DOI: https://doi.org/10.54393/pjhs.v4i12.1035

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 12 (December 2023)

Original Article

The Prevalence and Outcomes of Hepatorenal Syndrome in Chronic Liver Disease Patients in a Tertiary Care Hospital

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ARTICLE INFO

Key Words:
Acupuncture, UB-40, Pain, Disability, Lumbago

How to Cite:
Ali, R., Goswami, M., Talpur, M. T. H., Naeem, M., Kumar, S., Malik, F., Ghimire, S., Aslam, N., & Hasan, M. . (2023). The Prevalence and Outcomes of Hepatorenal Syndrome in Chronic Liver Disease Patients in a Tertiary Care Hospital : Hepatorenal Syndrome in Chronic Liver Disease. *Pakistan Journal of Health Sciences*, 4(12), 122–126. https://doi.org/10.54393/pjhs.v4i12.1035

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Received Date: 13th September, 2023
Acceptance Date: 27th December, 2023
Published Date: 31st December, 2023

ABSTRACT

Hepatorenal syndrome (HRS) leads to a severe kidney injury leading to its eventual failure in the background of chronic liver disease. **Objective:** This research's objective was to define the frequency of hepatorenal syndrome (HRS) in the background of cirrhosis and to find out the outcomes of the patients with HRS. **Methods:** This is a detailed prospective clinical series research. It was conducted in the Department of Medicine, Jinnah Postgraduate Medical Center (JPMC), Pakistan, from February 2020 to December 2020 after approval by the authorized review board. Jinnah Postgraduate Medical Center (JPMC). A sample size of 101 was calculated. The lab values including prothrombin time (PT), serum albumin, and chronic liver disease variations were established for confirmative diagnosis. Frequency tables were created for parameters to be determined (sex and Child-Pugh classification). The means and their SD of parameters of interest (age and weight) were calculated. **Results:** The demographic variables were the mean age of the patients was 62.5±10.2 and the mean bilirubin was 2.32 ± 2.3mg/dL. 68 (67.3%) of the patients had normal creatinine and 33 (32.7%) of the patients had raised serum creatinine. 2(10.5%) of the patients had a numerical score of 5-6, 13 (68.4%) of the patients had a total score of 7-9 and 4(21.1%) of the patients had 10-15 scores. Hepatorenal syndrome was detected in 11.9% of patients with cirrhosis, among whom 4 (33.3%) died. **Conclusions:** The hepatorenal syndrome is quite common in liver diseases and it needs to be assessed.

INTRODUCTION

Liver cirrhosis refers to late-stage diseases due to long-standing, continuous, and repeated damage to the liver parenchyma and its cellular structure that inevitably results in liver malfunction and default. It is a permanent disease state characterized by developing new nodules, loss of standard architecture, replacement of healthy cells, and gradual and extensive bridging fibrosis. It has the highest mortality rate globally. In Pakistan, a high disease burden exists owing largely due to Hepatotoxic hepatitis caused by Hepatitis A and [1, 2]. Transmission of both these organisms can be averted if improved food hygiene, sanitation, and community awareness can be carried out.

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The sequel of cirrhosis includes fatal outcomes such as variceal bleeding (top cause of death), kidney and liver failure, portal hypertension, and cerebrovascular involvement -encephalopathy [3]. The HRS is a prospective reason behind severe kidney injury leading to its eventual failure in the background of chronic liver disease [4]. Pathogenesis is unclear, but renal vascular and nervous outflow changes are the main cause. Portal hypertension leads to subsequent dilatation of the splanchnic vessels and insufficient perfusion leading to the release of Nitric oxide which is a vasodilator [5]. This response activates the renin-angiotensin system causing renal vasoconstriction (a hallmark of HRS) and reduced filtration function of kidneys. Three major and primary detected risk factors include reduced average arterial pressure (<80 mmHg), water intoxication, and withholding of excessive sodium in the urine (urine sodium <5 mEq/L). Patients with chronic liver abnormalities or diminishing liver function markers like serum albumin, prothrombin time, and bilirubin do not indicate greater susceptibility for HRS development. H.R. syndrome is frequent, with an occurrence rate of 10% in patients under observation at the hospital due to ascites and cirrhosis. The International Ascites Club has formulated a standard to confirm HRS diagnosis, of which four criteria must be present. Minor criteria have been included to point towards supplementary proof of the disease. Major standards are increased GFR which was noted by the raised serum creatinine concentration (>1.5 mg/dL or 24-hour creatinine clearance (CC) <40 mL/min), Presence of current contamination, loss of fluid volume, no evidence of shock, and ongoing therapy by nephrotoxic drugs, lack of evidence indicating improving function of the kidney (decline in creatinine concentration to 1.5 mg/dL or less or rise in creatinine clearance to 40 mL/min or more) after stoppage of diuretics and use of plasma expanders (1.5 L), and Proteinuria lesser than 500mg per day without supportive radiographic proof of obstructive renal disorders or uropathies [6]. The treatment of HRS is focused on management as symptomatic support (B.P. monitoring and anti-biotic cover) with hemofiltration if any possibility of improvement in hepatic function exists or with liver transplant [7]. Current experimental research on treatment is being done, but conclusive results have yet to be found. Trials regarding combined therapy with albumin/octreotide plus midodrine have shown promising renal function; however, this is only applicable in providing palliative care [8]. The ultimate cure is liver transplantation [7]. HRS syndrome presents in two forms [9]. Type 1 variant is the acute one in which those with significant liver disease experience involuntary kidney failure that progresses quickly. It is distinguished by a substantial reduction in the function of kidneys, as indicated by a decrease in initial 24-hour creatinine clearance to half its original value (20ml in two weeks). Clinical outcomes are unsatisfactory, with only a 10% survival rate. After the liver function has improved, renal function may return independently. The most common instances of this include fulminant or alcoholic hepatitis and sepsis. A clinical picture of DIC and tangible signs of jaundice are seen, with death resulting from co-existing liver and kidney collapse or internal bleeding. In Ascites, the type 2 HRS is seen in patients unresponsive to the administration of diuretics. Kidney failure has a slower path which might worsen over a few months. The mean survival time is six months that is longer than type I. Hence, research aimed to determine the occurrence of HRS in the background of cirrhosis and to analyze its prognosis.

METHODS

This is a detailed prospective clinical series research. It was conducted in the Medicine Department, Jinnah Postgraduate Medical Center (JPMC), Pakistan, from February 2020 to December 2020 after approval by the authorized review board. Jinnah. Non-probability sampling method was utilized to collect the data. After estimating it from the Roasoft sample size calculator with a margin of error of 5%, a confidence level of 95% and an expected incidence of 136 with a sample size of 101 was calculated [9]. Depending upon the clinical picture, serum laboratory study, and ultrasound imaging, patients over 14 years of age were evaluated. Following consultations with the OPD or a visit to an ER, patients were immediately referred. Patients of hepatic encephalopathy under medication with kidney-damaging drugs, severe infection, sepsis, hypovolemic state, and acute, and sub-acute liver failure are omitted. Patients were directly referred after a consult from the OPD or an emergency department visit. Patients of hepatic encephalopathy under medication with kidney-damaging drugs, severe infection, hypovolemic state, sepsis, and acute and sub-acute liver failure are omitted. Overall, 101 patients participated. The values of serum albumin, prothrombin time, and chronic hepatic disease (CHD) variations were established for confirmative diagnosis. Renal failure was set as a pre-requisite for inclusion in the study. Clinical examination and serum investigations (creatinine over 1.5 mg/dL) were measured. The confounding factor was determined by eliminating infections within the abdominal cavity. Spontaneous bacterial peritonitis (SBP) was set as one of the confounding variables. The patient's biodata was entered in the questionnaire and lab analysis (blood test and ultrasound) to verify cirrhosis, diagnosis, management, and hospital admission data. The clinical conclusions were classified as complete disease resolution, partial

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resolution, no outcome, fatality, and patient referral noted in the questionnaire. Hence, HRS was interpreted as the occurrence of kidney failure in the setting of Cirrhosis - fibrosis of the liver. It is supported by biochemical evidence of a major decrease in the functioning of the kidneys (> serum creatinine to a level greater than 1.5 mg/dL). Adding on, proteinuria (<500 mg/24 hours) was among the vital criteria to establish HRS. The effectiveness of treatment was evaluated using the following outcomes: 1) No effect: raised concentrations of serum creatinine 2) Partially recovered: decreased concentrations of serum creatinine but not < 1.5 mg/dl 3) Completely recovered: reductions in the concentration of serum creatinine concentrations < 1.5mg/dL 4) Mortality: patients died. The data were gathered using a questionnaire which was later imported into SPSS Version 20.0 IBM Corp and analyzed. The tables of frequency were created for parameters to be determined (gender and Child-Pugh classification). The means and SD of parameters of interest (age and weight) were also evaluated. Consent was obtained from all the patients along with notifying the Ethical Board Committee before initiating the research.

RESULTS

Table 1 demonstrates demographics where the mean age of the patients was 62.5 ± 10.2 and 74 (73.3%) of the participants were male. The bilirubin (mean) was 2.32 ± 2.3mg/dL.

Table 1: The demographic variables of the patients.

Variables	Categories	Mean ± Standard Deviation
Age (years)	-	62.5 ± 10.2
Gender	Male	74 ± 73.3%)
	Female	27 ± 26.7%)
Bilirubin (mg/dL)	-	2.32 ± 2.3
Albumin (g/dL)	-	4.1 ± 0.9
Prothrombin time (s)	-	18 ± 1.31
Creatinine (mg/dL)	-	1.9 ± 0.4
24-hour Urinary Proteins (mg/day)	-	122.1 ± 38.3

Table 2 shows that 68 (67.3%) of the patients had normal creatinine and 33 (32.7%) of the patients had raised serum creatinine.

Table 2: The values of serum creatinine among the cohort of patients.

Variables	Categories	Frequency (%)
Creatinine	0.6-1.4 mg/dL	68 (67.3%)
	>1.4 mg/dL	33 (32.7%)

Table 3 shows that of the patients HRS.A: 2 (10.5%) of the patients had a numerical score of 5-6, B: 13 (68.4%) of the patients had a total score of 7-9 and C: 4 (21.1%) of the patients had 10-15 scores.

Table 3: The Child-Pugh classification of patients comparison of the patient.

Child-Pugh Classification	Patient's diagnosis	
	Cirrhosis (n=82)	Hepatorenal syndrome (n=19)
A: Score of 5-6	3 (3.7%)	2 (10.5%)
B: Score of 7-9	51 (62.2%)	13 (68.4%)
C: Score of 10-15	28 (34.1%)	4 (21.1%)

Table 4 shows that the frequency of HRS in the cirrhotic patients was 12 (11.9%) while 89 (88.1%) of the patients with cirrhosis did not have HRS.

Table 4: The periodicity of HRS in patients.

HRS	Frequency (%)
Cirrhosis (not having HRS)	89 (88.1%)
Cirrhosis (having HRS)	12 (11.9%)

Table 5 shows that only 3(25%) of the patients fully recovered. In HRS patients, the mortality rate was 33.3%. Only 5 (41.7%) of the patients were partially recovered.

Table 5: Outcomes of the HRS patients.

Outcomes	Frequency (%)
No effect	0 (0%)
Completely recovered	3 (25%)
Patially (incompletely) recovered	5 (41.7%)
Death	4 (33.3%)

DISCUSSION

Globally, cirrhosis is becoming a bigger issue. Mortality rates from cirrhosis are rising globally. Acute renal damage is one of the most significant prognostic markers for cirrhosis [10]. About 20% of hospitalized cirrhotic patients with renal failure exhibited HRS. Many well-known causes can lead to HRS. By staying away from particular settings and receiving the proper care, the risk of having HRS can be decreased. Patients with HRS type 2 should be assessed for TIPS or liver transplantation as it is linked to end-stage liver disease [11]. Cirrhosis of the liver patients are more susceptible to problems that reduce life expectancy [12]. Kidney injury is one of the most common side effects, especially when portal hypertension is present [13]. In the context of severe liver illness, HRS is the final stage of a chronic loss of renal perfusion and is associated with a bad prognosis [14]. We conducted the current experiment to determine the prevalence and short-term outcomes of hepatorenal syndrome in people with chronic liver disease. There were 101 patients with hepatic cirrhosis in this study. Men made up 73.3% of the patients, while women made up 26.7%. The patients were, on average, 62.5±10.2 years old. The majority of the patients in these outcomes were between the ages of 40 and 60, and in several other studies, there were more male patients than female patients (between 45% and 60%) [15]. Due to the high rates of

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smoking and alcohol usage among men, men make up the majority of persons in Pakistan who have liver cirrhosis. In terms of the demographic factors, the findings of our study are consistent with the other studies as well [15, 16]. Hepatitis B and C were shown to be the root causes of chronic liver disease in the current study in 40 (38.10%), 54 (51.43%), and 9 (8.57%) of the patients, respectively. According to our findings, the illness persisted for 5.46 years and 3.82 months. According to Fida S *et al.*, analysis of the prevalence of HRS in cirrhotic patients, 24.26% of patients had hepatitis B, 30.88% had hepatitis C, 8.09% had hepatitis B and C equally and the remainder of the patients had cirrhosis due to a variety of etiological factors [9]. In a study by Ullah I *et al.*, the HRS frequency among cirrhotic patients was around 19.9%. It was a bit higher than the findings of our study showing 11.9% of such patients [17]. In the current study, there were 12 (11.9%) HRS patients; of these, 4 (33.3%) passed away, 5 (41.7%) made partial recoveries, and 3 (25%) made full recoveries. The findings of our study were consistent with the results of Khan S *et al.*, where 26.7% of patients with HRS died [18]. SHR1 was found in 35% of the 28 patients with HRS who needed hemodialysis for renal replacement treatment in the study by Rey R M *et al.*, accounting for 70% of the total [19]. Ninety percent of dialysis patients passed away within ninety days. Liver transplantation was the only treatment available for the remaining ten percent of patients. In a study by Wang H *et al.*, 58 (37.2%) of 196 patients demonstrated better renal function following terlipressin and albumin therapy. According to another research, 4 (28%) patients made a full recovery [20]. It was consistent with our findings where 25% of patients made the full recovery. The frequency of HRS was 11.9% in our study that is consistent with another study reported by Seetlani NK et al., where the frequency of HRS in Karachi having cirrhosis was 15% [16]. The major limitation of our study was a single institution. If multiple institutes were involved, a larger sample size could have been obtained and multiple variables could have been assessed.

CONCLUSIONS

Our study concludes that hepatorenal syndrome is quite common in chronic liver disease. It needs to be assessed immediately in such patients to avoid complications.

Authors Contribution

Conceptualization: MH, RA
Methodology: RA, MG, MN
Formal analysis: FM, SG
Writing-review and editing: MTHT, SK, NA, MH

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

All authors have read and agreed to the published version of the manuscript.

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