Original Article

RELATIVE FREQUENCY OF HEPATITIS B VIRUS AND HEPATITIS C VIRUS INFECTIONS IN PATIENTS OF LIVER CIRRHOSIS IN CHILDREN

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ABSTRACT

Objectives:

To determine the relative frequency of Hepatitis B virus and Hepatitis C virus infections in liver cirrhosis in children between 5 to 15 years.

Study design:

Descriptive case series.

Setting and Duration:

The Gastroenterology Department at The Children's Hospital, Lahore from August 2008 to July 2009

Subjects and methods:

A total of 100 children diagnosed as liver cirrhosis on the basis of clinical features and ultrasonography findings were analyzed for findings and viral serology.

Results:

Mean age was 10.14 years and male to female ratio was 2:1. Out of 100 patients, 14 were infected with HBV, 8 with HCV. No case was found positive for both viruses. In HBsAg positive group, 12 were male and 2 were female (p=0.045).

Conclusions:

Both viruses account for 22% cases of liver cirrhosis in children. Liver cirrhosis due to HBV is more common than HCV in this region.

Keywords: Liver cirrhosis, HBV and HCV

INTRODUCTION

Cirrhosis is the most common chronic liver disease (CLD) detected in all age groups, and in both sexes. Chronic liver disease is mostly attributed to cryptogenic, post hepatitis, metabolic and storage disorders. Hepatitis B is the leading cause of chronic liver disease in children followed by Wilson's disease and autoimmune liver disease.[1] Cryptsogenic causes account for 44% cases. Cirrhosis of liver is characterized by necrosis of liver followed by fibrosis and regenerative nodules. It is manifested clinically by features of chronic liver failure and portal hypertension.[2] Some research workers regard cirrhosis as a pre-malignant condition, since more than 80% cases of hepatocellular carcinoma (HCC) develop in cirrhotic patients.[3] Cirrhosis is generally thought to be progressive and irreversible disease. However this view is not accepted by other researchers who reported reversibility in their patients after anti viral therapy for hepatitis C.[4]

Hepatitis B virus (HBV) and Hepatitis C virus (HCV) are the most common causes of chronic hepatitis worldwide.[5] These viruses are mainly transmitted through contaminated blood and

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body fluids.[6] In Pakistan, Hepatitis B virus has been found to be the leading cause of cirrhosis according to a study conducted in DI Khan.[7] The risk of chronic Hepatitis B virus infection is related inversely to age. Infections in children account for 20–30% of all cases of chronic HBV infections.[8] Worldwide, the areas of highest prevalence of HBV infection are Sub-Saharan Africa, China, parts of Middle East, the Amazon basin, and The Pacific Islands.[8] HCV has a prevalence of 4-7% in different parts of Pakistan based on detection of anti HCV antibodies.[9]

Cirrhosis accounts for significant morbidity and mortality beyond childhood.[5] Morbidity and mortality in chronic Hepatitis B are linked to evolution to cirrhosis or HCC. The 5-year survival is approximately 80-86% in patients with compensated cirrhosis while it is 14-35% in patients with decompensate cirrhosis.[10]

Many studies have been conducted on this topic worldwide. This research work was undertaken in this part of the country where cirrhosis is not uncommon.

MATERIAL AND METHODS

The study was conducted in The Gastroenterology Department of The Children Hospital and The Institute of Child Health, Ferozpur Road, Lahore from August 2008 to July 2009. Hundred patients of liver cirrhosis diagnosed on the basis of clinical features and ultrasonographic findings fulfilling inclusion criteria were enrolled in the study. Liver cirrhosis was defined by the clinical features of portal hypertension (hemetemesis, malena, ascites, and splenomegaly) or chronic liver failure (jaundice, clubbing, spider nevi, bruises, ascites) and ultrasonographic features of coarse echogenicity, nodular pattern. Children less than 5 years and more than 15 years of age were excluded from study. Non probability convenience sampling was done. Demographic profile was recorded including age, gender and locality. A detailed history and clinical examination was performed on every patient to look for the symptoms and signs of liver cirrhosis. Venous blood was taken and immediately processed. In case of delay, serum was stored at 2-8 centigrade for not more than 2 hours. Serum was tested for HBsAg by Device method (Bioline, ISO 9001), confirmed by ELISA (Bio-Tech Co. Ltd.) and anti HCV was done by ELISA. Following supportive investigations like complete blood count (Hemoglobin %, total leukocyte count, platelet count). Liver function tests (Serum bilirubin, direct, indirect, alanine aminotransferase, alkaline phosphatase) and Prothrobin Time (PT) were also done. All this information was recorded on a standard proforma.

The collected data was entered into SPSS version 11.0 and analyzed. Graphs were prepared by using Microsoft Excel 2006. Male female ratio for gender distribution and mean ± SD for age distribution was calculated. Frequencies and percentages were computed to HBV+ve, HCV+ve and presenting complaints. Chi-square test was applied to compare the significance of proportion of these variables categorically at $p<0.05$ level of significance.

Table 1. Chi-Square Test for clinical features vs Hepatitis B and C infection leading to cirrhosis

P>0.05	P<0.05
Hepatitis B:	
	Edema
	Jaundice
	Palmar Erythema
	Purpra/Bruises
	Caput Medusae
Hepatitis C:	
	Malena
	Pallor

RESULTS

One hundred patients of liver cirrhosis were included in our study. Out Of them, 67% were males and 33% were females. Male to female ratio was 2:1. Sixty percent children belonged to rural area while 40% were from urban society. The age range was 5 to 15 years. The mean age was 10.14 ± 2.96 years. For male, the age range was 5 to 15 years and mean age was 10.11 ± 3.23 years. For females, the age range was 6 to 14 years and mean age was 10.19 ± 2.38 years. Fourteen patients were HBsAg positive (14%) and 8 patients were found to have anti-HCV antibodies (8%). Out of these 22 patients, none was positive for both HBsAg and anti HCV antibodies. A significant number (78%) of patients had no serological evidence of HBV or HCV infection. In HBsAg positive group, 12 were male and 2 were female while in anti HCV antibodies group, 2 were male and 2 were female. These figures show that the serology markers for Hepatitis B virus are significantly different in both sexes ($p=0.045$).

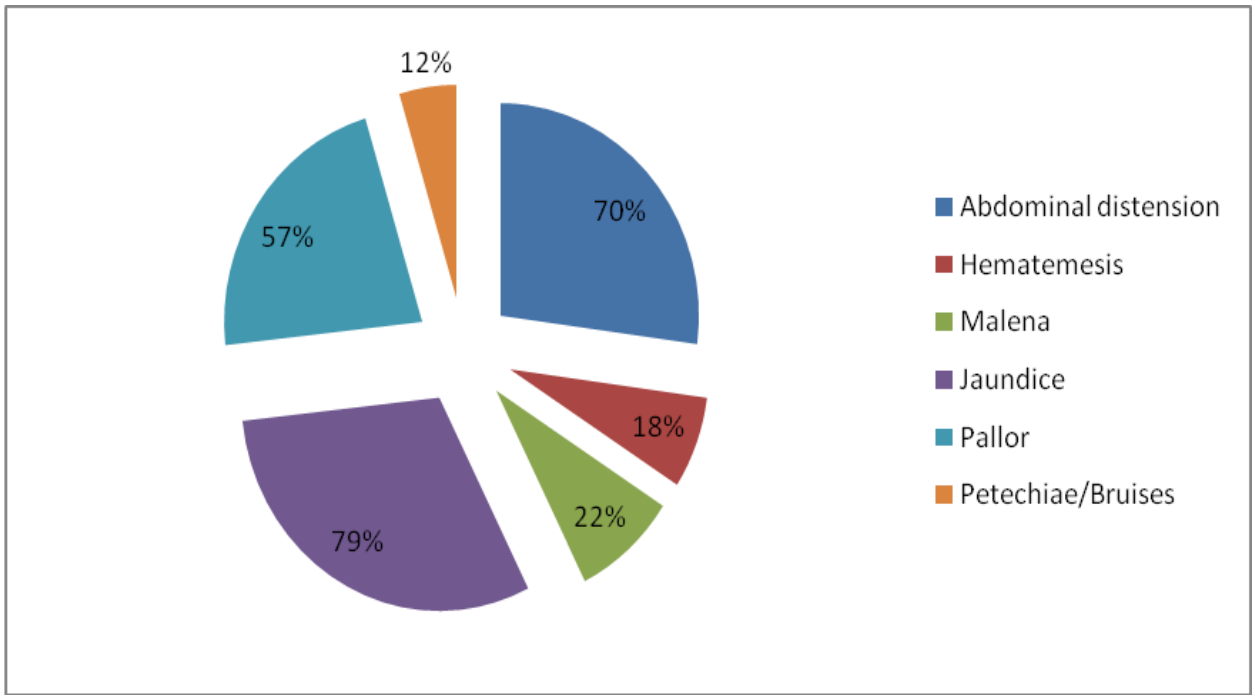

Figure 1. Symptoms among patients with cirrhosis

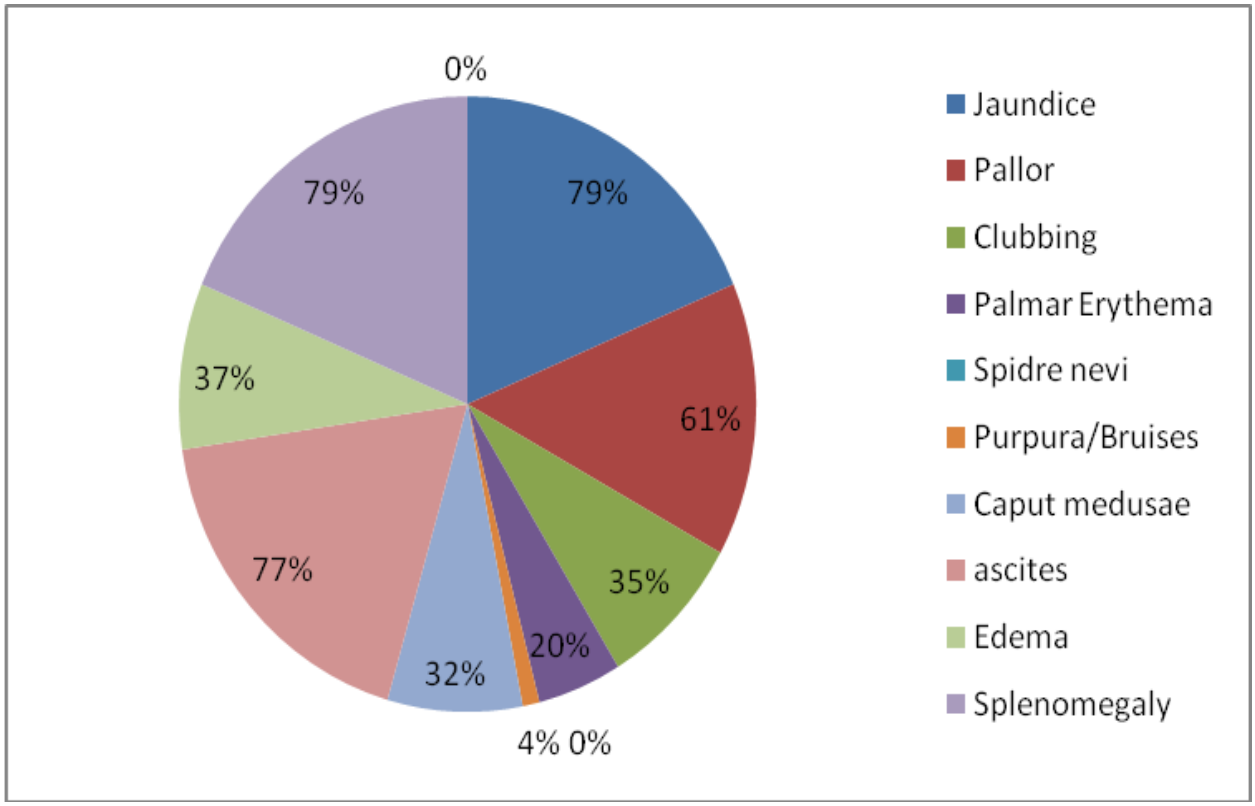

Figure 2. Signs among patients with cirrhosis

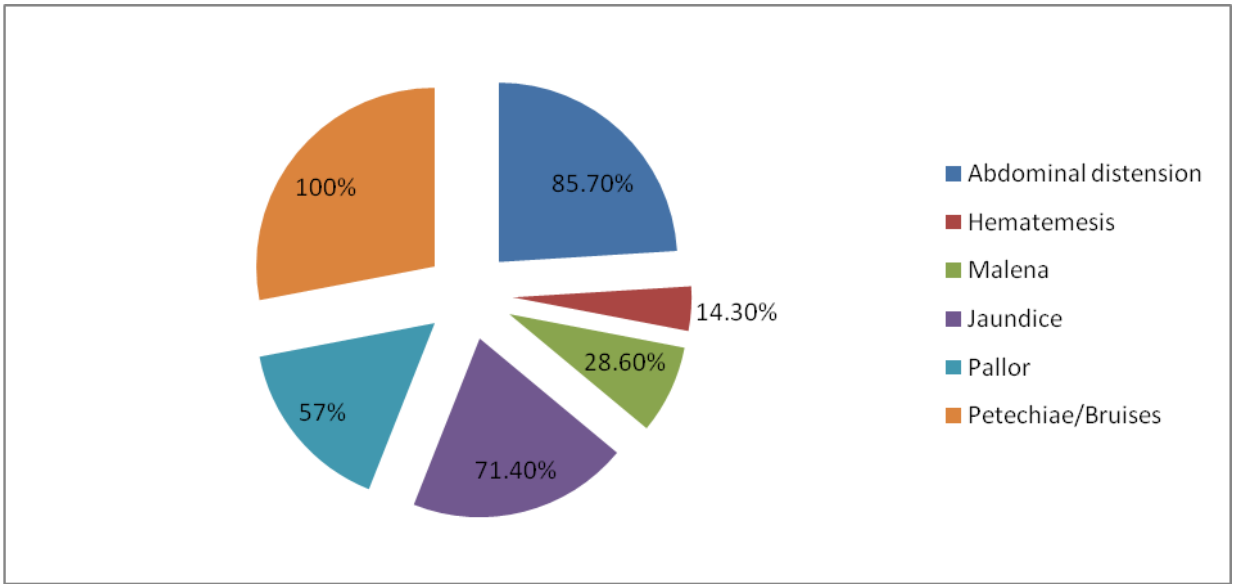

Figure 3. Symptoms among patients with cirrhosis due to HBV infection

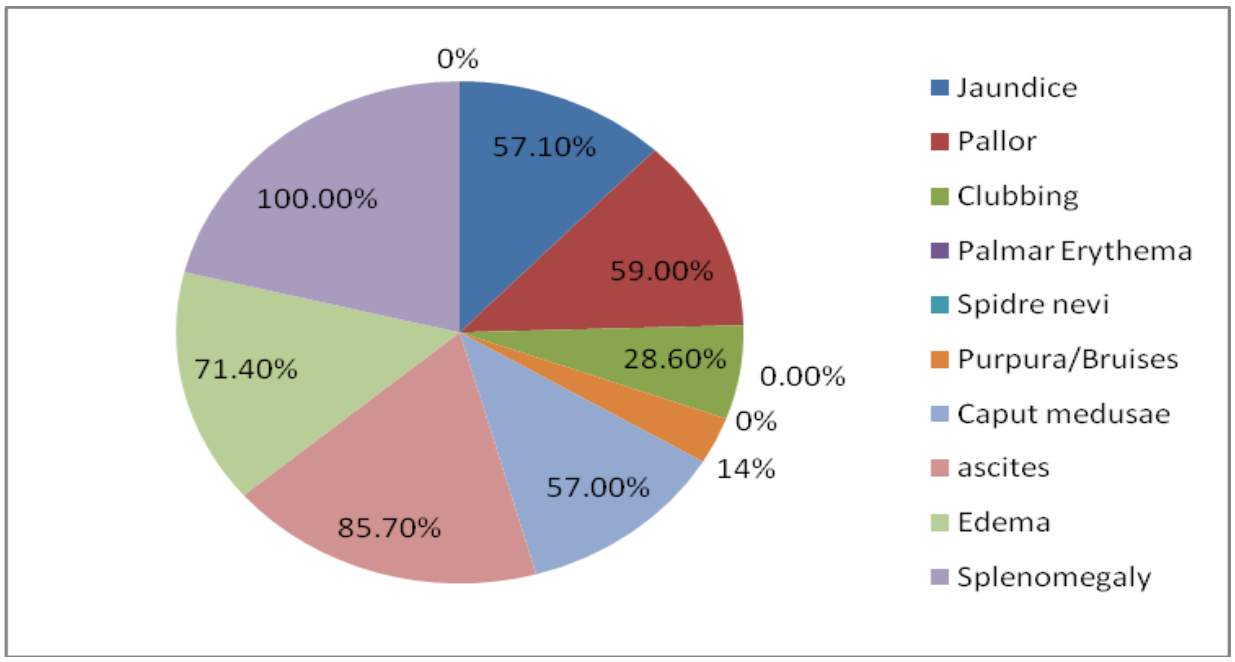

Figure 4. Signs among patients with cirrhosis due to HBV infection

The most common symptom found was jaundice that was present in 79% of patients. The percentages of symptoms and signs of liver cirrhosis are shown in Figs. 1 & 2, respectively. The percentages of symptoms and signs of liver cirrhosis due to Hepatitis B are shown in Figs. 3 & 4, respectively.

Among the laboratory parameters, the mean hemoglobin was 8.67 ± 1.79 Gm/dl, mean leukocyte count was 10597/cmm; leukocytosis (TLC >0,000/cmm) was present in 31% patients and thrombocytopenia (Platelets <150,000/ cmm) in 64%. Out of these 64 thrombocytopenic patients, 38 had platelet count less than 100,000/cmm (p=0.03). Hyperbilirubinemia (Total bilirubin ≥2 mg/dl) was seen in 77% patients, increase alanine aminotransferase (ALT >45 iu/L) in 82% patients, and prothrombin time (PT) more than 13 seconds in 92%. Out of these 92 patients, 10 had PT ≥60 seconds.

DISCUSSION

Cirrhosis is the most common chronic liver disease (CLD) detected in all age groups, and in both the sexes. In this study, a total 100 patients with liver cirrhosis were studied prospectively. This is one of few large series described from Pakistan and Asia. Before this Hanif M, Raza J, *et al.*[1] done a study in children but they included patients of chronic liver disease. The mean age in our study was 10.14 years. This is in contrast to a study done by Giacchino R *et al.*[11] in which the mean age at diagnosis was 6 years and 8 months but they had only 22 patients in their study.

In our study, cirrhosis due to HBV infection was found at a mean age of 10.60 years. In a large study done by Bortolotti F *et al.*[12] that included 292 consecutive children who were HBsAg positive and had an elevated serum ALT level. Cirrhosis was found at a mean age of 4.0 ± 3.3 years. In our study, cirrhosis due to HCV infection was found at a mean age of 10.53 years. This is comparable to a study done by Mohan P *et al.*[13] in which mean age of HCV infection was 7.1 months and 12% of patients were found to have significant fibrosis after 13 years of infection.

This study showed that among HBsAg positive group 85.71% were males and 14.28% were females. In anti-HCV antibodies positive group 50% were males, 50% were females and out of 78 patients having neither HBsAg nor anti-HCV antibodies, 64% were males and 36% were females. This is comparable to a study by Nazish Z *et al.*[14] in which among HBsAg positive group 75% were males and 25% females. In anti HCV antibodies group 62.50% were male, 37.50% were female and out of 24 patients having neither HBsAg nor anti-HCV antibodies 66.66% were male and 33.33% were female but this study was carried out in adults.

Splenomegaly was present in 79% patients in our study, that is comparable to a study conducted by Giacchino R *et al.*[11] which showed splenomegaly in 81.81% cases. In our study, distension of abdomen was present in 70% and hemetemesis in 18%. This is almost comparable to the study done by Umar M *et al.*[9] that showed ascites in 68% and upper GI bleeding in 26%. This is in contras to adult population in which distension of abdomen was seen less commonly and hematemesis was found in 36% of patients.[15]

Ali SA *et al.*[16] showed that weighted average of Hepatitis B antigen prevalence in pediatric populations of Pakistan was 2.4% (range 1.7-5.5%) and for Hepatitis C antibody was 2.1% (range 0.4-5.4%). We found HBsAg positivity in 14% and anti-HCV antibodies in 8% patients with cirrhosis. Out of these 22 patients, none was positive for HBsAg as well as anti HCV antibodies. Seventy eight percent of patients had no serological evidence of HBV or HCV infection. These results are clearly different from figures obtained in earlier study carried out in Rawalpindi and Islamabad on adult patients that showed HBsAg positivity in 46.6% and anti-HCV antibodies positivity in 13.3%. In this study, 1.66% patients had dual infection with HBV and HCV.[17] A single case of dual infection was reported by Mashud I *et al.*[7] in their study.

Similarly another study conducted by Shajee AS *et al.*[18] showed HBsAg positivity in 32% of patients with cirrhosis. According to a study carried out by Khan AA, *et al.*[19] on adult patients about 8% of patients had dual infection with HBV and HCV.

Our study showed that HBV is slightly more commonly associated with liver cirrhosis in pediatric population than HCV. This may be attributed to high prevalence of HBV infection than that of HCV in pediatric population in this area of Pakistan. Another possible reason for this difference could be that majority of patients in our study were having advanced cirrhosis at presentation as 77% patients were having ascites. Cirrhotic patients with Hepatitis C may remain asymptomatic for relatively longer time, and present late to a health care facility.

CONCLUSION

Hepatitis B virus is more common (as a cause of cirrhosis) than Hepatitis C virus in this area of our country. More male pediatric patients are affected as compared to female. Dual infection with HBV and HCV is not present in liver cirrhosis in this area. More studies are required to prove higher prevalence of HBV infection in pediatric population in other parts of the country.

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