Original Article

Pathologic causes of liver disease in Sudanese children: Results of 450 liver needle biopsies at a single children hospital

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ABSTRACT

The pathologic diagnoses of percutaneous 450 liver biopsies performed at the Gastroenterology Unit, Gaafar Ibnoof Specialized Children Hospital, Khartoum, Sudan during a five-year period (2005 to 2010) were reviewed. The cohort consisted of children aged between 1 month and 15 years, of whom 42% were less than 1 year of age. The male to female ratio was 1.4:1. The most common histological diagnosis was liver cirrhosis (26%), where no specific cause could be found, followed by neonatal hepatitis (20%), fatty liver (12%), billary atresia (10%), chronic hepatitis (8%), metabolic liver disease (6%), progressive intrahepatic cholestasis (5.5%), non specific pathological changes (4.4%) and hepatocellular carcinoma in (4%).

In conclusion, liver biopsy is a useful and practical tool for the appropriate diagnosis of pediatric liver diseases. Hepatocellular carcinoma has significantly higher prevalence in our pediatrics population.

Key words: Liver diseases; Histopathology; Child; Sudan.

INTRODUCTION

Liver disease in pediatrics is one of the most significant causes of morbidity and mortality in this age group and includes a broad spectrum of disorders such as infections, developmental abnormalities, metabolic and neoplastic disorders that finally result in hepatic dysfunction and cirrhosis. The histologic pattern and incidence of different disorders have not been studied before in Sudanese children.

Biliary Atresia and neonatal hepatitis are the two most common causes of cholestasis in the neonatal period [1,2]. Treatment modalities differ among each condition; therefore, it is obvious that an early and correct pathologic diagnosis has a crucial role in the proper management of these children. Various diagnostic tools including liver function tests, enzyme assays, or imaging techniques are available for the evaluation of liver disorders, but although liver biopsy is an invasive method, it is the corner stone for a precise diagnosis and

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differentiates between the foregoing conditions [1, 3, 4]. The objective of our study is to determine the frequency of different patterns of liver needle biopsies performed in Sudanese children and compare them with other studies.

MATERIAL AND METHODS

During a period of 5 years (January 2005 to January 2010), liver biopsies were obtained from 450 children in our Gastroenterology (GE) Unit and examined at Gaafar Ibn Oaf (GIO) Specialized Children Hospital Pathology Laboratory, Khartoum, Sudan. Indications for liver needle biopsies included abnormal liver function tests, prolonged jaundice, unexplained hepatomegaly and portal hypertension. The biopsies were taken by the use of Menghini needles and were immediately fixed in 10% formalin solution. Alcohol was used as another fixative solution. After processing in an automated tissue processor, paraffin-embedded blocks were serially sectioned and were then stained by H & E, trichrome and PAS with and without diastase methods. Other special stains such as perls stain, rhodanin stain and reticulin stain were used when required. Slides showing less than three portal spaces were considered as inadequate specimens. The frequency of each disorder, separately and in combination with the age group of the patients or gender, was calculated and compared with other similar studies.

RESULTS

A total of 450 liver biopsies were studied with a male to female ratio of 1.4:1. The age range was from 1 month to 15 years. Patients from 1 month to 1 year composed the most frequent age group (42%). A total of (32%) were between 1 and 5 years, whereas the rest were above 5 years of age.

The most common histological diagnosis (Table 1) was liver cirrhosis (26%) followed by neonatal hepatitis (20%), fatty liver (12%), biliary atresia (10%), chronic hepatitis (8%), metabolic liver disease (6%), progressive familial intrahepatic cholestasis (5%), non specific pathological findings (4.4%), and hepatocellular carcinoma (HHC, 4%). We found that neonatal hepatitis and biliary atresia, respectively, to be the two most common diagnoses from 1 month to 1 year of age. As age increased, liver cirrhosis, fatty liver and chronic hepatitis became the dominant diagnoses. A total of 18 children were diagnosed with HCC, 10 of whom were Hepatitis B positive.

Table 1 - Pathologic causes of liver disease in 450 Sudanese children

Liver disorder	Age			Total No (%)
	1month -1year	1-5years	5-15years	
Liver cirrhosis	0	53	64	117 (26%)
Neonatal hepatitis	84	6	0	90 (20%)
Fatty liver	15	39	0	54 (12%)
Billary atresia	42	3	0	45 (10%)
Chronic hepatitis	0	14	22	36 (8%)
Metabolic disease	15	5	7	27 (6%)
Progressive familial intrahepatic cholestasis	25	0	0	25 (5%)
No significant change	0	20	0	20 (4.4%)
Hepatocellular carcinoma	0	o	18	18 (4%)
Bile duct paucity	8	1		9 (2%)
Veno occlusive disease	0	0	6	6 (1.3%)
Hebatoblastoma, neuroblastoma, histocytosis	4	2	0	6 (1.3%)

DISCUSSION

For patients who suffer from hepatomegaly and present with abnormal liver function tests or unexplained jaundice, a liver biopsy is the best and the only way to attain the correct diagnosis [1]. Nevertheless, information on the patient's medical history, physical examinations, biochemical tests and viral, autoimmune markers and radiologic examinations are extremely valuable. In addition, we believe that epidemiologic and national criteria can play an important role in the primary evaluation of these patients. In this regard, we evaluated liver biopsies in Sudanese children to define the frequency of different histologic patterns of liver diseases. There are similar studies from South Africa [5] and Pakistan [1, 6-8], and we have used these as well as others [9-11] for comparison. The number of cases in the present study was higher than the other studies and over longer period of time. In our study also, cirrhosis without a cause composed the most prevalent histological diagnosis (26%). The next common group of disorders in the present study was neonatal hepatitis (20%); and all patients were under1- year- old with male predominance (male: female ratio, 4:1). Ramakrishna et al from India [12] and Akinbami et al from Oman [13] reported the higher incidence of neonatal hepatitis, as the most common diagnosis before the age of 2 years. Ahmad et al [1] found this disorder in 10% of their patients with male dominance. The next common disorder in our study was fatty liver which was mainly in the age group between 1 and 5 years, reflecting the high incidence of macro and micro nutrient deficiency in the present cohort.

Chronic hepatitis was noted in 10% of children referred to our GE unit during the 5 years of the study. All of them were older than 1 year. Our results are close to those reported by Ahmad et al [7] but in contrast to another later study [1], we detected a higher incidence of chronic hepatitis in our children, which was mainly due to hepatitis B infection and almost the same like what Zhang et al [10] found in Chinese children. Hanif and associates [11] evaluated the etiology of chronic liver diseases in children from Karachi and reached a similar result. Other rare diagnoses such as metabolic diseases, glycogenosis, or lipid storage disease should be kept in mind during the investigation of a liver disorder because, with proper management, we can prevent the progression to cirrhosis. The predominance of biliary atresia in our results may be due to the fact that our GE Unit is a main referral center for children with liver diseases. The high percentage of liver cirrhosis without a specific cause makes one wonder about the possibility of the presence of specific type of cirrhosis in Sudanese children, undiagnosed metabolic diseases or a sinister course of the fatty liver in the younger age group, which was thought previously to run a benign one. Further studies are required to investigate the cirrhosis in relation to the genetics and diet. Also a close follow up is needed for children with fatty liver due to malnutrition. On the other hand, the high incidence of chronic hepatitis may highlight the infants who acquired viral hepatitis in their perinatal period and would later develop a chronic liver disease, as Hepatitis B vaccination has been just started 2 years back. Whereas the prevalence of hepatoblastoma was low in our study, there was relatively high rate of HCC, which we hope it will come down with the recent introduction of Hepatitis B vaccine. Nevertheless, the incidence of childhood HCC may remain high for probably the next 15 years or so. We found that veno occlusive disease in Sudanese children is closely associated with tuberculosis infection.

In conclusion, liver biopsy is a useful and practical tool for the appropriate diagnosis of pediatric liver diseases. This study has provided background information on the occurrence of specific liver diseases in Sudanese children. We found, liver cirrhosis, chronic hepatitis and neonatal hepatitis are the most prevalent histological diagnoses. The

dilemma with cryptogenic liver cirrhosis in our children needs to be addressed and investigated. Hereditary and metabolic liver diseases are common due to high rate of consanguinity, and require to be included in the work-up of prolonged neonatal jaundice, as treatment is now available for most of these disorders if discovered early. Early referral of cholestatic jaundice needs to be stressed to different pediatrics health professionals to intervene surgically in billary atresia and medically in metabolic and hereditary liver diseases. Hepatocellular carcinoma is relatively high in our children and requires further research.

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