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Original Research Article

A clinical study of viral hepatitis in children: a prospective hospital-based study

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ABSTRACT

Background: Viral hepatitis is a major public health issue throughout the world affecting millions of children; Clinical presentation may vary from asymptomatic to hepatitis, cirrhosis, liver failure and cancer. This study is aimed at understanding the clinical profile of viral hepatitis in children.
Methods: Prospectively, 48 children admitted in paediatric unit with confirmed viral hepatitis from August 2015 to July 2016 at KIMS hospital, Bangalore were included. In each case, age, sex, clinical presentation and laboratory investigations were collected and analysed.
Results: Out of 48 patients, 26 were girls and 22 were boys. Out of which 40 cases were positive for IgM Hepatitis A, 1 case of HbsAg positive, 7 cases were non-A non B Hepatitis. All cases presented with fever (100%), jaundice found in 40 cases (83.3%), 33 cases had abdominal pain (68.7%), vomiting was present in 40 cases (83.7%), 34 cases presented with dark colored urine (70.8%), altered sensorium in 3 cases (6.2%). Icterus was found in 48 (100%) cases, pallor was found in 17 cases (35.4%), Ascitis in 8 cases (16.7%), hepatomegaly in 37 cases (76%), oedema in 10 cases (21%). Liver enzymes elevated at admission in almost all cases, 16 cases had SGPT b/w 200-500. 10 cases had SGPT b/w 500-1000, 19 cases had SGPT b/w 1000-3000 and 2 cases had SGPT of more than 3000. 18 cases had total bilirubin between 5-10 mg/dl, 6 cases had total bilirubin >10 mg/dl. 44 cases had PT <1.5 at admission, 1 case had PT INR between 1.5-2.5, 1 case had INR between 2.5-3.5, 2 cases had INR>3.5. Out of 48 cases 2 cases died. Out of 2 deaths, 1 case of hepatitis A and 1 case positive for Hepatitis B. The cause of death was hepatic encephalopathy in both the cases.
Conclusions: Majority of cases in children were hepatitis A cases, followed by non-A non B. Most of the cases were aged above 3 years with slight girl's predominance. Those cases with elevated liver enzymes (SGOT >3000) and those with PT INR >3 at admission has higher mortality.

Keywords: Children, Clinical profile, Hepatotropic, Viral hepatitis

INTRODUCTION

It is defined as infection of the liver caused by hepatotropic and/or non-hepatotropic viruses.[1] Hepatitis is an inflammation of the liver; the condition can be self-limiting or can progress to fibrosis (scarring).[2] Epidemics of viral hepatitis are seen in many developing countries including India.[3] It continues to be a major health problem in both developing and developed countries. Epidemic jaundice due to hepatitis was first described by Hippocrates.[4] This disorder is caused by at least 5 pathogenic hepatotropic viruses recognised to date: hepatitides A (HAV), B (HBV), C (HCV), D (HDV) and E (HEV) viruses. Many other viruses can cause hepatitis, usually as one component of multisystem disease. These include herpes *simplex virus, cytomegalovirus, Epstein-*

Barr virus, varicella.[5] The relative frequency of asymptomatic and symptomatic Hepatitis has been reasonably well characterized and appears to be age dependent.[6]

Hepatitis A is the commonest cause of viral Hepatitis in pediatric age.[7-9] Infection with HAV occurs predominantly in areas of lower socio-economic status and reduced hygienic standards, especially in developing, tropical countries. The route of transmission of Hepatitis A is through contaminated water and food (feco-oral). Usually only humans are affected. The HAV infection clinical course varies widely from asymptomatic cases to fulminant liver failure.[10] In children, most cases are likely to be asymptomatic or unrecognized, while older adolescents and Adults presents with symptoms like jaundice and hepatomegaly. The incubation period for hepatitis A ranges between 15 and 50 days with an average of 30 days.[10] Underlying liver disorder and immunocompromised state increases the risk for liver failure in cases with HAV infection. Acute HAV infection diagnosis is made based on the identification of HAV RNA or anti-HAV IgM antibodies.[10]

Hepatitis B infection either present or past is serologically evident in approximately one third of world population. However, its prevalence varies widely from place to place ranging 0.1% to 20%. Low prevalence (<2%) areas include Western Europe, The United States, Canada, Australia and New Zealand. Lifetime risk of infection in low prevalent area is less than 20%. Intermediate prevalence is defined as 2% to 7%, includes the Mediterranean countries, Japan, Central Asia, the Middle East, and Latin and South America. Lifetime risk of infection in these areas is 20-60%. High prevalence areas (≥8%), lifetime likelihood of infection is greater than 60%. It includes Southeast Asia, China, and sub-Saharan Africa. The diverse prevalence rates are probably linked to differences in age at infection. As age increases, the progression rate from acute to chronic HBV infection decreases. The risk of progression is approximately 90% in case of perinatal transmission, while it is 5% in adults.[10] The routes of HBV transmission include Sexual, Perinatal, transfusion, percutaneous (intravenous drug use), horizontal, nosocomial (including needle-stick injury).[10] Incubation period varies from 60 to 180 days.[11] There is a wide range of clinical manifestation in both acute and chronic HBV infection. During the acute phase, manifestations range from subclinical to icteric hepatitis and, in some cases, fulminant hepatitis. Fulminant hepatitis or acute liver failure (ALF) was defined as the presence of biochemical evidence of acute liver injury (<8 weeks duration); no evidence of chronic liver disease; and hepatic based coagulopathy defined as a prothrombin time (PT) >15 s or international normalized 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.[12] During the chronic phase, it can be asymptomatic or manifest as chronic hepatitis, cirrhosis or hepatocellular carcinoma. Only 0.1-0.5% of patients are seen to develop fulminant hepatic failure.[10] Infection due to HBV may either resolve or progress to chronicity. However, HAV infection doesn't progress to chronicity.[13]

Non-A Non-B Hepatitis is a disease entity whose diagnosis is made on exclusion of Hepatitis A and B infection. Non-A Non-B Hepatitis is said to be transmitted predominantly by blood transfusion, percutaneous inoculation, plasma derivatives and rarely feco-oral route.[14] 95% of Non-A Non-B hepatitis in people who have received blood transfusions are due to Hepatitis C. Hepatitis C also constitutes 50% cases of sporadic non-A, non-B hepatitis.[15] The Hepatitis C infection prevalence in younger children less than 12 year is 0.2% and in children older than 12 year is 0.4%.[9]

To the best of our knowledge there is no published study on clinical profile of acute viral hepatitis in children. Against this background, we carried out a study in our hospital to understand the epidemiology of endemic viral hepatitis and its clinical presentations in the children.

METHODS

This is a prospective observational hospital-based study conducted in department of paediatrics, KIMS Bangalore between August 2015 and July 2016. Children less than 18 years who presented with jaundice, fever, vomiting/nausea, abdominal pain, dark coloured urine was included in this study after informed verbal consent from the parent/guardian. Total of 61 cases were admitted to paediatric department with above history. Those cases with acute onset of symptoms and positive for viral markers like IgM Hepatitis A or HbsAg for Hepatitis B were included. Non-A Non B Hepatitis cases were included after ruling out other causes of Hepatitis like drug exposure, metabolic, haemolytic, toxins, parasitic infection, on anti-tubercular treatment or active tuberculosis. Other diseases with similar complaints like Malaria, Enteric fever, Dengue were also excluded by laboratory tests. Chronic liver disease is ruled out by history or laboratory test. Obstructive cause and anatomical defects are ruled out by history and ultrasonography. Total 48 cases met our criteria. Each case was followed till either recovery or death.

In each case the presenting complaints like fever, jaundice and examination finding at admission like clinical icterus, organomegaly noted and each symptom and signs are followed till recovery or death. Priority was given based on general status of the patient. Those with CNS symptoms like seizures, decreased level of consciousness were admitted to PICU, Other cases were admitted to paediatric ward. In each case detailed history regarding travel, blood transfusion, family contacts, occupation, drug intake history if yes then scrutinized for liver toxicity, source of drinking water, food habits, herbal medication intake, residence in urban/rural area and income were obtained. Detailed general physical

examination and systemic examination was carried out. Viral markers, IgM Hepatitis A or HbsAg for Hepatitis B sent for all cases. Liver function test, PT INR/APTT were done at admission and recorded. There after laboratory test were repeated according to the status of the patient, same was tabulated in excel format and analysed. Special investigation like serum ammonia was sent in selective cases like involvement of central nervous system. In each case examination finding and laboratory test was compared to clinical outcome.

RESULTS

Out of 48 cases, 26 were girls (54%), 22 were boys (46%). This represents slight girls' predominance in the present study (Figure 1). As shown in Figure 1, 16 cases (33.3%) were aged more than 10 years. 14 cases (29.1%) aged between 6 and 10 years. 12 cases (25%) between 3 and 6 years. Only 6 cases (12.5%) reported less than 3 years.

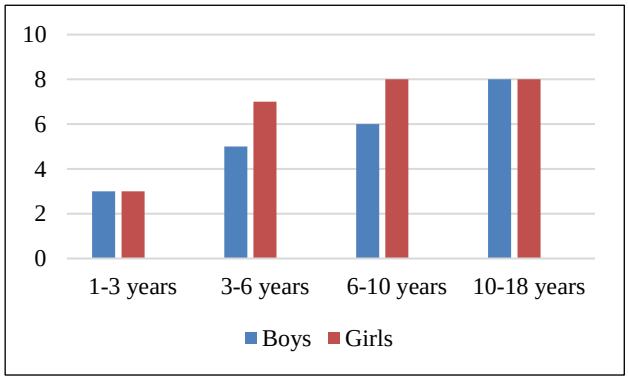

Figure 1: Distribution of patients according to age and sex.

Table 1: Symptoms distribution: fever, jaundice, abdominal pain, nausea/vomiting, anorexia.

Symptom	No. of patients (%)
Fever	100%
Jaundice	40 (83.3%)
Vomiting	40 (83.3%)
Abdominal pain	33 (68.7%)
Nausea	8 (16.7%)
Anorexia	4 (8.3%)
Dark colored urine	34 (70.8%)
Loose stools	4 (8.3%)
Altered sensorium	3 (6.2%)

On an average almost, all cases presented in second week. These cases presented with variety of symptoms, fever is presenting symptom in all cases (100%), jaundice and vomiting in 40 cases each (83.3%), these followed by dark coloured urine (70.8%), abdominal pain (68.7%), nausea (16.7%), anorexia and loose stools each accounting 8.3%, altered sensorium in 6.2%. when enquired about source of drinking water, 47% were using unsafe drinking water. Among them almost all were from rural areas. Table 2 describes physical findings distribution noted at the time of admission. This varied with each case. Icterus present in all cases (100%), hepatomegaly in 76% of cases followed by pallor in 35.4% cases, edema in 20.8%, ascitis in 16.7%, splenomegaly in 10.4%. As mentioned above icterus was the most common sign we encountered in the present study.

Table 2: Various physical findings distribution: icterus, ascitis, hepatomegaly, edema.

Physical finding	No. of patients (%)
Icterus	48 (100%)
Pallor	17 (35.4%)
Ascitis	8 (16.7%)
Hepatomegaly	37 (76%)
Splenomegaly	5 (10.4%)
Edema	10 (20.8%)

Table 3: SGPT, Serum bilirubin and INR at presentation.

SGPT at presentation	
Units/ml	**No. of patients**
100-200	1 (2.08%)
200-500	16 (33.3%)
500-1000	10 (20.8%)
1000-3000	19 (39.5%)
3000-5000	2 (4.16%)
>5000	Nil
Serum bilirubin at presentation	
Total bilirubin	**No. of patients**
1-5mg/dl	24 (50%)
5-10mg/dl	18 (37.5%)
>10mg/dl	6 (12.5%)
INR at presentation	
INR	**No. of patients**
<1.5	44 (91.6%)
1.5-2.5	1 (2.08%)
2.5-3.5	1 (2.08%)
>3.5	2 (4.16%)

Table 3 shows laboratory markers of liver at the time of admission. SGPT levels varies from 100 to 5000iu/ml. 19 cases (39.5%) had SGPT between 1000 and 3000, 33.3% of cases had SGPT between 200 and 500, 20.8% cases had SGPT between 500 and 1000, 2 cases (4.16%) had SGPT 3000 and 5000, only 1 case had SGPT between 100 and 200. 2 cases which had SGPT more than 3000 at the time of admission progressed to hepatic encephalopathy on follow up. 50% of cases had serum bilirubin between 1 and 5 mg/dl accounting for most of the cases, 18 cases (37.5%) had serum bilirubin between 5 and 10 mg/dl. 6 cases (12.5%) had bilirubin more than 10 mg/dl at the time of presentation. PT INR varied from less than 1.5 to more than 3.5. PT INR of less than 1.5

seen in most of the cases about in 44 cases (91.6%), INR of more than 3.5 seen 2 cases (4.16%), INR between 1.5 and 2.5 seen only in 1 case (2.08%). Those cases with elevated liver enzymes, PT INR of more than 3.5 progressed to hepatic encephalopathy.

As shown in Table 4, out of 48 cases of hepatitis, majority of cases are due to Hepatitis A: 40 cases (83.3%); followed by 7 cases (14.5%) of Non-A Non-B Hepatitis; 1 case (2.08%) of hepatitis-B. This indicates highest prevalence of Hepatitis A in children in the present study.

Table 4: Distribution of spectrum of hepatitis.

Reactivity	No. of patients
HbSAg	1 (2.08%)
IgM ANTI-HAV	40 (83.3%)
Non-A Non-B hepatitis	7 (14.5%)

Table 5: Hepatic encephalopathy.

Reactivity	Grade 1	Grade 2	Grade 3	Grade4	Outcome	
					Discharged	Expired
IgM anti HAV	2 cases		1 case		2 cases	1 case
HbSAg			1 case			1 case

As described in Table 5, out of 48 cases, 4 cases progressed to hepatic encephalopathy, 2 cases to grade 1, 2 cases to grade 3. Both 2 cases of Grade 3 hepatic encephalopathy expired during the course of treatment one was Hepatitis A case and other was Hepatitis B case. This indicates here highest mortality of Hepatitis B in the present study.

Table 6: SGPT, bilirubin and PT INR of death cases at presentation.

	SGPT (IU/ml)	Serum Bilirubin (mg/dl)	PT INR
Case-1	4860	14.2	7
Case-2	4986	15	8.2

As we observed in Table 6, the liver enzymes were elevated almost 100 times the normal range, serum bilirubin was elevated 14 to 15 times the normal range, coagulation profile was grossly disarranged in both the death cases. out of 48 patients, 46 patients recovered however 2 cases died in the course of treatment, overall mortality being 4.17%.

DISCUSSION

The etiology of viral hepatitis and its associated complications varies with the geographical location, depending upon prevalent hepatitis virus types. In our study there is a high prevalence of Hepatitis A. A study by Behera MR et al in eastern part of India also showed highest incidence of HAV infection among children.[16] Not only in children even in adults, Das AK et al reported highest incidence of HAV infection[17]. Despite of availability of vaccine and improved sanitation HAV infection is still a major issue in developing countries. This is probably due to lack of knowledge regarding availability of vaccine, lack of awareness on mode of disease transmission among lower socio-economic status. coming to sex distribution, Girls predominance is observed in in the present study, this is comparable with study done by Parekh Z et al, in which there also reported girls' predominance, whereas other studies reported boys' predominance.[18-20] This study suggests majority of cases (80%) were aged above 10 years. The adolescent age group has been affected more because of their food habits like eating unhygienic food etc. Study done in southern India also reported 10-20-year age group being most commonly affected.[21] On the contrary, another study done in eastern India reported higher prevalence in age group 5 to 10 years.[16] Another study done by Kamath et al also reported maximum number of cases (61.6%) in 5-10 year age group.[22] This study attempts highlighting symptoms and examination findings in case of viral hepatitis. Fever (100%) is the most common symptoms with jaundice (83.3%), vomiting (83.3%) reported in this study. Parekh Z et al reported almost similar presenting complaints most common being jaundice (94%) followed by fever (82%).[18] Behera AK et al reported yellowish discolouration of eye and urine as the most common symptoms in their study.[23] Icterus (100%) is the most common sign reported in our study, followed by hepatomegaly (76%). This is consistence with other study who reported jaundice and hepatomegaly as most common sign.[24]

Laboratory markers will give an idea about extent of liver damage. Liver enzymes were elevated in all cases; most cases had SGPT levels between 1000-3000 iu/ml at presentation. This is in contrary to the study which showed most cases had SGPT less than 500 at presentation. This is probably due to rural people coming here delay in seeking medical advice.[16] The total bilirubin at presentation varies with most cases presented between 1-5mg/dl (50%). PT INR in most cases (91.6%) was less than 1.5 at presentation. Out of 48 cases included 4 cases progressed to hepatic encephalopathy. We found the

cases with elevated liver enzymes (SGPT >3000IU/ML), bilirubin more than 10mg/dl, PT INR of more than 3.5 had higher rate of mortality. 2 cases died; in both the above laboratory readings are noted. Out of 40 cases of Hepatitis A, 1 case died, and 1 case of Hepatitis B died. This gives an idea of higher mortality of Hepatitis B virus. The other study also showed higher mortality with Hepatitis B virus.[18] A study conducted in adults showed gall bladder thickening in Ultrasound.[25] We couldn't find this in the present study.

The drawback of the present study is that patients were not evaluated for Hepatitis C, D and E due to limited set up and most studies from India report HEV as the major cause, ranging from 12.6-78.6% in both sporadic and epidemic hepatitis from different parts of country.[26-31] Thus further studies are required to delineate HEV as a major cause and to evaluate its implications. Also, the effect of chronic liver disease on acute viral hepatitis with respect to its mortality was not correlated.

Present results encourage further well-designed studies that would elaborate precisely on the clinical profile of viral hepatitis.

CONCLUSION

Hepatitis is a major public health problem. It's important to create awareness in the society regarding preventive measures including availability of vaccine especially in rural side. It is also important to educate the society regarding clinical presentation of disease so that they can seek medical intervention early and can reduce significant mortality associated with it.

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