common cause for the childhood hepatitis and, Hepatitis B (2%) and dengue fever (1%) were next in the frequency.

The hepatitis was common in 6 to 13 years (72%) age group which was slightly different from previous study by Panda SK et al, they found that Hepatitis A largely (59.5%) affects younger children of 1-5 yr.[10] while some other studies showed similar results and concluded that Hepatitis A virus infection starts dramatically high in school-age children, and then rises gradually with an increase in age.[6,11,12]

We found male to female ratio of 1.45:1. Although a slight preponderance of male as compared to females which was different from Poddar U et al study, spectrum of sporadic acute viral hepatitis in Indian children where they found that male to female ratio of 2.3:1.[13] It however would be difficult to conclude whether this disease shows any predilection for either sex.

Yellow discoloration of sclera was most common complaint that brings notice to parents, while anorexia, vomiting, weakness and malaise were common complaints which were also main commonest complaints in children. Yellow discoloration of sclera was found in 99% of patients, high colored urine in 68%, vomiting 93%, Fever in 89%, hepatomegaly in 78%, splenomegaly in 31%, which were corresponds with the earlier study done in at PGI Chandigarh.[14]

We observed that average period of this morbidity ranges from 2-14 days. Liver function tests were deranged in all hepatitis patients irrespective of etiology. Follow up of liver enzyme for various duration of the illness showed that, decreasing trend of SGOT/SGPT signifies recovery of the patient and average time for biochemical recovery ranges from 24-59 days. Derangements of biochemical parameters cannot signify etiology of hepatitis but are helpful in assessment of recovery of patient.

Two of 100 patients had fulminant hepatitis failure, one patient recovered and other patient was referred for liver transplantation. Both these patient were diagnosed with hepatitis A. Studies reported that commonest causes of acute liver failure in Indian children is acute viral hepatitis due to infection with Hepatitis A and E virus either alone or in combination while in the west, it is due to Hepatitis B, C viruses and drugs and toxin related.[13-18]

The difference in clinical presentation, in children with severe hepatitis and those with non-sever hepatitis with different etiology group were not significant in present study. Biochemical derangement in sever hepatitis group were not significantly higher than in non-sever hepatitis patient as would be expected from sever nature of liver damage in severe cases. It may point out that degree of biochemical abnormality may not be necessarily reflects on severity of infection.

Out of 100 children with hepatitis, one patient was referred for liver transplantation while other 99 patients were followed by various means of communication and on the OPD basis, found that all patients were recovered. Average period of illness from first contact was in a range of 24 to 59 days. Average time required for clinical recovery was far less (12-24 day) than time required for biochemical recovery (23-59 days).

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