Original Article

Paediatric Cholestatic Liver Disease

Aetiology and Clinical Presentation of Paediatric Cholestatic Liver Disease - A Single Centre Experience

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ABSTRACT

Objective: To evaluate the causes, clinical presentation and outcome of paediatric cholestatic liver disease in a tertiary centre.

Study Design: Observational / descriptive study.

Place and Duration of Study: This study was conducted at Pediatric Gastroenterology, KFSH&RC, Jeddah from September, 2006 to September, 2016.

Materials and Methods: A data sheet was designed to collect data from hospital ICIS power chart system. Children with initial presentation of cholestatic liver disease below the age of six months were included in this study. Children with autoimmune hepatitis, wilson disease and hepatitis B and C were excluded from the study.

Results: Among 25 children 18 were male and 7 were female and male to female ratio was 2.5:1. Regarding the aetiology of cholestatic liver disease 8 children (32 %) were diagnosed with PFIC II. There were 6 cases (24%) of idiopathic hepatitis , 4(16 %) with Alagille syndrome , 3 (12%) with biliary atresia, 2 children (8%) of sclerosing cholangitis and 2 (8%) with mitochondrial disease. In our study almost all children 25(100%) presented with jaundice, 7(28%) children were with failure to thrive, 5(20%) children had significant abdominal distension, 7(28%) children had developmental delay ,only two (8%) children have pruritis. Out of 25 children 23 (92%) survived and only two children (8%) died.

Conclusion: In our study the PFIC II remains the most common cause of cholesatic liver disease. The most common clinical presentation was jaundice and with early management the outcome was good.

Key Words: Cholestasis, liver disease, Ideopathic hepatitis, PFIC, Alagille Syndrome, Biliary atresia

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INTRODUCTION

Cholestasis is defined as an impairment in the excretion of bile, which can be caused by defects in intrahepatic production or transmembrane transport of bile, or mechanical obstruction to bile flow. Elevated conjugated bilirubin is the predominant characteristic in most of the causes of cholestasis. [2]

Cholestatic Liver disease has major impact on children. The clinical presentation of liver disease can vary greatly between individuals. By reviewing other studies, the causes of cholestatic liver diseases differ from country to country. For instance, biliary atresia was the most common cause of liver disease in Korea.[3] whereas metabolic liver diseases account for most of cases of acute liver failure in infants and young children in Europe [4]. Clinically, pruritus, fatigue, pale, stools, or even steatorrhoea may present with fat-soluble vitamins deficiency [5]. Early evaluation for patency of the extra-hepatic biliary system is important as early surgical intervention results in a better outcome [6]

Liver transplantation is a life-saving procedure for paediatric patients who have severe or end-stage liver disease. [7] Therefore early identification of disease is important in paediatric age group to avoid any delay to improve the outcome.

MATERIALS AND METHODS

It is a observational / descriptive study which was conducted at Paediatric gastroenterology, hepatology & nutrition, King Faisal Specialist Hospital and research centre (KFSH&RC), Jeddah, Saudi Arabia. The hospital is a tertiary specialist centre which provides modern medical care to patients in western region of the Kingdom of Saudi Arabia. Children with initial presentation of cholestatic liver disease below the age of six months were included in this study. Children with hepatitis, B, hepatitis C, wilson disease and autoimmune hepatitis were excluded from the study.

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The data was collected from September, 2006 to September, 2016.

A data sheet was designed to record the aetiology of choestatic liver disease, demographic data for age, gender, age of presentation, clinical presentation and outcome. The data was collected from hospital ICIS power chart. The data was presented in percentages and frequencies in form of a pie chart and tables.

RESULTS

Among 25 children 18 were male and 7 were female and male to female ratio was 2.5:1. Regarding the aetiology of cholestatic liver disease 8 children (32 %) were diagnosed with progressive familial intrahepatic cholestasis (PFIC), all were of type II. There were 6 cases (24%) of idiopathic hepatitis, 4(16 %) with Alagille syndrome, 3(12%) with biliary atresia, 2 children (8%) of sclerosing cholangitis and 2(8%) with mitochondrial disease as shown in figure 1.

Table No.1: Clinical Presentation of patients with cholestatic liver Disease

Clinical Presentation	Children affected	Percentage
Jaundice	25	100%
Failure to thrive	7	28%
Developmental delay	7	28%
Abdominal distension	5	20%
Pruritis	2	8%
UTI	1	4%
Sepsis	1	4%
Hepatocellular carcinoma	1	4%
Recurrent Diarrhea	0	0%
Recurrent chest infections	0	0%

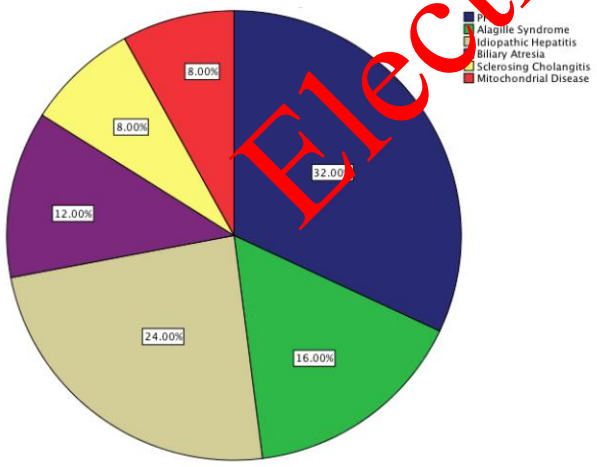

Figure No.1: Causes of cholestatic liver disease

In our study almost all children 25(100%) presented with jaundice, 7(28%) children were with failure to thrive, 5(20%) had a significant abdominal distension, 7(28%) children had developmental delay , only two (8%) children have pruritis, one (4%) had one (4%) presented with sepsis and one child (4%) had urinary tract infection with underlying cholestatic liver disease. Recurrent diarrhoea and chest infections were not observed in any child as shown in table 1.

Out of 25 children 23 (92%) survived and only two children (8%) died. Thirteen children (52%) were referred for liver transplantation and two children have had hepatoportoenterostomy (Kasai procedure). The rest of our patients are doing well on conservative medical management.

DISCUSSION

Several studies had been done to evaluate the causes and clinical presentation of cholestasis. They have reported variable results with the neonatal hepatitis remaining the commonest causes of cholestatic syndromes ranging from 38% to 79% .[8,9,10] Danks et al (1977) and Dick et al (1985) suggested idiopathic hepatitis remained as the main cause of Cholestasis, but their studies antedate the descriptions of recently recognized metabolic causes of cholestasis[11] On the other hand advances in preventive medicine may result in the lower incidence of congenital infections compared to idiopathic hepatitis in some recent studies.[12] However the study done in Brazil showed 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.[13]

In our study the progressive familial intrahepatic cholestasis (PFIC) is the most common cause of cholestatic liver disease in children (32%), however interestingly all of our PFIC cases are of type 2. As more and more metabolic diseases involving the liver are being diagnosed and due to advancement in medical science and diagnostic methods, the incidence of idiopathic hepatitis is decreasing gradually.[14,15]

Our data showed only 24% of children were diagnosed with idiopathic hepatitis. This is similar to a study done in Iran by Seyed Mohsen Dehghani et al in 2015 in which biliary atresia (24.6%) and Idiopathic hepatitis (24%) were found to be the most common causes of cholestatic liver disease.[16] But our study showed only 12% of our cases were found to have biliary atresia. This difference was due to children below three months of age were recruited in Iranian study while in our study children above three months were also included. The most common clinical presentation in our study was jaundice but a significant number of children have had growth failure, abdominal distension and developmental delay. Pruritis is a recognised feature of chronic cholestasis in children.[17] But in our study due to early diagnosis and management it is seen in only 8% of children. The recurrent diarrhea and chest infections were not observed in our study and again it may be due to early management. Another important complication in PFIC II is the development of hepatocellular carcinoma or cholangiocarcinoma in 15% of the

patients.[18,19,20] Our data revealed one out of 8 patients (12.5%) developed hepatocellular carcinoma who did not undergo liver transplantation as his parents declined the offer. These findings emphasise the need to maintain a close surveillance for the development of malignancy in children with PIFC II.

CONCLUSION

In our study the progressive familial intrahepatic cholestasis was the most common cause of cholestatic liver disease followed by Idiopathic hepatitis. The most common clinical presentation was jaundice. More than half of our patients needed liver transplantation to improve the outcome of disease. Based on our small study we suggest that more research work should be done in relation to genetic and metabolic aetiology of children with cholestatic liver disease

Conflict of Interest: The study has no conflict of interest to declare by any author.

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