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Clinical Profile of Liver Diseases in Children Attending Usmanu Danfodiyo University Teaching Hospital Sokoto, Nigeria

Baba Jibrin,[1] Yusuf Tahir,[1] Usman Muhammad Sani,[1] Murtala Muhammad Ahmad,[1] Abubakar Sadiq Mayaki,[2] Kabir Abdullahi,[3] Ibrahim Haruna Gele,[4] Fatima Bello Jiya,[1] Modupe Omoshalewa Ugege.[1]

[1]*Department of Paediatrics, Usmanu Danfofiyo University Teaching Hospital, Sokoto, Nigeria*
[2]*Department of Internal Medicine, Usmanu Danfofiyo University Teaching Hospital, Sokoto, Nigeria*
[3]*Department of Histopathology, Usmanu Danfofiyo University Teaching Hospital, Sokoto, Nigeria*
[4]*Department of Radiology, Usmanu Danfofiyo University Teaching Hospital, Sokoto, Nigeria*
Corresponding author: Baba Jibrin

Abstract

Background

Liver diseases are significant causes of morbidity and mortality in children and include a broad spectrum of infectious, developmental, genetic, metabolic and immunologic disorders that eventually result in hepatic dysfunction and cirrhosis. There is the need to know the epidemiological distribution of liver disease in children in our settings particularly common hepatic disorders in order to institute prompt management and preventive measures.

Objectives

This study was aimed in determining the pattern of liver disease among children in a teaching hospital, Sokoto, Nigeria.

Materials and Method

It was a retrospective study that described the clinical profile of liver disease among children aged 0 – 15 years managed at the Paediatric Gastroenterology and Hepatology clinic, Emergency Paediatric Unit and Paediatric Medical Ward of Usmanu Danfodiyo University Teaching Hospital, Sokoto, over a 3-year period (February 2018 – January 2021). The hospital medical records of children with liver diseases were retrievedand diagnosis of liver diseases was made up of combined evidence based clinical and laboratory features.

Results

Sixty- three cases seen over the study period. The subjects age ranged from 0- 15years with the mean age of 8.36 and SD (± 3.94) years and male-to-female ratio of 3.8:1. Majority of the children 37 (58.7%) were from low socio-economic class. The common presentations among the study subjects were yellowness of the eyes 28(23.9%), fever 23(19.7%), abdominal pain 22(18.8%), abdominal swelling 21(17.9%) and hepatomegaly 27 (31.8%). Diagnosis recorded were viral hepatitis 46(73.0%), 3(3.7%) chronic liver disease (CLD) of unknown/idiopathic cause, 3(4.7%) hepatoblastoma and 3(4.7%) portal hypertension with oesophageal varices. Others were cholecystitis 2 (3.2%), 2 (3.2%) cirrhosis, one cases of each of hepatic fibrosis (Schistosomiasis), hepatic cyst, biliary atresia, and neonatal hepatitis syndrome.

Conclusion

Hepatitis B infection is highly prevalent and the commonest cause of liver disease in children in our community.

Keywords: *Liver disease, children*

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I. Introduction

The liver has an enormous task of maintaining the body's metabolic homeostasis, which makes it highly vulnerable to a wide variety of toxic, microbial, metabolicand circulatory injuries.[1,2,3] Liver diseases are significant causes of morbidity and mortality in children and include a broad spectrum of infectious, developmental, genetic, metabolic and immunologic disorders that eventually result in hepatic dysfunction and cirrhosis.[3,4,5]In children, liver disorders are age specific and differ from those of adults;and may take an acute or chronic course.[4,5,,6] The pattern of liver disease varies according to geographical location in different countries and communities.[2,6,7,8,9]

Common causes of liver diseases seen from newborn age to first few years of life include biliary atresia, choledochal cysts, congenital hepatic fibrosis, metabolic disorders such as galactosemia, tyrosinemia as

well as alpha one antitrypsin deficiency.[3,5,6,9,10] While in older children, thecauses of liver diseases include chronic viral hepatitis B and C, autoimmune hepatitis, Wilson's disease, cystic fibrosis and Primary sclerosing cholangitis.[4-10]Non-alcoholic fatty liver disease (NAFLD) is currently an emerging and common cause of liver disease in children particularly the obese [4,5,11,12]

Acute hepatitis in children may occur as pathological changes in the liver within six months whereas chronic hepatitis is an inflammatory condition of the liver characterized by the persistence of biochemical and histologic abnormalities for more than six months.[1,13]However, the concept of 6 months duration of symptoms required for making a diagnosis of autoimmune hepatitis has been recently abandoned.[14]

The features of pediatric liver disease include jaundice, symptoms and signs related to digestion problems such as abnormal fat absorption and metabolism, hepatomegaly, coagulopathy elevation of liver enzymes as well as features of cholestasis, portal hypertension,ascites and oesophageal varices.[1,9,13]

Evaluation of liver disease warrants a complete clinical assessment and thorough biochemical and serological testing including histopathological findings of liver biopsy[2,15,16] Other specific tests include Liver function tests (LFT), enzyme assays and imaging.[2,15] Liver biopsy is an invasive procedure but a cornerstone for precise diagnosis.[15,16]

Since the pattern of liver disease has been shown to varies according to geographical location in different countries and communities,[2,6,7,8,9] there is need to know the epidemiological distribution of liver disease in children in our setting.This will help to identify particularly common hepatic disorders within the area so that prompt management and appropriate preventive measures can be put in place, which will go a long way in reducing the risk of irreversibleliver damage of the affectedchildren. This study, therefore was aimed at determining the pattern of liver diseases among children seen at a teaching hospital in Sokoto, North-Western Nigeria.

II. Methodology

It was a retrospectivestudy that described the clinical profile of liver diseasesamong children aged 0 – 15 years managed at the Paediatric Gastroenterology and Hepatologyclinic, Emergency Paediatric Unit (EPU) and Paediatric Medical Ward (PMW) of the Usmanu Danfodiyo University Teaching Hospital, (UDUTH) Sokoto, over a 3-year period (February 2018 – January 2021). The clinic runs every Monday as a specialist, referraland for follow-up care. Children with liver diseases who were on admission in EPU and PMW were also included.

The hospital medical records of all children with diagnosis of liver diseases were retrieved from the Medical Record Department after obtaining due permission. The diagnosis of liver diseases was made up of combined evidence based clinical and laboratory features. The data obtained included demographic characteristics, symptoms and signs suggestive of liver diseases such as jaundice, abdominal pain, swellings, itching, pale stools, bleeding, fever, weakness, vomiting, anorexia, pallor, hepatomegaly, splenomegaly and ascites.

The results of liver function tests such as serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), Alkaline phosphatase (AP), prothrombin time (PT) and partial thromboplastin time (PTT), international normalization ratio (INR), serum protein and albumin were also documented. The results of viral serology markers such as HBsAg, and HBV-DNA for hepatitis B infection; anti-HCV and HCV- RNA for hepatitis C infection as well as HIV screening were also obtained. Other investigation reports studied were liver biopsies, abdominal ultrasonography and abdominal computed tomography (CT). Three patients had liver biopsies done, but there was limitation in conducting genetic analysis and enzymatic assay in our center due lack of facilities.

The children were classified into three broad categories; namely, infective, non- infective (metabolic, congenital, cholestatic, neoplastic) and idiopathic liver diseases. Specific diagnoses were categorized as chronic liver disease (CLD) when symptoms persisted beyond six months of disease onset or follow-up care, with or without identifiable viral serological markers while acute hepatitis had symptoms with resolution within less than six months and were negative for serological markers. The group classified as idiopathic had no identifiable cause.Outcome of the care for the children were also recorded.Data obtained were sorted, entered and analyzed using SPSS 23 version. Data were presented in frequencies and percentages, Chi-squared test was used for the comparison of categorical data and p values< 0.05 was considered significant.

III. Results

A total of Sixty- three cases of liver disease were seen over the study period. The age ranged from 2 days to 15years, with the mean age of 8.4±3.9 years. There were 50 (79.4%) males and 13(20.6%) females giving a male-to-female ratio of 3.8:1. More than half of the children 49(77.8%) were within the age range of 5 – 15 years with 24(38.1%) subjects in the age group of 5.0 -10.0 and 25(39.7%) in age group 10.1– 15.0 years

respectively.Fourteen (22.2%) were aged less than 5 years. The differences in age groups were notstatically significant (p = 0.486) (Table 1).

Majority of the children 37 (58.7%) were from low socio-economic class, whereas 20 (31.8%) were from middle class and the remaining 6 (9.5%) from high socio-economic class. The socio-economic classification was made according to Oyedeji.[17]

Table I:Age group and gender distributionof the Children with Liver Diseases in UDUTH, Sokoto.

Age group (years)	Male	Female	Total
<1.0	1	1	2
1.0 - 5.0	11	1	12
5.1 - 10.0	19	5	24
10.1 -15.0	19	6	25
Total	50	13	63

$X^2 = 0.198$

P = 0.486

The commonest presenting symptom among the study subjects was yellowness of the eyes 28(23.9%), followed by fever 23(19.7%), abdominal pain 22(18.8%), abdominal swelling 21(17.9%), body weakness 11(9.4%), vomiting 5(4.3%) and anorexia 3(2.6%). Others were bleeding, body itching and pale stool with 2(1.7%),1(0.85%) and 1(0.85%) each respectively. The highest physical sign elicited was hepatomegaly 27 (31.8%), then pallor 20(23.5%), jaundice 14 (16.5%) and the least frequent finding were splenomegaly and ascites with 12 (14.1.%) each respectively as depicted in Table II

Table II: Symptoms and signs among children with Liver Diseases in UDUTH, Sokoto.

Clinical Features	Frequency	Percentage
Symptoms		
Yellowness of the eyes	28	23.9
Fever	23	19.7
Abdominal pain	22	18.8
Abdominal swelling	21	17.9
Weakness	11	9.4
Vomiting	5	4.3
Anorexia	3	2.6
Bleeding	2	1.7
Pale stool	1	0.85
Itching	1	0.85
Signs		
Hepatomegaly	27	31.8
Pallor	20	23.5
Jaundice	14	16.5
Splenomegaly	12	14.1
Ascites	12	14.1

The highest diagnosisrecorded were due to viral hepatitis46(73.0%). Chronic viral hepatitis 27{42.9%}, acute viral hepatitis 13{20.6%}, and chronic viral hepatitis with secondary Nephrotic syndrome 6{9.5%}). Three (3.7%) cases were due to chronic liver disease (CLD) of unknown/idiopathic cause, 3(4.7%) hepatoblastoma and 3(4.7%) portal hypertension with oesophageal varices. Others were cholecystitis 2(3.2%), 2(3.2%) cirrhosis, one cases of each of hepatic fibrosis (Schistosomiasis) 1.6%, hepatic cyst 1.6%, biliary atresia 1.6% and neonatal hepatitis syndrome NHS 1.6% each respectively. Table III

Table III: Diagnoses of liver diseases among children in UDUTH Sokoto

DiagnosisFrequency(%)	
Chronic viral hepatitis	27 (42.9)
Acute viral hepatitis	13 (20.6)
Chronic viral hepatitis with secondary Nephrotic syndrome	6(9.5)
CLD (unknown cause)	3(4.7)
Hepatoblastoma	3 (4.7)
Portal Hypertensionwith oesophageal varices	3 (4.7)
Cholecystitis	2 (3.2)
Cirrhosis	2 (3.2)
Hepatic fibrosis (Schistosomiasis)	1 (1.6)
Hepatic cyst	1 (1.6)
Biliary atresia	1 (1.6)
Neonatal hepatitis syndrome (NHS)	1 (1.6)
Total	63 (100)

The serum levels of liver enzymes, serum levels of total/conjugated bilirubin as well as total protein and albumin levels are depicted on Table IV.Forty-six (73%) subjects were positive with viral serological markers, among which 43 (93.5%) were positive for Hepatitis B surface antigen (HBsAg) and 3 (6.5%) children were positive for anti- HCV antibodies. Of the 43 children positive for HBsAg, elevated HBV DNA viral load was recorded in 22 (51.2%)of the subjects (lowest = 879iu/ml, highest = 5.75 x 10^9iu/ml) and <25iu/ml HCV RNA load was recorded in 2(4.7%) children with positive Anti-HCV.

Twenty-one (63.6%)of the children with chronic hepatitis B, elevated HBV DNA load of ≥ 2000iu/ml and /or with cirrhosiswere treated with antiviral agents (Entecavir and Tenofovir respectively). In addition, patients with chronic viral hepatitis and secondary nephrotic syndrome were co-managed with Paediatric Nephrologist. There was significant improvement with sustained virological response in 9(42.9%) of the subjects that had treatment with antiviral agents.

Twenty-two other cases of viral hepatitis plus another 2 cases (a case of biliary atresia and NHS each respectively) constituting 38.1% of our study subjects were lost to follow up. The 2 cases of cholecystitis (acute) had medical conservative treatment with very good response, one case of portal hypertension with variceal bleeding had successful endoscopic band ligation. The subjects with hepatic fibrosis (due to schistosomiasis) and hepatic cyst are being followed upregularly with the remaining children on treatment at paediatric gastroenterology clinic. There were 3(4.8%) deaths, these includesa case of cirrhosis who had severe repeated variceal bleeding and 2 cases of hepatoblastoma.

Table IV: Results of Liver Function Test in children with liver disease

Parameters	Mean	SD
Serum Alanine aminotransferase (ALT)IU/L	62.014	125.98
Serum Aspartate aminotransferase (AST)IU/L	60.845	78.752
Serum Alkaline phosphatase (AP)IU/L	261.23	196.22
Conjugated serum bilirubin (mg/dL)	2.89	4.53
Total serum bilirubin (mg/dL)	3.13	3.75
Total serum proteins (g/dL)	6.42	1.31
Serum albumin (g/dL)	3.46	0.65

IV. Discussion

Early recognition of features of liver disease in children at initial presentation is very important. This study looked at pattern of liver disease among children aged 15 years and below in a tertiary center over a 3-year period. The demographic data of the subjects showed age ranged from day 2 of life to 15 years. Half of these children were from low socio-economic classand more than 2/3 of the children studied were males. Similar findings reported in previous studies onchildren with liver disease with similar age range, more males and from low socio-economic status being affected.[2,8,10,13]

In this study, specific age group that were mostly affected were 5-15 years constituting77.8%, high percentage of 62% was recorded in similar age group 5 years and above in Abuja.[13]However,a similar study in Sudan[10]showedhighest prevalence (42%)in children within age group <1 year, and lowest percentage (26%) in ages above 5 years. The reason for this similarity (higher percentages 77.8%,62%) in relation to our own study to that of Abuja may be attributable to same risk factors of liver disease in children including socio-cultural factors as well as geographical location.On the other hand, the lower percentage (26%) recorded in Sudan study,

may be as a result of differencesin geographical location with possible different risk factors as well as socio-cultural factors.

The most common clinical features in this study werehepatomegaly (31.8%), yellowness of the eyes (23.9%),pallor (23.5%) and jaundice (16.5). Other presentations that were relatively common included fever, abdominal pain, abdominal swelling followed by splenomegaly and ascites. Very fewcases of variceal bleeding, pale stool and body itching were recorded in this study. Similarly, previousstudies done reported jaundice, hepatomegalyand/orsplenomegaly as the commonest presentations.[4,5,6,9,18,19]The reason why jaundice and hepatomegaly are the most frequent features in this study and other afore-mentioned studies may be due to the fact that jaundice represent almost an invariable finding of liver disease regardless of the cause[1]whereas hepatomegaly is often the only manifestation of liver disease.[15]Hepatosplenomegaly or splenomegaly on the other hand is a manifestation of portal hypertension[1,19]one of the complications of chronic liver disease that can result into oesophageal bleeding. It is of note, that4.7% of our subjects had bleeding oesophageal varices.This is in contrast to a study by Hanif *et al*[19]in Karachi, which observed a very high number (42%) of patients with variceal bleeding among their study cohorts. The reason for the higher prevalence reportedby Hanif *et al*[19]is because there were more cases of chronic hepatitis (82%) and cirrhosis(18%)in their study compared to ourstudy 42.9% and 3.2%. respectively.Similarly, Behera *et al*[6]in India, reported higher number of patients having chronic hepatitis andcirrhosis (73.9% and 26.08% respectively), andconsequently higher proportion of subjects (39.97%) with variceal bleeding.

The most prevalent aetiologic agent causing liver disease in this present study was viral infection by Hepatitis B virus,HBV (68.2%).Previous studies had also reportedHBV infection as the commonest aetiologyof liver disease with prevalenceranging from 18 – 32%.[5,19,20,21] The reason for the much higher percentage of HBV infection observed in this study may be due to the fact that Nigeria is an endemic area for hepatitis B with prevalence of HBsAg of≥8%.Within this geographical area, mother to child transmission is typically high, early childhood infection is very common and life time risk of hepatis B is >60%.[22]

We recorded 4.8% of hepatitis C infection as aetiological factor.This was in sharp contrast to what was reported in a similar previous study by Awais *et al* in Pakistan, in which 31.66% of their patients had hepatitis C.[23] The higher figure recorded in Awais *et al* study was attributable to history of blood transfusion in more than 2/3 (72.7%) of their patients with viral hepatitis.[23]

Other aetiologic factors we recorded in this study include: chronic liver disease of unknown/idiopathic cause 4.7%, hepatoblastoma, a rare solid tumour in childhood 4.7% and cirrhosis 3.2%.Idiopathic cause of liver disease in children was also reported in various studies previously but in higher percentages,35% - 52.5%.[5,6,19,23]The lower percentage of unknown cause in our study was also reported by Ahmed *et al* (9.5%).[13] The reason for the low rates may be because frequency of idiopathic CLD varies in different parts of world[5] and also may be as result of the lower sample size. Some other causes of liver disease we recorded but in very low frequencies were cholecystitis 3.2%, hepatic fibrosis (Schistosomiasis) 1.6%, hepatic cyst 1.6%, biliary atresia 1.6% and neonatal hepatitis syndrome1.6%. The low frequency rates of these diseases recorded may bedue to probable low prevalence's of these diseases in our setting and very few neonatal cases presented to our clinic hence the possibility of underdiagnosis.In this present study, no single record of genetic or metabolic cause of liver disease in our patients and the reason is not far-fetched,as this is attributable to non-availability of specific diagnostic tools in our center which was a major limitation in the study.

V. Conclusion

Hepatitis B infection is highly prevalent in our environment and it is the commonest cause of liver disease in children in our community.Therefore, there is the need to strengthen preventive measures against Hepatitis B and C particularly on general health promotion, including provision for screening, prompt/early diagnosis and treatment. It is also strongly recommended that specific diagnostic tools should be made available, this will provide a means for further studiesin identifying the burden of genetic and metabolic causes of liver disease in our settings.

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