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Research Article

Study of Clinico-Etilogical Profile of Hepatocellular Jaundice in Children at Tertiary Care Hospital

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Abstract

Introduction: Aim and objective to study the clinical spectrum of jaundice due to liver disease in children. And determine the clinic-etiological manifestation of liver disease.

Material and Method: The study was done in the department of pediatrics SCB Medical College and SVP PG institute of Pediatrics Cuttack from October 2016 to September 2018.

Summary: The incidence of acute hepatitis is 79.9% and chronic liver disease was 20.1%. The most common age of presentation was 5 to 9 years. The mean age of presentation was 6.62 years. There was male preponderance with male to female ratio was 1.4:1. The most common population belonged to upper lower socioeconomic class. Most common presentation being was jaundice (95.1%) followed by fever (84.1%). The most common sign of presentation was icterus (96.3%) followed by hepatomegaly (74.4%).

Conclusion: Hepatitis is commonly seen in children with acute viral hepatitis being the most common. Wilson's disease was the most common cause of chronic hepatitis.

Keywords: Jaundice; Liver Diseases; Acute Liver Failure

Background

Jaundice is a yellowish pigmentation of the skin, the conjunctival membrane over the sclera and the mucous membrane caused by hyperbillirubenimia [1]. Hepatitis is an inflammation of the liver. The condition can be self limiting or can progress to fibrosis (scaring), cirrhosis or liver cancer. Hepatitis virus are most common causes of hepatitis in the world but other infections, toxins substances (e.g. alcohol, certain drugs), and autoimmune diseases can also cause hepatitis. There are 5 main hepatitis virus [2,3] referred to as types A, B, C, D and E. These 5 types are of greatest concern because of the burden of illness and death they cause and the potential for outbreaks and epidemic spread. In particular, types B and C lead to chronic disease in hundreds of millions of people and, together, are the most common cause of liver cirrhosis and cancer. Hepatitis A and E are typically caused by ingestion of contaminated food or water. B, C and D usually occur as a result of parenteral contact with infected body fluids. Rarely for unknown reasons, 1-20% of these of viral hepatitis develop massive liver cell necrosis resulting in fatal fulminant liver cell failure within 8 weeks of icteric phase of acute viral hepatitis [4].

Chronic liver disease (CLD) [2] refers to a wide spectrum of disorders characterized by ongoing liver damage with a potential for progression to cirrhosis or end stage liver disease. CLD implies long standing liver disease (usually 3-6 months), leading to various manifestations and complications of liver cell failure. Unlike in adults, long duration of the disease should not be considered as mandatory aspect of the definition of CLD in children, as progressive irreversible changes can occur in children, even with symptoms as short as one week. It accounts for 1-5% of the pediatric ward admissions up to 20% ward mortality in our country. Today Indian childhood cirrhosis, a dreadful disease of the past is a rarity, whereas diseases like Wilsons disease, Gaucher's disease, autoimmune hepatitis, Budd-chiary syndrome are being

diagnosed with increasing frequency. The early detection and treatment protocol have resulted in greater life expectancy with better outcome and have therefore become relatively important forms of pediatrics liver disease.

Acute liver failure (ALF) is manifest by the presence of coagulopathy (international normalized ratio [INR]>1.5) and any degree of encephalopathy without 24 weeks of the first onset of symptoms in patients without underlying liver disease [5,6]. Multiple organ failure is the most common cause of death (>50%) from ALF, with intracranial hypertension (ICH)and infection accounting for most of the other deaths in this patient population [7].

Primary hepatic tumors are rare in children, where they account for about 5-6% of all intra-abdominal masses and represent between 0.5% and 0.2%of all pediatric neoplasms [8]. They are a diverse group of epithelial and mesothelial and mesenchymal tumors, which constitute the third most common group of childhood solid abdominal tumors. The incidence is 0.4to 1.9 per million children each year and can vary with patient age. Liver masses in children can be benign, malignant, or indeterminate. About one third of pediatric primary liver masses are benign [9-14]. Knowledge of pediatric liver disease and their imaging appearance is essential in order to make an appropriate differential diagnosis [11]. Differentiation of masses is still complex, and biopsy or resection for histological diagnosis sometimes becomes necessary [15-17]. The incidence of complications after percutaneous liver biopsy in pediatric patient was 6.83%, of which 2.4% were major complications as reported by Scheiman., *et al*. [18].

Material and Method: after obtaining the clearance from the institutional ethical committee the study was conducted in the indoor ward of department of Pediatrics S C B Medical college and SVP PG IP, Cuttack from October 2016 to September 2018. All the investigations were done in the department of pathology, biochemistry and central laboratory of the institution. It was a hospital based cross sectional study.

Inclusion criteria

1. Children 1 year to 14 years, 2. hepatic origin.

Exclusion criteria

1. Transfusion dependent anemia, 2. Congestive hepatopathy, 3. Hemolytic anemia. 4. Obstructive jaundice, 5. Surgical cases of liver disease like liver abscess, trauma, malignancy etc. 6. Severe acute malnutrition

All total of 164 cases were taken into the study that were fulfilling the study group.

Investigation included were

1. Complete blood count
2. Liver function test. a. SGOT and SGPT: it is a serum analysis measured by Reitman and Frankel method. It measures the brown color produced at the end of the reaction calorimetrically. Normal value 5 to 40U/L b. Serum Alkaline Phosphatase (ALP): done by King, Abdul Fade and Walker method. It measured the yellow color produced at the end of the reaction calorimetrically. Normal value: 3-13 KA units/ml.c. Serum Protein: measured by Burette method Normal value: 6.5-8.5g/dl, d. Serum Albumin: measured by spencer and price modification of Doumas method normal value: 3.5-5.5g/dl, e. Serum billirubin: measured by Evelyn and Malloy method normal value 0.2-0.8mg/dl f. prothombin time: measured by Quick on stage method. Normal value 12-16 seconds.
3. Viral markers for hepatitis –Immuno combo HBsAg test, micro ELISA-HAV, HCV, HEV.
4. Serum ceruloplasmin: done by Nephelometric Assay. Normal value 63.7-140.12µg/dl. A value below 20 µg/dl is suggestive of Wilsons disease.
5. 24 hour urinary copper: done by quantitative inductively coupled plasma mass spectrometry. Normal value: 20-50 µg. Individuals with symptomatic Wilson disease usually excrete more than 100 µg copper per day. D-penicillamine challenge test: At least 2 baseline measurements of 24 hour urinary copper should be made prior to the test. the patient is given two doses of d-penicillamine 500mg 12 hours apart. The urinary copper is estimated similarly 24 hours after first dose.
6. Ultrasonography of the abdomen.
7. Auto-immune marker for ANA and Anti-KLM 1
8. Optional investigations; Upper GI endoscopy, Liver biopsy (when indicated and feasible)

Statistics

Simple statistics involving mean with range was used along with graphs and charts which were obtained via Microsoft excel data assessment. Microsoft word was used to prepare the study and incorporated the various charts and data. No special software was used for the study.

Observation

Onset of hepatitis	Male		Female		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Acute	76		55		131	79.88
Chronic	20		13		33	20.12
Total	96	58.54	68	41.46	164	100

Table 1: Distribution of cases depending on onset of hepatitis along with sex.

A total of 164 patients were undertaken for the study. Out of which 131(7.9%) had acute and 33(20.1%) had chronic liver disease. There was male preponderance with male to female ratio was 1.4:1.

Age in years	1-4	5-9	10-14	Total
Number	42	110	12	164
Percentage	25.6	76.1	7.3	100

Table 2: Age distribution.

The mean age of presentation to the hospital was 6.62 years, most common being 5 to 9 years of age.

Socioeconomic class	Lower	Upper lower	Lower middle	Upper middle	Upper	Total
Number	40	84	26	12	2	164
Percentage	24.4	51.2	15.9	7.3	1.2	100

Table 3: Distribution of cases depending on socio-economic class.

The most common population belonged to upper lower socioeconomic class (51.2%).

Presenting complaints	Jaundice	Fever	Nausea and vomiting	Abdominal distention	Abdominal pain	Rash
Number of cases	156	138	125	104	46	35
Percentage	95.1	84.1	76.21	63.4	28	21.3

Table 4: Presenting complaints at the time of presentation.

Most common presentation being was jaundice (95.1%) followed by fever (84.1%).

Clinical features	Icterus	heapatomegaly	Abdominal tenderness	Pyrexia	Splenomegaly	Ascitis	Altered sensorium
No of cases	158	122	110	104	96	46	6
Percentage	96.3	74.4	67.1	63.4	58.5	28	3.7

Table 5: Clinical features at the time of presentation.

The most common sign of presentation was icterus (96.3%) followed by hepatomegaly (74.4%).

Parameter	Values	Number	Percentage
Serum billirubin level	1 to 2 mg/dl	11	6.7
	2 to 4 mg/dl	23	14
	4to6mg/dl	102	62.2
	>6mg/dl	28	17.1
SGPT	<100IU/L	26	15.9
	100-400U/L	80	48.8
	>400U/L	58	35.4
SGOT	<100IU/L	22	13.4
	100-400U/L	92	56.1
	>400U/L	50	30.5
Sr ALP	<240IU/L	28	17.1
	>240IU/L	136	82.9
Sr Albumin	<2.5 gm/dl	32	19.6
	2.5-3.5gm/dl	78	47.5
	>3.5gm/dl	54	32.9
Prothombin time	Normal	43	26.2
	Elevated	121	73.8
Hb levels	<7mg/dl	20	12.2
	7-11mg/dl	96	58.5
	>11mg/dl	48	29.3

Table 6: Different parameter in hepatitis.

Serum Billirubin was elevated in all cases with most of the cases being 4 to 6mg/dl. SGOT and SGPT were also elevated in all cases, most of the patients having a moderate elevation. Serum ALP was also elevated in 82.9% cases. Hypoalbuminemia was seen in 78.1% cases. Prothrombin time was elevated in 73.8% cases. Hemoglobin was low in 70.7% cases.

Etiology	Cryptogenic	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis E	Hepatitis A& E	Auto-immine Hepatitis
Number	76	29	2	1	11	8	4
Percentage	46.3	17.7	1.2	0.6	6.7	4.9	2.4

Table 7: Etiology of acute liver disease.

Hepatitis A virus being the most common in acute liver disease.

Etiology	Cryptogenic	Wilson's disease	Budd-chiari syndrome	Auto-immine Hepatitis	Drug induced hepatitis	Hepatitis C
Number	15	8	2	3	1	2
Percentage	9.1	4.9	1.2	1.8	0.6	1.2

Table 8: Etiology of chronic liver disease.

Most common cause of chronic hepatitis remained unknown but commonly Wilson's disease was detected in 4.9% of cases.

USG Finding	hepatomegaly	Spleenomegaly	Liver parenchymal disease	Ascitis	Incidental gall stone
Number	164	108	162	46	5
Percentage	100	65.9	98.8	28	3

Table 9: Ultrasound finding of the Liver.

On ultrasound of the liver, Hepatomegaly is found in all cases of jaundice, splenomegaly was found in 65.9% of cases, liver parenchymal disesse was found in 98.8% of cases, ascitis was found in 28% of cases.

Auto-antibody analysis	Anti-LKM1 positive only	ANA positive only	Both
Number cases	4	1	2
Percentage	2.4	0.6	1.2

Table 10: Auto-antibody analysis in auto-immune hepatitis.

Auto-immune hepatitis was seen in 7 cases with 6 of them testing positive for Anti-LKM1.

Discussion

In our study with 164patients, 131 (79.88%) cases presented with acute onset hepatitis and 33(20.22%) cases with chronic hepatitis. males were 96(58.54%) and females were 68(41.46%) in the whole study with male to female ratio of 1.4:1 in a hospital based study in kerala [19], across all age group, the male to female ratio was 3.2:1. In another study by Arora NK., *et al*. [20] the ratio was 1.9:1. The above two studies were for acute liver disease. A study by Gulzar., *et al*. [21] had a ratio of 1.67:1. The results were similar to our study in studies with Akinbami., *et al*. [22] and Hanif., *et al*. [23].

The mean age of presentation to the hospital was 6.62 years, majority of the patient 110(67.1%) were from5-9 years. The youngest child was 15 months presenting with cryptogenic hepatitis of acute origin. Our finding here matched all the studies discussed here.

In our study 75.6% cases belongs to the lower and upper lower class. Various schemes by the government help these cases getting subsidized yet quality care at our centre [24].

Jaundice presented in 95.1% cases in our study. the symptoms were most commonly yellowish discoloration eyes and passage of high colored urine. In studies by Dangwal., *et al*. [25], Hanif., *et al*. [23], Arora NK., *et al*. [20] and Deore P., *et al*. [26] similar result were found. Also in our study non-specific gastro – intestinal symptoms like nausea, vomiting and malaise was seen in 76.21 cases similar to Deore P., *et al*. [26] in a study by Dangwal., *et al*. [25] in the north India, the most common presenting features were jaundice (70%), fever(67%) and abdominal distention (60%).

Icterus was the most common clinical features in our study in 96.3% of the cases under study followed by hepatomegaly identified clinically in 74.4% cases. Hanif., *et al*. [23] and Dangwal., *et al*. [25] found jaundice in 70% and 80% of the cases in their respective studies. Hepatomegaly was found in 70% cases in study by Hanif., *et al*. [23], 64% cases by Ira shah., *et al*. [27] and 80% cases by Dangwal., *et al*. [25].

Sple nomegaly was found in 58.5% cases and in 65.9% cases by USG. In studies by Ira Shah., *et al*. [27] and Dangwal., *et al*. [25], it was 47.5% cases where as it was seen in 76% cases by Hanif., *et al*. [23] and in 65% cases by Gulzar., *et al*. [21]. Splenomegaly can be attributed to many causes, in India being a tropical country the incidence of splenomegaly is 5-10% in pediatric population. No specific association to hepatic involvement can be made.

6 cases i.e. 3.7% cases had altered sensorium during presentation. These were referred cases which later progressed to fulminant course. Out of 6 cases 4 cases succumbed to the disease process in spite of giving adequate treatment in ICU. The cause of sudden detoriation could not be noted and were classified as cryptogenic hepatitis.

Pallor was seen in 151 (91.5%) cases under study. however due to its association with multiple factors was not included in the results section. Lower socio economic group have more anemia. A similar result was seen in study by Hanif., *et al*. [23].

Liver enzymes were elevated in all cases under study indicating a definite hepatic involvement in jaundice. These results correlated studies by Wolf., *et al*. [28], Sherlock., *et al*. [2] and Hanif., *et al*. [23]. In our study, serum billirubin was elevated in all 164 patients. Most of the cases, 102(62.2%) had serum billirubin levels between 4 to 6 mg/dl. the highest value noted was 11.8mg/dl with a mean of 5.3mg/dl. in studies by Sherlock., *et al*. [2] and Hanif., *et al*. [23] the finding were similar.

In our study, serum glutamic pyruvic transaminase (SGPT) was elevated in all 164cases. 48.8% had it between 100 to 400 units per liter which is considered moderate elevation of the enzyme. There was moderate elevation of SGOT in most of the cases under study; here also it was elevated to some extent in all cases. Sherlock., *et al*. [2] proposed in her study that these enzymes values do not correlate to the severity of hepatitis. They are prognostic indicator.

Serum alkaline phosphatase levels were elevated in 72.5% cases highest value being 2240 U/L. Sherlock., *et al*. suggests that serum ALP is elevated in acute cases but in chronic cases it normalizes generally except in severe hepatic involvement.

Serum albumin was below 3.5gm/dl I 67.1% cases in our study. Owing to many confounding factors like socio-economic group, hemoglobin level and level of malnutrition. Hence this finding seems to be inconsistent to the finding except in our study. Further all cases of chronic liver disease were hypo-albuminemic.

Prothrombin time was elevated in 73.7% cases which correlated to study by Sherlock., *et al*. [2] and Haif., *et al*. [23].

Majority of the patient were of acute hepatitis the common cause being unknown i.e. cryptogenic (43.6%). Acute viral hepatitis was the most common known cause of hepatitis comprising of 17.7% of entire study group followed by hepatitis E seen in 6.7%. Co-infection with both hepatotropic viruses A and E seen in 8 cases. two case presented acutely tested positive for HBsAg and one case for HCV DNA. In a study P. Jain., *et al*. [29], HAV (29.96%) was identified as the most common cause of acute hepatitis followed by HEV(17.97%), HBV(11.10%)and HCV(11.98%). Co-infection with more than one virus were present in 34 cases; HAV-HEV co-infection being the most common. Similar finding were also seen in studies by Anthony., *et al*. [19], where HAV was 24.41%, HEV was 34.73%, HBV was 13.46% in the pediatric age group.

Among the case of chronic hepatitis, majority (9%) cause remained unknown. Most common cause of chronic hepatitis in our study was Wilson's disease. We diagnosed 8 cases with KF ring seen in one case however none of the cases had developed any neurological manifestations. Similar finding were studied by Yachha., *et al*. [30] Rajeshwari., *et al*. [31], Dhole., *et al*. [32] and Roy A., *et al*. [33].

Two cases presented with Budd-chiari syndrome. Drug induced hepatitis was noted in 4 cases due to chronic intake of hepatotoxic drugs.

Hepatitis C was seen in two cases here as a chronic cause of hepatitis. The cases of Hepatits B and C were seen in patients with history of blood transfusion. Out of total 5 cases of hepatitis B and C in our study, 4 cases were of transfusion dependant anemia, suffering from thalassemia major.

Auto-immune hepatitis was noted in 7(4.3%) cases. anti-LKM-1 was positive in most of the cases (6 out of7) which is known and correlates with our study. similar finding were found by Yachha., *et al*. [30], Raffe., *et al*. [34] and Zhang., *et al*. [35].

Gall stones were seen in five cases in our study. However they did not show any specific related symptoms.

Summary: A total of 164 patients were undertaken for the study. Out of which 131(7.9%) had acute and 33(20.1%) had chronic liver disease. The most common age of presentation was 5 to 9 years. the mean age of presentation was 6.62 years there was male preponderance with male to female ratio was 1.4:1. The most common population belonged to upper lower socioeconomic class. Most common presentation being was jaundice (95.1%) followed by fever (84.1%). The most common sign of presentation was icterus (96.3%) followed by hepatomegaly (74.4%). Serum

Billirubin was elevated in all cases with most of the cases being 4 to 6mg/dl. SGOT and SGPT were also elevated in all cases; most of the patients having a moderate elevation. Serum ALP was also elevated in 82.9% cases. hypoalbuminemia was seen in 78.1% cases. Prothrombin time was elevated in 73.8% cases hemoglobin was low in 70.7% cases. Most common cause of acute hepatitis remained unknown with the most common detected cause being acute viral hepatitis. Hepatitis A virus being the most common in them. Most common cause of chronic hepatitis remained unknown but commonly Wilson's disease was detected. Auto-immune hepatitis was seen in 7 cases with 6 of them testing positive for Anti-LKM1.

Conclusion

Hepatitis is commonly seen in children with acute viral hepatitis being the most common. Wilson's disease was the most common cause of chronic hepatitis. Most of these presenting with hepatitis evaded diagnosis despite of conducting an array of tests under an extensive rational approach. There are many viruses which are associated with hepatitis which could not be tested for due to limited resources hence were classified as cryptogenic. The low prevalence of chronic hepatitis B and C might be owed to the extensive screening of blood and blood products, usage of universal precaution in suspected cases, adequate available treatment and immunization.

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