Association of Hepatorenal Syndrome with Liver Cirrhosis

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Abstract
Hepatorenal syndrome is the complication of end stage liver disease in which renal shut down occur. There might be some geographical variations in the disease pattern of liver cirrhosis and the frequency of different complications. So the aim of the current study was to find out the frequency of hepatorenal syndrome among patients with liver cirrhosis in Lahore Pakistan. A descriptive cross-sectional study was conducted at the department of medicine, Azra Naheed Medical College, Lahore during January to September 2021. For confirmation of liver cirrhosis, laboratory findings including prothrombin time and serum albumin and ultrasound finding of parenchymal changes in the liver were noted. For diagnosing hepatiorenal syndrome, serum creatinine level, 24-hour urinary protein and detailed urinary examination were performed. Data was analyzed by using Statistical Package for Social Science (SPSS) version 20. The mean age of the study participants was 45 ± 7.1 with male predominance (65%). Out of total 163 patients of liver cirrhosis, about 11.6% patients were confirmed cases of hepatorenal syndrome. Liver cirrhosis was graded on the basis of Child-Pugh classification, 4 patients fall in Group A, among them only 1 patient was confirmed for hepatorenal syndrome. Group B consisted of 107 patients and 13 were having hepatorenal syndrome while 52 patients were in Group C, out of them 7 were labelled for hepatorenal syndrome. It can be concluded that the frequency of hepatorenal syndrome is 11.6% among patients of liver cirrhosis. Diagnosis of hepatorenal syndrome at early stage and early initiation of treatment can minimize the mortality rate due to hepatorenal syndrome.

Keywords: Hepatorenal syndrome, Cirrhosis, Child-Pugh classification

Introduction

Prolonged hepatocellular injury leads to liver cirrhosis which ends up to hepatic failure. Liver cirrhosis is an irreversible disease, the characteristic features include fibrosis and nodular regeneration. It is one of the leading cause of increased mortality worldwide (1). In Pakistan, there is high prevalence of liver cirrhosis with rising mortality rate due to its complications including hepatic encephalopathy, hematemesis, pulmonary fibrosis and hepatorenal syndrome. Unfortunately, hepatitis B and hepatitis C, preventable diseases, are the most common etiological factor in 65% of cases (2).

Hepatorenal syndrome is the complication of end stage liver disease in which renal shut down occur (3). Anand et.al reported that nonsteroidal anti-inflammatory drugs are administered in cirrhotic patients which decreases the glomerular filtration rate by altering the renal blood flow (4). Literature review revealed the detailed pathophysiology that there is vasoconstriction of renal vasculature causing activation of renal sympathetic nervous system, resulting in decreased filtration fracture (5). Besides that, there is excessive systemic vasodilation so total peripheral resistance decreases in systemic circulation resulting in hypotension (6). The hallmark of hepatorenal syndrome is renal vasoconstriction and systemic vasodilation as per "Arteriolar vasodilation theory" and "Hepatorenal reflex theory" (7).

There are two types of hepatorenal syndrome, in type-I there is spontaneous occurring of renal failure with rapid progression and poor prognosis, on the other hand type-II appear in diuretic-resistant ascites patients and is chronic in nature take few months to progress, poor prognosis but survival time is longer than type-I (8, 9). About 10% of patients with liver cirrhosis undergoes into hepatorenal syndrome. There might be some geographical variations in the disease pattern of liver cirrhosis and the frequency of different complications. So the aim of the current study was to find out the frequency of hepatorenal syndrome among patients with liver cirrhosis in Lahore Pakistan.

Material and Methods

A descriptive cross-sectional study was conducted at the department of medicine, Azra Naheed Medical College, Lahore during January to September 2021. The study got approval from the concerned institute. OpenEpi calculator was used to calculate sample size and it was 180 at the confidence interval of 95%. All the patients, above 18 years of age, who were diagnosed as the case of liver cirrhosis, on the basis of signs, symptoms, laboratory findings and ultrasonography, were included in the study. Patients from in-patient and out-patient department were enrolled. Those patients were excluded who were either having hepatic encephalopathy or hepatic failure or taking nephrotoxic drugs or sepsis. Spontaneous bacterial peritonitis was the confounding factor so the patients with intra-abdominal infections were also excluded.

For confirmation of liver cirrhosis, laboratory findings including prothrombin time and serum albumin and ultrasound finding of parenchymal changes in the liver were noted. For diagnosing hepatiorenal syndrome, serum creatinine level, 24-hour urinary protein and detailed urinary examination were performed. A self-designed proforma was used, consisting of demographic variables like age, gender, laboratory investigations and ultrasound findings. Hepatorenal syndrome was diagnosed on the basis of four major criteria including serum creatinine level $\geq$1.4 mg/dL, ultrasonography to assess renal parenchyma, 24-hour urinary protein $\geq$500mg/dL and detailed urinary examination. Data was analyzed by using Statistical Package for Social Science (SPSS) version 20. All the numerical variables were calculated as mean with standard deviation while categorical variables were presented in frequency and percentages.

Results

The mean age of the study participants was 45 $\pm$ 7.1 with male predominance (65%) as compare to their female counterpart (35%). For the diagnosis of cirrhosis few laboratory investigations

were used including bilirubin with mean value 2.10 ± 0.8 mg/dL, serum albumin 3.3 ± 0.2 g/Dl, prothrombin time 16 ± 1.85 seconds, creatinine 1.6 ± 0.9 mg/dL and 24-hours urinary proteins with mean value of 124.7 ± 119.9 mg/day as presented in Table 1.

Table 1 Characteristics of study participants

Variables	Mean ± SD
Age (years)	45 ± 7.1
Bilirubin (mg/dL)	2.10 ± 0.8
Albumin (g/dL)	3.3 ± 0.2
Prothrombin time (sec)	16 ± 1.85
Creatinine (mg/dL)	1.6 ± 0.9
24-hours urinary proteins (mg/day)	124.7 ± 119.9

To assess renal function, serum creatinine level was checked, about 68.33% patients were having normal value of serum creatinine i.e. ≤1.4 while 31.6% were having deranged values of serum creatinine above 1.4 as mentioned in Table 2.

Table 2 Serum creatinine among study participants

Serum Creatinine	n=180 (%)
Normal serum creatinine (0.6-1.4 mg/dL)	123 (68.33%)
Raised serum creatinine (≥1.4 mg/dL)	57 (31.67%)

Hepatorenal syndrome was labeled by using four major criteria including serum creatinine level ≥1.4 mg/dL, ultrasonography to assess renal parenchyma, 24-hour urinary protein ≥500mg/dL and detailed urinary examination. Out of total 180 patients, 19 were having serum creatinine level ≥1.4 mg/dL but the renal parenchyma on ultrasonography was normal, 24-hour urinary protein was less than 500mg/dL and slightly altered urinary examination. Out of total 163 patients of liver cirrhosis, about 11.6% (21) patients were confirmed cases of hepatorenal syndrome. Liver cirrhosis was graded on the basis of Child-Pugh classification, 4 patients fall in Group A, among them only 1 patient was confirmed for hepatorenal syndrome. Group B consisted of 107 patients and 13 were having hepatorenal syndrome while 52 patients were in Group C, out of them 7 were labelled for hepatorenal syndrome as presented in Table 3.

Table 3 Association of diagnosis with Child-Pugh classification

Child-Pugh classification	Liver Cirrhosis	Hepatorenal syndrome
	n= 180	
Grade A (score of 5-6)	4 (2.2)	1 (0.5)
Grade B (score of 7-9)	107 (59.4)	13 (7.2)
Grade C (score of ≥10)	52 (28.9)	7 (3.8)
Total	163 (90.5%)	21 (11.6%)

Discussion

Globally cirrhosis has the high morbidity and mortality rate because of its irreversible nature. There are many complication at the end stage of cirrhosis like hepatorenal syndrome (10). Amin et.al. conducted a study and reported that the frequency of hepatorenal syndrome is 10-21% in the patients of liver cirrhosis and is the most common reason behind the admission in intensive care unit (3). There is a high incidence rate of hepatitis B and hepatitis C in developing country, specially Pakistan, so cirrhosis is a very commonly occurring disease (11). Seetlani et.al. conducted a study in Karachi, included 240 patients of liver cirrhosis and reported that the incidence of hepatorenal syndrome with ascites was 15%. Although the study limitation was small sample size but it was the first study which highlighted the incidence rate of hepatorenal syndrome among patients of liver cirrhosis (12). Current study found 11.6% frequency of hepatorenal syndrome among patients of liver cirrhosis. Current study took sample size of 180 which was a very small sample size so there is a need to conduct study on larger scale.

In Spain, a prospective study was performed by Gines et.al. to report the incidence of hepatorenal syndrome in liver cirrhosis patients. The study results revealed that the incidence rate was 18% at 1-year after the diagnosis of liver cirrhosis while the incidence rate was increased to 39% after 5 years of liver cirrhosis (13). Another study conducted in United States of America revealed that 40% of patients of liver cirrhosis were misdiagnosed as hepatorenal syndrome because of no diagnostic criteria was established at that time. But still a high incidence of hepatorenal syndrome was recorded i.e. 13-45.8%, the reason behind this might be the lack of awareness regarding hepatorenal syndrome among physicians (14-16).

Hepatorenal syndrome is difficult to cure as there is poor treatment options. Liver transplantation is the only treatment of choice which can revert back the renal function to normal but the availability of donor is the difficult task that is why the mortality rate is still high. The other limitations of liver transplantation are poor post-operative recovery, high morbidity and mortality rate and prolong duration of hospitalization (17). Gonwa et.al. revealed that post-operative hemodialysis is also required for short duration only 5% of the patients required long-term hemodialysis after liver transplantation (18).

Conclusion

It can be concluded that the frequency of hepatorenal syndrome is 11.6% among patients of liver cirrhosis. Diagnosis of hepatorenal syndrome at early stage and early initiation of treatment can minimize the mortality rate due to hepatorenal syndrome.

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