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INCIDENCE PREDICTIVE FACTORS, AND PROGNOSIS OF THE HEPATORENAL SYNDROME IN CIRRHOSIS WITH ASCITES

Abdul Qadir[1], Adam Khan[2], Basit Ali[3], Mohammad Umar[4], Muhammad Talha[5], Aamer Ahmad[6], Faizan Banaras[7*]

[1]Senior Registrar, Nephrology Division Khyber Teaching Hospital, Peshawar
[2]Postgraduate Resident, Nephrology Division Khyber Teaching Hospital, Peshawar
[3]House Officer, Nephrology Division Khyber Teaching Hospital, Peshawar
[4]House Officer, Nephrology Division Khyber Teaching Hospital, Peshawar
[5]House Officer, Nephrology Division Khyber Teaching Hospital, Peshawar
[6]House Officer, Hayatabad Medical Complex, Peshawar
[7*]Postgraduate Resident, Nephrology Division Khyber Teaching Hospital, Peshawar
Email address: faizanbanaras958@gmail.com

***Corresponding Author:** Faizan Banaras
*Postgraduate Resident, Nephrology Division Khyber Teaching Hospital, Peshawar
Email address: faizanbanaras958@gmail.com

Abstract

Background and Aim: Renal failure, especially in its acute phase, is common in patients with liver cirrhosis and ascites. The incidence of hepatorenal syndrome varies from 18% to 39% in a span of 1 to 5 years. The present study aimed to determine the prevalence, predictive factors, and prognosis of hepatorenal syndrome (HRS) in cirrhosis with ascites.

Patients and Methods: This prospective study was carried out on 68 cirrhotic patients admitted for the treatment of ascites in the Departments of Nephrology and Gastroenterology, Khyber Teaching Hospital, Peshawar from January 2022 to December 2022. The median GFR, median values of serum sodium, and urine sodium concentrations were measured for each individual. All the patients underwent physical examination and detailed history. The abdominal tapped fluid was used to measure the concentration of protein ascetic fluid. Descriptive statistics were done in SPSS version 27.

Results: Of the total patients, there were 46 male and 22 females. The overall mean age was 48.64±4.8 years. Out of 68 patients, the incidence of cryptogenic cirrhosis and hepatitis B surface antigen (HBsAg)-positive cirrhosis was 76.5% (n=52) and 23.5% (n=16) respectively. Based on physical examination, the incidence of hepatomegaly, splenomegaly, and hepatic stigmata was 57.4% (n=39), 38.2% (n=26), and 79.4% (n=54) respectively. About 58.8% (n=40) patients had previous episodes of ascites. Gastrointestinal hemorrhage and hepatic encephalopathy was found in 26.5% (n=18) and 19.1% (n=13) respectively. Serum bilirubin levels increased in majority of patients 76.5% whereas serum albumin concentration decreased in 85.3% cases.

Conclusion: The present study found that HRS is a comparatively common complication in cirrhosis patients with ascites that is significantly associated with higher mortality rate and short survival rate.

Hepatorenal syndrome could be easily predicted by plasma renin activity, liver size, and concentration of serum sodium.

Keywords: Hepatorenal syndrome, Cirrhosis, Ascites, Predictive factors

INTRODUCTION

Advanced liver failure and cirrhosis patients are susceptible to hepatorenal syndrome (HRS) characterized by splanchnic vasodilatation leading to severe renal failure in cirrhotic patients causing the renal vasoconstriction by decreasing effective circulating volume and glomerular filtration reduction [1, 2]. The incidence of hepatorenal syndrome varies from 7% to 45% [3, 4]. Based on severity and progression, HRS is classified into two main types: HRS type 1 and HRS type 2 in which HRS type 1 is more severe and progresses rapidly [5]. HRS type 1 is considered as the most fatal complication in cirrhotic patients. A significantly higher mortality rate of 80% in HRS type 1 is reported in 2-weeks without treatment and 10% survival rate in 3 months [6, 7]. The incidence of HRS in hepatic cirrhosis with ascites patients varies from 18% to 39% after one to five years [8]. Therapeutic paracentesis, bacterial infections, and gastrointestinal hemorrhage are various precipitating factors for HRS.

HRS is characterized by the reduction in glomerular filtration rate (GFR) and renal blood flow associated with marked renal vasoconstriction, absence of renal tissue histological changes, and tabular renal function preserved. It is usually caused by chronic liver disease related to the low artery pressure due to circulatory dysfunction [9]. Knowing the pathophysiology of HRS allows the introduction of treatment modality and pharmacological interventions till the liver transplant [10]. With the introduction of these therapy, the short term survival rate has been increased [11]. HRS frequently follows an advanced sequence that appears in close chronological association with bacterial infections and gastrointestinal hemorrhage like complications with poor prognosis. However, very limited or no previous research has been carried out on the prevalence of HRS in cirrhotic patients with ascites. The prediction of developing HRS in cirrhotic patients with ascites based on analytical or clinical data is still to be determined. Therefore, the current study aimed to determine the incidence, predictive factors, and prognosis of hepatorenal syndrome in cirrhotic patients with ascites.

METHODOLOGY

This prospective study was carried out on 68 cirrhotic patients admitted for the treatment of ascites in the Departments of Nephrology and Gastroenterology, Khyber Teaching Hospital, Peshawar from January 2022 to December 2022. Patients with ascites and having clinical data and histological findings for cirrhosis diagnosis, absence of gastrointestinal hemorrhage, bacterial infection, and hepatic encephalopathy were enrolled. The median GFR, median values of serum sodium, and urine sodium concentrations were measured for each individual. All the patients underwent physical examination and detailed history. The abdominal tapped fluid was used to measure the concentration of protein ascetic fluid. The abdominal tapped fluid was used to measure the concentration of protein ascitic fluid. All the cases underwent 24-hour urinary excretion of electrolytes, osmolality, liver function tests, and arterial pressure were measured. Nutritional status of all the cases were categorized into poor, good, and excellent. Insulin clearance was used to measure the GFR and creatinine clearance. Endoscopy was used for investigating the presence of esophageal varices. After 2 hour bed rest, mean arterial pressure, PRA (plasma renin activity), and norepinephrine concentration were measured. Diuretics (spironolactone plus furosemide) or plasma volume expansion and paracentesis were given as a treatment modality. After discharge, diuretics were given to each individual to avoid ascites reaccumulation based on individual responses. SPSS version 27 was used for data analysis. Quantitative variables were expressed as mean and standard deviation whereas qualitative variables were expressed as frequency and percentages.

RESULTS

Of the total patients, there were 46 male and 22 females. The overall mean age was 48.64±4.8 years. Out of 68 patients, the incidence of cryptogenic cirrhosis and hepatitis B surface antigen (HBsAg)-positive cirrhosis was 76.5% (n=52) and 23.5% (n=16) respectively. Based on physical examination, the incidence of hepatomegaly, splenomegaly, and hepatic stigmata was 57.4% (n=39), 38.2% (n=26), and 79.4% (n=54) respectively. About 58.8% (n=40) patients had previous episodes of ascites. Gastrointestinal hemorrhage and hepatic encephalopathy was found in 26.5% (n=18) and 19.1% (n=13) patients respectively. Serum bilirubin levels increased in the majority of patients 76.5% whereas serum albumin concentration decreased in 85.3% cases. Based on Child Pugh classes, the incidence of Child Pugh Class A, B, and C was 4.4% (n=3), 64.7% (n=44), and 30.9% (n=21) respectively. The prevalence of HRS was 50% (n=43) chronologically developed due to precipitating factors: gastrointestinal bleeding 16.3% (n=7), IV albumin 9.3% (n=4), paracentesis 9.3% (n=4), and severe bacterial infection 65.1% (n=28). Of the total 28 cases of severe bacterial infection, the incidence of septicemia, pneumonia, and spontaneous bacterial peritonitis was 14 cases, 2 cases, and 12 cases respectively. Demographic details and baseline features are represented in Table-I. The overall mean value of various predicting factors such as GFR, serum sodium, urine sodium, free water clearance, and mean arterial pressure during admission are shown in Table-II. Various factors such as GFR, serum sodium, urine sodium, free water clearance, and mean arterial pressure during HRS diagnosis are shown in Table-III. Different factors that chronologically develop HRS in cirrhotic patients with ascites are shown in Table-IV.

Table-I Demographic details and baseline characteristics

Parameters	**Values**
Age (years)	48.64±4.8
Gender N (%)	
Male	46 (67.6)
Female	22 (22.4)
Physical examination N (%)	
Hepatomegaly	39 (57.4)
Splenomegaly	26 (38.2)
Hepatic stigmata	54 (79.4)
Previous episodes of ascites	40 (58.8)
Gastrointestinal hemorrhage	18 (26.5)
Hepatic encephalopathy	13 (19.1)
Child Pugh Classes N (%)	
A	3 (4.4)
B	44 (64.7)
C	21 (30.9)

Table-II various factors such as GFR, serum sodium, urine sodium, free water clearance, and mean arterial pressure during admission

Factors	**Mean value (±SD)**	**P-value**
GFR (mL/min)	72±14.8	0.0001
Serum sodium (mEq/L)	134±4.9	0.0001
Urine sodium (mEq/day)	13.6±10.98	0.05
Free water clearance (mL/min)	6.1±4.8	0.007
Mean arterial pressure (mm Hg)	86±8.9	0.006
PRA (ng/mL-h)	10.2±8.8	0.01

Table-III various factors such as GFR, serum sodium, urine sodium, free water clearance, and mean arterial pressure during HRS diagnosis

Factors	Mean value (±SD)	P-value
GFR (mL/min)	29±9.8	0.0001
Serum sodium (mEq/L)	122±1.9	0.0001
Urine sodium (mEq/day)	0.2±0.1	0.05
Free water clearance (mL/min)	-0.3±0.6	0.007
Mean arterial pressure (mm Hg)	73±9.6	0.006
PRA (ng/mL-h)	41.3±22.6	0.01

Table-IV Different factors that chronologically develop HRS in cirrhotic patients with ascites

Parameters/Factors	N (%)
Gastrointestinal bleeding	7 (16.3)
IV albumin	4 (9.3)
Paracentesis	4 (9.3)
Severe bacterial infection	28 (65.1)
Septicemia	14
Pneumonia	2
spontaneous bacterial peritonitis	12

DISCUSSION

The present study mainly focused on the prognosis of HRS in cirrhotic patients with ascites and found that hepatorenal syndrome is a somewhat common complication in individuals with cirrhosis who have ascites, and it is related with a greater death rate and a shorter survival rate. Plasma renin activity, serum sodium content, and liver size might all be used to predict hepatorenal syndrome. Furthermore, HRS is a severe complication associated with cirrhosis and ascites. Renal failure might be caused by HRS due to bacterial infections and gastrointestinal bleeding complications. HRS significantly arises spontaneously indicated by the half cases with no HRS. Renal function recovery is exceedingly rare in HRS patients. The endogenous vasoconstriction system involvement in HRS development has been investigated both analytically and clinically as reported in numerous investigations [12-14].

Despite the recent literature emphasizing that arterial splanchnic vasodilatation is the major cause of increased nitric oxide releases due to hypertension and hepatic failure [15, 16]. HRS is the ultimate outcome of continuous renal perfusion loss in the context of advanced liver disease; it is linked with a bad prognosis [17]. Several studies have been conducted to establish the prevalence of HRS, with considerable variations found based on the HRS definition employed and the inclusion and exclusion criteria used [18, 19].

Numerous clinical and laboratory indicators can predict the incidence of HRS in cirrhosis patients with ascites. Three exploratory findings were related with a significant risk of HRS: the lack of hepatomegaly, esophageal varices presence during endoscopy, and poor nutritional status. The liver size's prognostic effect is not unexpected given that this metric has previously been proven to predict cirrhosis and ascites patient's survival [20, 21].

Patients with slightly lower GFRs exhibited a considerably greater risk of HRS incidence indicating that the baseline GFR had predictive significance. Lastly, arterial BP, plasma norepinephrine levels, and PRA were all predictive with HRS development. This phenomenon was substantially more common in individuals with high plasma renin, norepinephrine levels, and arterial hypotension [22-24].

A significant finding was that Aetiology associated with cirrhosis and liver tests had little predictive value for HRS. Similarly, another criteria for HRS development is the Child-Pugh score criteria which generally measure the liver failure's degree and cirrhotic patient's prognosis [25].

HRS is now thought to be a severe manifestation of arterial vascular under filling caused by peripheral arteriolar vasodilation [26, 27]. This assertion is supported by our findings. Patients are more susceptible to HRS development where individual had higher PRA, lower arterial BP, and higher plasma norepinephrine levels. In contrast, the HRS onset was constantly related with a considerable rise in PRA and decrease in mean arterial pressure in individuals evaluated before and during HRS [28].

In-hospital mortality following liver transplantation is considerably greater in cirrhotic patients. These findings and observations suggest that individuals with cirrhosis and ascites should get transplants before HRS develops. In this context, the discovery that the incidence of HRS may be predicted by a number of easily accessible clinical and analytical indicators [29, 30].

CONCLUSION

The present study found that hepatorenal syndrome is a comparatively common complication in cirrhosis patients with ascites that is significantly associated with higher mortality rate and short survival rate. Hepatorenal syndrome could be easily predicted by plasma renin activity, liver size, and concentration of serum sodium.

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