RENAL DERANGMENT IN CIRRHOSIS: EXPERIENCE IN HAYATABAD MEDICAL COMPLEX, PESHAWAR

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Objective of the Study: To identify different causes of renal impairment in patients with cirrhosis.

Patient and Methods: This study was conducted in the Gastroenterology and Hepatology Department of Hayatabad medical complex Peshawar from January 2017 till December 2017. Patients with liver cirrhosis having ascites and impaired renal functions were included in the study. Detailed history taking and relevant systemic examination were carried out. Relevant investigations including hematological, biochemical, urinalysis, ascitic fluid analysis and radiological assessment were done for all patients. All this information was entered into a specially designed proforma. All data was analyzed using SPSS Program 10.0. Descriptive statistics were calculated for the study variables.

Results: A total of 100 patients with cirrhosis and ascites were included in this study out of which 59 (59 %) were male and 41 (41 %) were female patients with male to female ratio of 1.43:1. Most patients were in the age group of 51-60 years i.e. 47 (47%) patients. Cirrhosis in 48 (48%) patients was due to hepatitis "C", in 30 (30%) patients it was due to hepatitis "B" while in 22 (22%) patients it was due to other causes. Among cause of renal impairment hepatorenal syndrome was found in 49 (49%) patients, followed by hypovolemia in 33 (33%) and spontaneous bacterial peritonitis in 11 (11%) patients among other causes.

Conclusion: Renal impairment in patients with cirrhosis is a relatively common and serious complication. Hepatorenal syndrome is not the only cause to be considered in such patients and it should be the diagnosis of exclusion in these patients. Among other causes which needs to be excluded include hypovolemia, intrinsic renal disease, active infection or sepsis and diuretics and nephrotoxic drug usage.

Key Words: Hepatorenal syndrome, renal impairment, cirrhosis.

INTRODUCTION

Among complication of cirrhosis, renal failure is a serious and difficult to manage complication[1] with poor prognosis and increased risk of death as compared to those who do not have renal impairment[2,3]. It is also a component of Model for End stage Liver Disease (MELD) score and this has increased the number of cirrhotic patients with renal impairment to receive liver transplant and thus reduce mortality in these patients[4-6]. Patients with advanced cirrhosis having circulatory dysfunction and systemic underfilling are particularly at risk of developing renal derangement either spontaneously or initiated by other events like hypovolemia, diuretics, intrinsic renal disease or obstructive uropathies, spontaneous bacterial peritonitis or other infections\sepsis and nephrotoxic drugs. The aim of this study is to find different causes of renal derangement in patients with cirrhosis and emphasis on the fact that every patient with cirrhosis having renal derangement does not have hepatorenal syndrome.

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OBJECTIVE

To identify different causes of renal impairment in patients with cirrhosis.

PATIENTS AND METHODS

This study was conducted in the Gastroenterology and Hepatology Department of Hayatabad medical complex Peshawar, from January 2017 till December 2017. Written informed consent was obtained from all the participating patients.

All adult patients from 30-65 years of age of either sex who were diagnosed cases of cirrhosis on the basis of history, clinical examination and investigations and were having renal impairment were included in the study on the basis of non-probability convenience sampling.

Patients were interviewed and data regarding demographic profile, history of associated medical illnesses and medications used were collected. All patients were given 1.5L normal saline fluid challenge followed by repeat renal functions on next day. All patients had ultrasound abdomen for renal size and corticomedullary differentiation along with examination for any obstructive lesion in the urinary tract. Ascitic fluid and urine analysis was done for all patients.

Data was recorded in a specially designed proforma. All data was analyzed using statistical package SPSS 10.0. Descriptive statistics were used. Mean a

standard deviation was calculated for age. Frequencies and percentages for variables were calculated.

RESULTS

A total of 100 patients were enrolled into the study. Out of them 59 (59%) were male and 41 (41%) were female (Table I) with a male to female ratio of 1.43:1.

Age range was from 30 to 65 years with a mean age ± s.d of 54.96 ± 8.80 years. Most of the patients were in the age range of 50 to 60 years as shown in Table II.

Hepatitis "C" was the most common cause of cirrhosis among our study population being 48% (n=48) followed by hepatitis "B" 30% (n=30) as shown in Figure 1.

Among causes of renal impairment hepatorenal syndrome was found to be the most common cause in our study population having frequency of 49% (n=49) followed by hypovolemia 33% (n=33) among other causes shown in Table III.

DISCUSSION

Renal derangement in the setting of cirrhosis carries poor prognosis and thus routine monitoring of renal functions in such patients can promptly identify this problem. Patients with serum creatinine more than 1.5 are considered to have deranged renal functions[1]. Among many causes of renal derangement in such patients hepatorenal syndrome carries the worst prognosis[9, 13]. However other causes of renal derangement should be excluded first as many of them are reversible.

Hepatorenal syndrome is defined as the development of renal failure in patients with advanced liver failure (acute or chronic) in the absence of any identifiable causes of renal pathology. The first detailed description of HRS was made by Hecker and Sherlock in 1956[7]. Cirrhotic patients are more prone to develop renal impairment as they already have altered circulatory function in the form of decreased systemic vascular resistance. It is due to increased production and activity of various vasodilators such as nitric oxide, carbon mono oxide and endogenous cannabinoids. All these lead to splanchnic arterial vasodilatation [8-12]. The decreased systemic vascular resistance in such patients lead to activation of vasoconstrictor systems such as sympathetic nervous system, rennin- angiotensin system and arginine vasopressin. This leads to sodium and free water retention ultimately leading to ascites, edema and renal derangement due to intra renal vasoconstriction and hypoperfusion[8, 9]. Diagnostic criteria for HRS is shown in table IV. In current study 49 % patients had HRS after other causes of renal derangement were excluded. In a similar study from Raj Kumar and his colleagues HRS was also found to be the most common cause of renal derangement among patients with cirrhosis showing that 47.37 % of patient

Table 1: Gender wise distribution of patients.

Gender	Number of patients	Percentage
Male	59	59%
Female	41	41%
Total	100	100%

Table 2: Age wise distribution of patients

Age groups	Number of patients	Percentage
30 – 40	11	11 %
41 – 50	30	30 %
51 – 60	47	47 %
61 -65	12	12 %
TOTAL	100	100 %

Table 2: Age wise distribution of patients

Age groups	Number of patients	Percentage
30 – 40	11	11 %
41 – 50	30	30 %
51 – 60	47	47 %
61 -65	12	12 %
TOTAL	100	100 %

Table 3: causes of renal impairment

Cause of renal impairment	Number of patients	Percentage
Hepatorenal syndrome	49	49 %
Hypovolemia	33	33 %
Spontanious bacterial peritonitis	11	11 %
Nephrotoxic drugs	4	4 %
Primary renal disease	3	3%
	100	100 %

Cirrhosis with ascites
Serum Creatinine level ≥ 1.5 mg/dL (133 umol/L)
No or insufficient improvement in serum creatinine level (remains ≥ 1.5 mg/dL) 48 hr after diuretic withdrawal and adequate volume expansion with intravenous albumin
Absence of shock
No evidence of recent use of nephrotoxic agents
Absence of intrinsic renal disease

Table 4: Diagnostic criteria of Hepatorenal syndrome

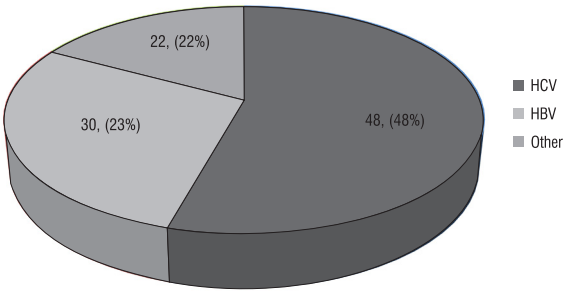

Figure 1: Causes of cirrhosis

having cirrhosis and renal derangement had HRS[13].

Among other causes of renal derangement in cirrhotic patients, infections play an important role, specifically spontaneous bacterial peritonitis[14-17]. Cirrhotic patients are particularly more prone to infections due to reduce activity of neutrophils and other immune cells leading to significant morbidity and mortality[18]. Among the sites of infection, ascitic fluid is most commonly infected causing spontaneous bacterial peritonitis which is the most common cause of renal derangement due to infections. In such cases infection is caused by translocation of gram negative bacteria most commonly[19, 20]. In these patients the already compromised circulatory function of these patients is further deteriorated by long lasting production of vasoactive mediators and increased level of proinflamatory cytokines elicited by sever inflammatory response in the peritoneal cavity[21, 22]. All these events lead to renal derangement in patients with SBP. Renal derangement can also be caused by other infections as well but the severity of inflammation and renal derangement is not that sever as in SBP[23, 24.] In our study 11 % of patients had renal derangement secondary to SBP.

Hypovolemia is another common cause of renal derangement in patients with cirrhosis as these patients already have poor effective circulatory blood volume and they may easily develop renal derangement in the setting of hypovolemia. Hypovolemia can occur due to gastrointestinal bleed, diarrhea, aggressive diuresis and large volume paracentesis[17, 25]. Patients with cirrhosis are at risk of upper gastrointestinal bleed from esophageal or gastric varices, portal hypertensive gastropathy and peptic ulcer. Hypovolemia and decreased renal perfusion develop rapidly in such patients which may lead to derangement of renal functions. Diarrhea and vomiting are other causes of hypovolemia in such patients. Usually the cause is gastrointestinal infections and over use of lactulose in such patients. Aggressive paracentesis is another reason due to which patients may develop renal derangement. It may lead to further reduction in effective circulatory blood volume and activation of vasoconstrictive mechanism thus leading to reduction of renal circulation and resulting in renal derangement[26]. In a study 10% of patients undergoing total paracentesis developed HRS[27]. Other than the above mentioned causes over use of diuretics can also lead to reduction in circulatory volume and thus reduction in renal perfusion which lead to impairment of renal functions. In our study 33% of patients developed renal impairment due to hypovolemia. It is among one of the reversible causes of renal derangement in such patients however it can act as a trigger for development of HRS in such patients as well.

Nephrotoxic drugs are another cause of renal derangement in patients with cirrhosis. Among them NSAID's are of particular importance. Renal perfusion in patients with advance cirrhosis is highly dependent on renal production of prostaglandins like prostaglandin E2 and prostacycline which have a vasoprotective effect on renal circulation. NSAID's inhibit the production of these prostaglandins and thus may lead to loss of this vasoprotective effect of prostaglandins on renal circulation. This may lead to renal derangement in such patients. NSAID's should be avoided in such patients as they can induce renal derangement in up to 33% of such patients[28]. Beside this NSAID's can also confer resistance to diuretics as well[29]. Even short term use of celecoxib in such patients can lead to significant reduction in GFR[30]. Other hypotensive drugs like angiotensin converting enzyme inhibitors (ACEI) and angiotensin II blockers may also cause renal derangement in patients with cirrhosis as hemostasis of arterial pressure is dependent on the activity of various vasoconstrictive mechanisms in such patients and inhibition of these mechanisms may lead to reduction of renal perfusion and thus renal derangement[31-33]. It has been shown that even low doses of ACE inhibitors, which may have no effect on arterial blood pressure, can lead to significantly reduced GFR[33]. Aminoglycosides is another class of drugs that can cause renal derangement in such patients. In our study 4% of patients had renal derangement secondary to nephrotoxic drug usage.

Intrinsic renal disease is another cause of renal derangement in patients with cirrhosis. It can be either due to the primary disease responsible for cirrhosis like hepatitis C or due to other systemic or metabolic causes like sepsis and diabetes. In patients with cirrhosis intrinsic renal disease should be suspected when they have protienuria and hematuria on urine analysis. Among intrinsic renal diseases associated with chronic hepatitis C membranoproliferative glomerulonephritis, membranous nephropathy, focal glomerulosclerosis and IgA nephropathy are common[34-38]. Acute tubular necrosis (ATN) is another intrinsic renal pathology responsible for renal derangement in such patients and should be suspected when renal derangement is preceded by sepsis, hemorrhagic shock, dehydration or use of nephrotoxic drugs[39]. It can be at times difficult to differentiate from HRS but clues to its diagnosis include presence of granular or epithelial cast in urine, urinary sodium concentration >20 mEq\L and fractional excretion of sodium >1. Patients having cirrhosis and other

systemic diseases may also develop renal derangement due to these systemic diseases like diabetes. These patients may have protienuria on urine analysis and on ultra sound examination there kidneys may show increased corticomedullary echogenicity with reduced size of the kidneys. In our study 3% patients having renal derangement were found to have intrinsic renal disease.

CONCLUSION

Renal impairment in patients with cirrhosis is a relatively common and serious complication. Hepatorenal syndrome is not the only cause to be considered in such patients and it should be the diagnosis of exclusion in these patients as more than half of the patients with cirrhosis and renal derangement has causes other than HRS for their renal derangement. Among other causes which needs to be excluded include hypovolemia, intrinsic renal disease, active infection or sepsis and diuretics and nephrotoxic drug usage. Detailed understanding of different pathophysiological events involved in producing renal derangement in these patients is important for their proper management and prompt diagnosis.

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