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Assessment of Risk Factors and Clinical Presentations in a Liver Cirrhotic State-Pakistan

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Abstract: *Background:* Liver cirrhosis is one among most common causes of death throughout the world. Pakistan is known as cirrhotic state with high number of cirrhosis anywhere in the world. Aims: The objectives of this study were to assess risk factors, clinical features and complications of liver cirrhosis. Method: This study was done at medical wards of Khyber Teaching Hospital and Lady Reading Hospital Peshawar. Data was collected from 74 patients with cirrhosis through structured questionnaire. Results revealed that in our results showed that Prevalence of liver cirrhosis is high in age group > 45 years(68.9%) and in male patients(79.7%), low in intermediate age group (29.7%) and infrequent in young age group (1.4%). Out of 74 cases 38 were attributed to HCV only, 12 to HBV and HCV co-infection, 7 to HBV only, 6 to HBV and Alcohol and HCV and Alcohol each, 3 to HBV, HCV and Alcohol acting conjointly and 1 to Fatty liver disease. For 1 patient the cause was unknown. More than 75% hepatitis (B and C) was associated with clinical mal-practices. Most frequent signs and symptoms in decreasing order were anorexia and weight loss (100%), jaundice (90.5 %), abdominal disturbances and spleenomegaly (75%), bleeding tendencies, decreasing mental function, itching and palmer erythema (<20%). Complications were ascites (97.3%), peripheral oedema(73%), recurrent infections (43.2), hepatic encephalopathy (28%), GIT bleeding (4.1%) and hepatocellular carcinoma (1.4%). Serum ALT and total Bilirubin were raised in 80 % and 90.7% patients respectively. Conclusion: Hepatitis C is the most frequent cause of liver cirrhosis mostly acquired through prick by contaminated syringes or blades or through blood transfusion.

Key words: Hepatitis · Liver Cirrhosis · Hepatocellular Carcinoma · Body Mass Index · Viral Transmission

INTRODUCTION

Liver cirrhosis is a degenerative condition that causes scarring of liver tissue and resultant malfunctioning. National Digestive Diseases Information Clearinghouse states that liver cirrhosis prevents body from food processing, controlling infections, absorbing of fats, hormones and medications [1] due to chronic injury. In Cirrhosis Scar tissue replaces healthy liver tissue, partially blocking the flow of blood through the liver and also impairing the liver's ability to function optimally and to replace its damaged cells [2]. Cirrhosis is the end stage result of many types of long-term liver injury with excess alcohol use and chronic infection with hepatitis viruses (such as HBV,HCV and HDV) as the major causes and others minor causes including non-alcoholic fatty liver disease, inherited metabolic disorders (including heamachromatosis. alpha-1 antitrypsin deficiency, Wilson disease, cystic fibrosis, glycogen storage diseases), drug-induced injury (methyl dopa), bile duct disorders (primary

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biliary cirrhosis. Primary sclerosing cholangitis) and autoimmune hepatitis. Some patients may have more than one cause for cirrhosis (such as alcohol excess and viral hepatitis). In about 20% of cases the cause is unknown termed as cryptogenic cirrhosis [2,3]. Because of long term exposure to the hepatotoxin and viruses advanced age is also considered as risk factor for cirrhosis. It is also shown that cirrhosis develop in Obese children with steatohepatitisin childhood [3,5]. Clinically Cirrhosis is divided into two stages (a) compensated cirrhosis in which the liver is heavily scarred but still usually asymptomatic, (b) Decompensated cirrhosis in which the liver function is lost. At this stage the patient develops variety of symptoms [6]. These symptoms include fatigue and weakness, Itching, peripheral oedema, Jaundice, Recurrent infections, Palmer erythema, Spider nevi, congestive spleenomegaly, bleeding tendency and decrease mental function. Untreated liver cirrhosis progress gradually to complications which include ascites, GIT bleeding, hepatic encephalopathy, diabetes mellitus, hepatorenal syndrome, hepatopulmonary syndrome, congestive cardiac failure and Hepatocellular carcinoma.

Liver cirrhosis is among top 10 leading causes of illness and death in the United States. Approximately 5.5 million population of United State are having liver cirrhosis constituting the seventh leading cause of death among age group 25-64year. Viral hepatitis (HBV and HCV) and excess use of alcohol are the two major contributors. Eliminating alcohol abuse only can prevent 75 to 80 percent of cirrhosis [7]. The number of people affected by cirrhosis will continue on increasing in the near future [3]. In 2000 there were 360,000 US hospital discharge related to cirrhosis and liver failure. In 2002 cirrhosis accounted for about 27257 deaths (9.5 per 100,000 persons) with slight male predominance [8].

It is also showing an increase in its trends in incidence and prevalence in Pakistan[9]. Majority of patients (90%) with chronic liver disease are infected with HBV or HCV or have co-infection. Disease is considered more severe in patients with co-infection and cirrhosis is recorded in 74% of patients [10,11].

Reliable study carried out in 2002 showed HBV (46.67%) as the major cause of cirrhosis with HCV for 13.33% and other causes for 40% of cases and male predominance. Another study in 2005 showed HCV(52%) as the major cause of cirrhosis [12]. This change may be due to recent increase in HCV prevalence and decrease in HBV due effective HBV vaccination.

Study Design: This was hospital based observational and descriptive cross-sectional study carried out in two tertiary care hospitals of Peshawar over a period of 21 weeks from 20th March 2013 to 26thAugust 2013.

Study Area and Studied Population: This study was conducted in medical wards of Khyber teaching Hospital (KTH) Peshawar and Lady Reading Hospital (LRH) Peshawar. Patients from all over Khyber Pakhtonkhaw (KPK), Federal Administered Tribal Areas (FATA) as well as from Afghanistan come to these hospitals to get their aliment by specialized faculty of these hospitals. Patients diagnosed for liver cirrhosis admitted in medical wards of Khyber Teaching Hospital and Lady Reading Hospital Peshawar during period of 5 weeks (from 10th may 2013 to 16th June 2013) was our study population. Total of 74 patients diagnosed for liver cirrhosis were enrolled for this study. Informed consent was obtained from each subject and the study was approval by the scientific and ethics committees of Khyber Medical College Peshawar.

Data Collection: Data was collected from 74 patients through questionnaire based person to person interview, clinical examination and from hospital charts and laboratory reports. A printed data sheet containing information such as age, sex, ethnic group, weight, height, body mass index (BMI), history of risk factors for cirrhosis, history of risk factors for Hepatitis viruses, history of clinical presentations and complications of cirrhosis. All the procedures followed in this study were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki declaration of 1975, as revised in 1983.

Data Analysis: Data was coded, compiled in statistical package for social sciences (SPSS) software for window 7.

Limitation

- Lack of education in most of our respondents created difficulties even to answer simple questions such as about age, weight loss etc.
- Some of patients were seriously ill and were not ready to give permission.
- Lack of co-operation of some patients.
- Use of convenient sampling technique.

RESULTS

Gender and Age Wise Distribution of Patients with Liver Cirrhosis: The proportion of male and female in study population is given in table 1. Our sample size was 74 patients with cirrhosis belonging to different walks of life with different occupations. Out of 74 patients fifty nine (79.7%) were males and fifteen (20.3%) were female. On the basis of age we have divided study population into three age groups i.e. 15y–30y: one patient (1.4%) is recorded in this age group, 31y – 45y: twenty two (22.9%) patients are recorded in this age group and Greater than 45 y (>45y) fifty one (68.9%) patients are Included in this age group. Analysis for data of age is given in Table 2.

To Determine a Relation Between B.M.I and Liver Cirrhosis: On the basis of B.M.I calculated we divided our study subjects into two categories i.e. normal and overweight. Sum of sixty one (82.4%) patients fall in normal category while thirteen (17.6%) patients fall in overweight category. Analysis for data of B.M.I is given in table 3.

To Determine Contribution of Different Causes to Liver Cirrhosis: Out of 74 cases Hepatitis C accounts for 38(51.4 %) cases, Hepatitis B and C co-infection for 12(16.2%) cases, Hepatitis B for 7 (9.5%) cases, HBV and Alcohol and HCV and Alcohol for 6 (8,1%) cases each, HBV,HCV and Alcohol for 3 (4.1%) cases and fatty liver disease for 1 (1.4%) case of cirrhosis. Cause for 1 (1.4%) case is unknown (cryptogenic). Analysis of data is shown in Table 4.

To Determine Risk Factors for Cirrhosis Associated Hepatitis (B and C): As analyzed above 72 out of 74 cases are associated with hepatitis (B and C) in some way. In above 72 patients the possible risk factor for Hepatitis (B and C) is prick by contaminated syringe /blade for 27 (37.5%) cases, prick by contaminated syringe /blade or blood transfusion for 24 (33.33%) cases, sexual contact with infected person for 07 (9.72%) cases and Blood transfusion for 03(4.16%) cases. In 11 (15.27%) cases the risk factor is unknown. Analysis for data of risk factors for Hepatitis (B and C) is given in Table 5.

To Determine the Frequencies of Different Signs and Symptoms and Complications of Liver Cirrhosis: Clinical presentation of liver cirrhosis varies from subject to subjects. Some study subjects are presented with few and minor sign and symptoms while other with more and major complications. Figure 1 and figure 2 representing frequency distributions of sign and symptoms and complications in our study population are given. The most common sign and symptoms found in Cirrhotic patients are weight loss in 74(100%), anorexia in 74(100%), Jaundice in 67(90.5%), fatigue and weakness in 66(89.2%), abdominal disturbance in 56 (75.7%), splenomegaly in 55(75.3%), Bleeding Tendency 15 (20.5%), decreased mental function 13(17.6%), itching 10(13.5%), palmer erythema and cyanosis in 6(8.2%) respectively.

Table 1: Frequency Distribution and Chi-square for gender of Study subjects (n=74)

Gender	Frequency (% age)	Chi-Square and Degree of Freedom; $\chi 2(df)$	Significance P = 0.05
Male	59 (79.7)	26.162 (1)	< 0. 0005
Female	15 (20.3)		

Table 2: Frequency Distribution and Chi-square for Age range of Study subjects (n=74)

Age Range	Frequency (% age)	Chi-Square and Degree of Freedom; $\chi 2(df)$	Significance P = 0.05
15-30 Years	1 (1.4)	51. 108 (2)	< 0. 0005
31-45 Years	22 (29.7)		
> 45 Years	51 (68.9)		

Table 3: BMI Distribution of Patients with Liver Cirrhosis

BMI	Frequency (% age)	Chi-Square and Degree of Freedom; $\chi 2(df)$	Significance P = 0.05
Normal	61 (82.4)	31.135 (1)	< 0. 0005
Overweight	13 (17.6)		

Table 4: Frequency Distribution and Chi-square for Causes of Cirrhosis in Study subjects (n=74)

Parameter	Options	Frequency (% age)	Chi-Square and Degree of Freedom; $\chi 2(df)$	Significance P = 0.05
Risk factors	Hepatitis B only	07 (9.5)	111.946 (7)	< 0. 0005
	Hepatitis C only	38 (51.4)		
	Hepatitis B and C	12 (16.2)		
	HBV and Alcohol	06 (8.1)		
	HCV and Alcohol	06 (8.1)		
	HBV and HCV and Alcohol	03 (4.1)		
	Fatty Liver Disease	01 (1.4)		
	Unknown	01 (1.4)		

Table 5: Risk factors for Hepatitis B and C in study subjects

Parameter	Options	Frequency (% age)	Chi-Square and Degree of Freedom; $\chi 2(df)$	Significance P = 0.05
Causes/ Risk				
factors of liver cirrhosis	Blood transfusion	03(4.16)	31.056(4)	< 0. 0005
	prick by contaminated syringe /blade	27(37.5)		
	prick by contaminated syringe /blade,			
	blood transfusion	24(33.3)		
	sexual contact with infected person	07(9.72)		
	Unknown	11(15.27)		

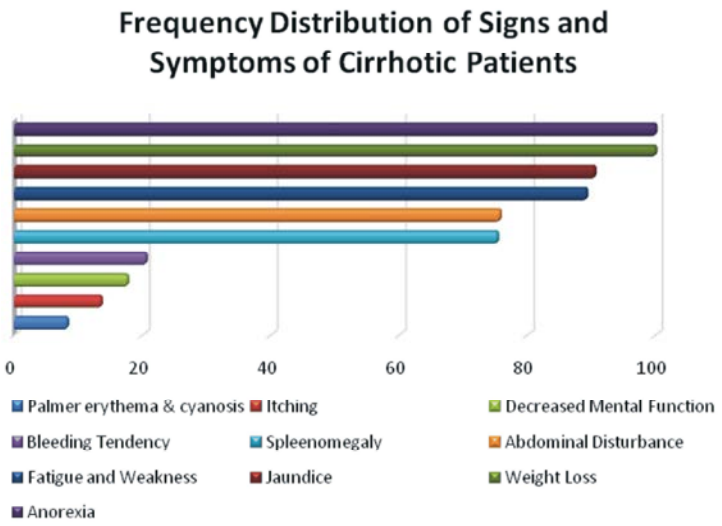

Fig. 1: Frequency Distribution of Signs and Symptoms of Cirrhotic Patients

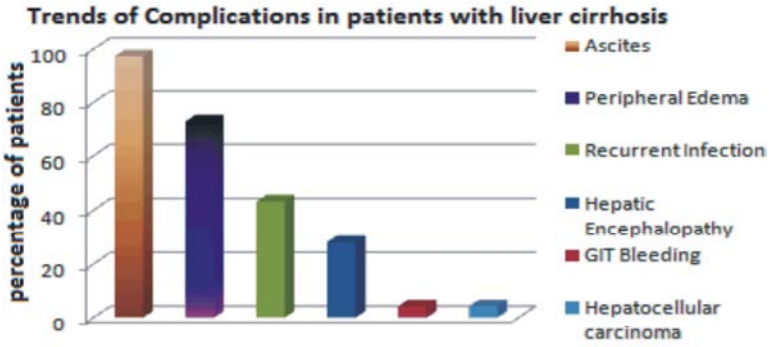

Fig. 2: Trend of Complications with Cirrhosis in Cirrhotic Patients

Among complications the most frequent presented is Ascites in 72 (97.3%) subjects, followed by peripheral oedema in 54 (73%) subjects, recurrent infections in 32 (43.2%) subjects, hepatic encephalopathy in 21 (28%) subjects, Upper GIT bleeding in3 (4.1%) subjects and hepatocellular carcinoma in 1 (1.4%) subject. Trends of complications in patients with liver cirrhosis are shown in Figure 2.

DISCUSSION

Liver cirrhosis is defined as a diffuse hepatic process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules as a consequence of chronic liver disease characterized by replacement of liver tissue by fibrosis, scar tissue and regenerative nodules [13,14]. Cirrhosis is caused by both known and unknown factors. Among the known causes, the most common are alcoholism, hepatitis (B and C) and fatty liver disease. Some patients with cirrhosis are completely asymptomatic and have a reasonably normal life expectancy. Other individuals have a multitude of the most severe symptoms of end-stage liver disease and a limited chance for survival. Cirrhosis is not less common in Indo-Pakistan subcontinent [15,16] along with rising frequency attributable to a more widespread awareness of this disease among gastroenterologist and hepatologists.

In this study, we are able to determine a relationship of age and body mass index (BMI) with cirrhosis and identify the clinical features and risk factors for cirrhotic patients. Majority of our patients were male. In the current cohort, the demographic features and clinical profiles were consistent with those of previous studies [2-4,17,18].

As per one of the findings of this study, advancing age is a risk factor for liver cirrhosis irrespective of the cause as cirrhosis was found significantly high ($p<0005$)in patients above the age of 45 years. These findings were similar to the results obtained by Mashud *et al*. [19] in Dera Ismail Khan, Khyber PakthtoonKhwa (KPK) Pakistan. Surprisingly frequency of cirrhosis was higher in normal patients as compared to overweight patients when a relation between BMI and liver cirrhosis was observed.

Next important finding of the current study is the observation that chronic Hepatitis C infection accounts for more than 50% of the total cirrhotic cases followed by Hepatitis B and C co-infection (16.2%) and alone Hepatitis B (9.5%). Cirrhosis has many possible causes. Worldwide, 57% of cirrhosis is attributable to either hepatitis B infection (30%) or chronic Hepatitis C infection (27%) (70). Alcohol consumption is another important cause, accounting for about 20% of the cases. (70), however our majority of patients were non-alcoholic. Sometimes more than one cause is present in the same patient that has been confirmed by this study. The reason for so high number of HCV related cirrhotic patients is the high prevalence of HCV infection in Pakistan [16]. Infection with the HCV causes inflammation of the liver and a variable grade of damage to the organ that over several decades can lead to cirrhosis. Cirrhosis caused by hepatitis C is the most common reason for liver transplant in the world.

Just like HCV, the HBV also causes liver inflammation and injury that over several decades can lead to cirrhosis. Hepatitis D virus (HDV) that is a defective virus and is dependent on the presence of HBV accelerates cirrhosis in co-infection. Unfortunately we were unable to detect HDV in HBV infected cirrhotic patients of our study due to the unavailability of reliable HDV RNA detection method in our country.

Clinical presentation of liver cirrhosis varies from subject to subjects. Some study subjects are presented with few and minor sign and symptoms while other with more and major complications. the tables and bar charts representing frequency distribution of sign and symptoms and complications in our study population is given.

Among complications the most frequent presented in subjects was ascites in (97.3%), followed by peripheral oedema in (73%), recurrent infections in (43.2%), hepatic encephalopathy in (28%), Upper GIT bleeding in (4.1%) and hepatocellular carcinoma in (1.4%). Here it is important to point out that some of the above mentioned signs and symptoms may occur in the presence of cirrhosis or as a result of the complications of cirrhosis. Many are nonspecific and may occur in other diseases and do not necessarily point to cirrhosis. Likewise, the absence of any does not rule out the possibility of cirrhosis.

CONCLUSION

Based on the results of this study it is concluded that various risk factors are responsible for liver cirrhosis such as advancing age, male sex, hepatitis B, hepatitis C, alcohol and fatty liver disease. Among these, hepatitis C is the risk factor having highest impact on symptomatic liver cirrhosis risk in Peshawar. Second major risk factor with high impact on liver cirrhosis is hepatitis B. more ever in the presence of more than one risk factors the progression to liver cirrhosis is rapid.

It is further concluded that major risk factor for hepatitis (B and C) are pricked by contaminated syringe or blade, blood transfusion and sexual contact with infected persons. Among them major risk factor associated with hepatitis, turn out to be prick by contaminated syringe or blade. It is also concluded that the majority of cases reports hospital when cirrhosis has already progressed to decompensate stage, frequently with complications such as Ascites, peripheral oedema, recurrent infections and hepatic encephalopathy

Competing Interests: The authors declare that they have no competing interests.

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