Original Article

Pathology

Miscellaneous Liver Diseases in Infancy & Childhood in Several Hospitals

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ABSTRACT

Introduction: Most of the liver diseases are different in pediatric age group, as compared to those in adult in many respects. Beside inflammatory, neoplastic and metabolic liver diseases; pediatric liver diseases also exhibit specific features of genetic predisposition, as well as environmental or other acquired diseases. In congenital diseases choledochal cyst, biliary atresia and cholestasis are included. While in environmental or acquired/nutritional diseases, fatty change liver and Kawashiorkor are found.

Objectives: A study is done to overview the miscellaneous congenital and acquired liver diseases in infancy and childhood which are important but less common as compare to inflammatory, metabolic and other liver diseases.

Study Design: Retrospective Study.

Place and Duration of Study: This study was conducted at Department of Pathology, Basic Medical Science Institute (BMSI), Jinnah Postgraduate Medical Center, Karachi from 1995 to 2004

Materials and Methods: Slides / paraffin blocks of liver biopsies were taken from patients under 15 years of age. The cases were retrospective.

Result: The distribution of 100 cases of miscellaneous liver diseases in infancy and childhood were according to age and sex. Total 48 (48%) cases were encountered in the youngest of 0-5 year's age group, 36 (36%) cases in 6-10 years and only 16 (16%) cases in 11-15 years age group.

Conclusion: It is observed that the tendency of miscellaneous liver diseases are higher up till 5 years of age and sexual differentiation showing male predominance with male to female ratio of 3:2. The miscellaneous liver diseases in younger children, may be congenital like biliary atresia, intra hepatic biliary hypoplasia and cholestasis or acquired; like tuberculosis and the Kawashiorkor (malnutrition).These are well known in third world countries and in Pakistan.

Key Words: Fatty change liver, Biliary atresia, Cholestasis, Choledocal cyst, Kawashiorkor.

INTRODUCTION

Liver diseases which are not included in inflammatory, storage or metabolic disorders of liver, are known as miscellaneous liver disorders/diseases in infancy and childhood[1]. There are congenital and acquired liver diseases. Congenitally there are extra hepatic biliary atresia, intra hepatic biliary hypoplasia, choledochal cyst, and hepatic fibrosis. In the acquired cases inflammatory (tuberculosis) and nutritional disease like Kawashiorkor are included.

Fatty change may be acquired or occurs due to inherited metabolic disturbances.Three most common causes of jaundice in infant are hepatitis, biliary atresia and choledochal cyst.

In the Children fatty liver disease is asymptomatic or with nonspecific symptoms like abdominal pain and fatigue. The children are overweight or obese mostly[2]. Hepatomegaly is often present. Acanthosis nigricans, and fatty liver is present 30-50% in insulin resistance diabetic children[3,4] In these children family history of fatty liver, insulin resistance, or type 2 diabetes mellitus is present[5].

Biliary atresia is a rare congenital or acquired disease of the liver causing, obliteration or discontinuity of the extrahepatic biliary system. It is idiopathic and causes obstruction to bile flow or cholestatic jaundice in neonates[6,7,8]. The fetal/perinatal form is occurred within the first 2 weeks of life; the postnatal type presents in infants from 2-8 weeks. In acquired cases, chronic rejection of a transplanted liver allograft is a known cause[8].

In the world, the incidence of Biliary atresia is varies from 5/100,000 to 32/100,000 live births, and is highest in Asia and the Pacific region. Females are affected more than males[9,10].

Inherited syndromes of intrahepatic cholestasis and biliary atresia are the most common causes of chronic liver disease and the prime indication for liver transplantation in children[11]. Cholestasis in children often result from pathologic processes that begin early in postnatal life, when the liver has not reached functional maturity and may be more susceptible to the adverse consequences of endogenous (metabolic, genetic) or environmental insults[12]

Hepatic tuberculosis is rare and most of the cases have been reported from South Africa and the Phillipines[13,14]. It may occurs with an active pulmonary or miliary tuberculosis. The Tubercle bacilli reach the liver by hematogenous route (hepatic artery), while in focal liver tuberculosis by portal vein. The granuloma (caseating and noncaseating) formation take place in

the periportal areas[15]. Clinically Jaundice is very rare, but high fever, weight loss, right hypochondriac pain and hepatomegaly are commonly present[16].

Choledochal cyst, is a cystic dilatation of the biliary tree, in infancy. It may be found with biliary atresia or without biliary atresia. Similar clinical symptoms appear in both the choledochal cyst and biliary atresia in infants[17].

Kwashiorkor is one of the type of protein energy malnutrition.It is serious nutritional disorder and since last 70 years it is occurring in endemic[18,19,20,21]. Its severity is hardly decreased within last seventy years and about one third of all children are affected by Protein Energy Malnutrition; in which about 20 % of children are lived in Africa. Many infectious diseases can occur in Kwashiorkor and about 10 million children are killed under 5 years of age per year[22]. The surviving children have gotten the complications and different type of diseases[23,24].

Extramedullary hematopoiesis (EMH) occurs outside of the bone marrow is a rare and asymptomatic disease. The site of occurrence are spleen, liver, or lymph nodes, and less commonly the posterior mediastinum[25,26].

MATERIALS AND METHODS

100 Slides / paraffin blocks of liver biopsies from patients under 15 years of age. The cases were retrospective from 1995 to 2004.

Retrospective Cases:

1- 40 Slides / paraffin blocks of liver biopsies received during last 10 years in the Department of Pathology, Basic Medical Science Institute (BMSI), Jinnah Postgraduate Medical Center, Karachi.

2- 60 Slides / paraffin blocks of liver biopsies received in Department of Pathology, National Institute of Child Health (NICH) Karachi during last 10 years.

Slides / paraffin blocks of liver biopsies received during last 10 years in the Department of Pathology, Basic Medical Science Institute (BMSI), Jinnah Postgraduate Medical Center and National Institute of Child Health (NICH) Karachi. A clinical protocol including the particulars about the patients name, age, sex and diagnosis were obtained from the surgical pathology registers, request cards and copies of report. Haemotoxylin and eosin (H&E) stained slides of all cases were used with special staining help in reaching a specific diagnosis.

RESULTS

In the study total 100 cases of miscellaneous liver diseases are taken. According to age and sex the maximum 48 (53.77 %) cases are found in 0-5 years, 36 (31.7%) cases in 6-10 years and 16 (14.6%) cases in 11-15 years age group. The male to female ratio is 3:2.

Table No.1: Distribution of 100 cases of Miscellaneous liver diseases

Sr. No.	Diagnosis	Males	Females	Total	%age
1	Unremarkable	10	10	20	20
2	Fatty change liver	31	19	50	50
3	Biliary atresia	5	7	12	12
4	Cholestasis	8	2	10	10
5	Tuberculosis	3	1	4	4
6	Choledochal cyst	3	1	4	4
	Total	**60**	**40**	**100**	**100**

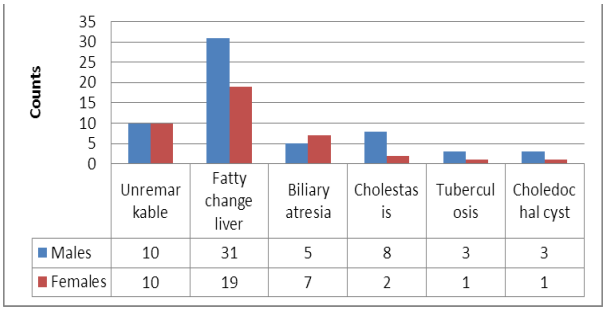

Figure No.1: Distribution of miscellaneous liver disease

Table No.2: Showing age and sex distribution of 100 miscellaneous cases of liver diseases

Age	Male	%	Female	%	Total	%
0-5	40	40	8	8	48	48
6-10	10	10	26	26	36	36
11-15	10	10	6	6	16	16
Total	60	60	40	40	100	100

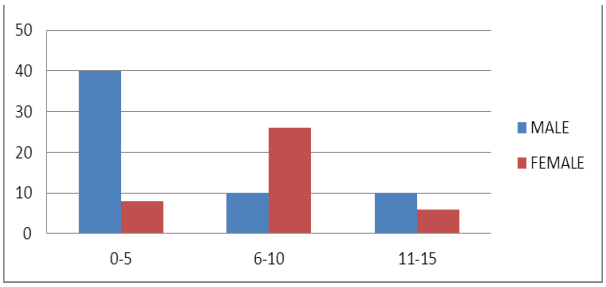

Figure No.2: Age and sex distribution of miscellaneous cases of liver disease

DISCUSSION

In "Miscellaneous liver diseases" different congenital and acquired diseases are included. Some liver diseases which could not be placed under inflammatory, cirrhotic and metabolic diseases, were described under miscellaneous group. Craig et al.(1980) described 13% of " miscellaneous disorders " which finally caused liver cirrhosis[27]. Shakoor (1987) described 19% cases

with 5 % cholestasis and fatty change each and 9 % under biliary atresia and obstruction[28].

Fatty change or fatty infiltration of the liver, can occur in diffuse or in focal form, it is caused by increased levels of triglycerides in hepatocytes. It can occur in infant and children due to diabetes, obesity, steroid therapy,chemotherapy, malnutrition, hyperalimentation, cystic fibrosis, jejunoileal bypass surgery, and inherited metabolic disturbances. In adults, it is occured most commonly due to alcohol abuse [29,30,31,32,33,34,35,36,37].

In congenital biliary atresia**,** acute liver failure and biliary hypoplasia**,** there is elevated levels of serum bilirubin (hyperbiliru-binemia) occured, which is deposited in liver and soft tissues[38].

Chronic liver failure may occur due to persistant jaundice, either inherited biliary hypoplasia or extrahepatic biliary atresia, in neonates.while in older children, autoimmune liver disease or cystic fibrosis are the most common causes of liver failure[39].

Histopathologically, in biliary atresia, the inflammatory damage to the intra- and extrahepatic bile ducts with sclerosis and narrowing or obliteration of the biliary tree is present[40]. Progressive fibrosis and biliary cirrhosis occur in children due to no proper drainage of bile and cirrhosis can cause hepatocellular carcinoma[41]. In untreated cases, cirrhosis and death can occur within the first years of life[42].

The 29 infants were surgically identified of choledochal cyst, by Kim and associates retrospectively, younger than 1 year of age from 1991 to 2004. There were 18 patients with Chronic Hepatitis and 11 were with Biliary Atresia and Chronic Hepatitis. Marked fibrosis, bile duct proliferation and portal inflammation were also seen[43,44].

In Cholestasis, the bile salts are accumulated in hepatocytes, which may cause hepatic failure. In cases of hepatitis with Cholestasis and fibrosis hepatic failure may occur. While in congenital hepatic fibrosis with hepatomegaly and normal liver function tests (LFTs) are accompanied by impairmed renal function may not be diagnosed until biopsied[28]. In a study by Alverez et al. (1981) 27 cases of congenital hepatic fibrosis were described in children in which 13 were males and 14 were females[1].

Sometimes minilaparotomy is done for histopathological examination or culture of the scrapings from the abscess wall, to rapidly settle the diagnosis and expedite treatment[45]. Recently, the PCR has been used for the detection of M. tuberculosis DNA. About 57% of hepatic granulomas caused by tuberculosis gave positive PCR test results. It also distinguish M. tuberculosis from other species of Mycobacterium[46].

In the present study not a single case of extensive fibrosis was noted. However, there were 100 miscellaneous cases in which 20 (20%) were unremarkable with no significant change, had minimal inflammatory infiltrate in portal areas, slightly dilated portal vein and/or negligible periportal fibrosis. The cases with fatty change were 50 (50%) and other including 12 cases (12 %) biliary atresia, 10cases (10%) cholestasis, 4 cases (4%) tuberculosis and 4 cases (4%) choledochal cyst.

However differentiation between biliary atresia which is a congenital disorder and neonatal hepatitis which is acquired, is mandatory. Amanullah (1976) suggested different tests e.g. RBC peroxide hemolysis tests, vitamin E absorption studies, determination of 5 nucleotidase and determination of serum alpha – fetoproteins to differentiate between neonatal hepatitis and biliary atresia[47]. Shakoor (1987) described the modified Rose Bengal test, in which lipoprotein – X determination need more advanced technology[28].

There are different types of choledochal cyst. Cyst in the proximal part of common bile duct is common. Stones or sludge may be present within the cyst. Microscopically there is thick fibrous wall of choledochal cysts with chronic inflammation. Mucosa and submucosa may show ulceration. Chronic inflammatory changes are more marked in older children then younger children[48,49,50,51,52,53].

CONCLUSION

Hepatomegaly is the commonest finding in infants and children. Some times with no obvious cause it can be diagnosed by taking history, physical examation and laboratory investigations. If the cause is not decteded on these ground, it could be due to miscellanous diseases of liver. Liver biopsy must be performed to find out the pathological process or cause of disease. This study can be used for future research and provides an overview of miscellaneous liver diseases to facilitate the analysis of past research discoveries and provide essential information for prioritizing directions.

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