

Spectrum of Renal Disorders in Patients with Liver Cirrhosis: How Grievous Is It ?

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ABSTRACT

Introduction: Globally the burden of cirrhosis is enormous. Few of the events which determine the prognosis of cirrhosis in the patient includes renal dysfunction, hepatic encephalopathy, appearance of ascitis and / infections etc. The purpose of this study was to study the spectrum of renal dysfunction among CLD patients.

Material and methods: This hospital-based study was carried on 102 cirrhotic patients, admitted from April 2019 to November 2019. Details of the patient including history, clinical examination findings and results of laboratory investigations were collected.

Results: A total of 102 patients were included in this study. Male patients were in majority 85.3% (n=87). The most common etiology was Alcohol, aggregating to 74.5%. Renal failure was observed in 45.1% of the total population. PreRenal Azotemia (PRA), HepatoRenal Syndrome (HRS), Acute Tubular Necrosis (ATN) & Chronic Kidney Disease / Acute on chronic kidney disease accounted for 47.8%, 28.2%, 17.4% & 6.6% of all the cases of renal failure respectively. The Odds of renal failure was more in cirrhotic patients with infection and / SBP (p value <.05). A moderately positive correlation (Pearson correlation r = 0.199) was seen between CTP Score and renal failure (p value <.05 level).

Conclusion: Renal dysfunction is a frequent complication among cirrhotic patients. The Authors suggest that cirrhotic patients who are decompensated and have any evidence of SBP / infection should have a more frequent monitoring of their renal parameters so that AKI can be diagnosed early or prevented.

Keywords: Cirrhosis, Hepatorenal syndrome (HRS), PreRenalAzotemia (PRA), Renal failure

INTRODUCTION

Globally the burden of cirrhosis is enormous. A person with cirrhosis has a load of morbidity and mortality related to liver disease. These counts up to the gigantic amount of economic burden on the country and devour medical resources. India is not trailing when it comes to figure of cirrhotic patients in India.

As an estimate, the number of prevalent cases of decompensated cirrhosis worldwide is 10.6 million (2017), of which 6.42 million prevalent cases were in males and 4.23 million were in females.¹ Cirrhosis currently causes 1.16 million deaths worldwide, making it the 11th common causes of death, each year.² India accounts for one-fifth (18.3%) of all cirrhosis deaths globally.³

As the cirrhosis advances, liver decompensate, more and more sign and symptoms crop up in the patients. Few of the

events which determine the prognosis of liver disease in the patient includes renal dysfunction, hepatic encephalopathy, appearance of ascitis and / infections etc.

Patients with cirrhosis are susceptible for renal dysfunction. Hepatorenal syndrome (HRS) is a specific form of acute kidney injury which is unique among cirrhotic patients.⁴ The Circulatory dysfunction among cirrhotic patients plays a key role in pathogenesis of HRS. It is not just HRS due to which cirrhotic patients are prone for renal dysfunction, but there are multiple other reasons. These other risk factors include volume depletion secondary to diuretic use, Gastrointestinal (GI) losses secondary to lactulose therapy, GI bleed, large volume paracentesis leading to circulatory disturbances etc. Chronic hepatitis B and C can also directly cause glomerular diseases.⁴

It is not just the multifarious risk factors that make the cirrhotic patient exposed to renal dysfunction, but even the instant identification and management of renal dysfunction is difficult at times. Hemodynamic disturbances in cirrhotic patients is a key cause of renal dysfunction in the majority of the patients.⁵ Decent assessment of intravascular volume status remains the cardinal step in management, however in cirrhotic patients proper volume status assessment is an arduous task. This is so because cirrhotic patients have hyperdynamic circulation with the total body hypervolemic state and low effective circulatory volume status. Unluckily, there is no sole valuable monitoring tool to assess the volume status in these patients.⁵

Depending on the cause of renal dysfunction the treatment also varies from medical therapy to Simultaneous liver and kidney transplant. Early recognition of renal dysfunction is of utmost importance and concurrently precipitating factors for renal dysfunction needs to be determined. International Club of Ascitis-AKI (ICA-AKI) criteria was introduced in 2015.⁶ This criteria is useful for classification of the type of Acute Kidney Injury (AKI) as well as for prognosis of

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patients with cirrhosis (Pre Renal Azotemia [PRA], HRS and Acute Tubular Necrosis[ATN]).

The purpose of this study was to study the spectrum of renal dysfunction among CLD patients.

MATERIAL AND METHODS

This hospital-based study was carried on 102 cirrhotic patients admitted in the Department of Gastroenterology of a Tertiary care center, from April 2019 to November 2019. All cirrhotic patients admitted during the study period and with age more than 18 years were included in this study. Patients with previously known renal disease, any organ transplant, any malignancy were excluded from the study. Details of the patient including history, clinical examination findings and results of laboratory investigations were collected. CTP (Child Pugh) score and MELD (Model for End Stage Liver disease) Score of patients were also noted. Diagnosis and classification of AKI was considered as per ICA-AKI criteria 2015. Patients with any evidence of Chronic Kidney Disease (CKD) were not included in AKI. The study protocol conformed to the ethical guidelines and was approved by the institutional review board.

Results for continuous variables were expressed as means and standard deviation. Variables with non normal distribution were described by a median. Categorical variables were expressed as percentages. Significant factors associated with the presence of renal dysfunction were analyzed using

binary logistic regression analysis Bivariate analysis was carried out using pearsons coefficient of correlation. Odds Ratio (OR) was used to ascertain the strength of relationship between two variables. A p value of less than 0.05 was considered statistically significant. SPSS21 software was used for statistical analysis.

RESULTS

A total of 102 patients were included in this study. Male patients were in majority constituting 85.3% (n=87) of the total population, the rest were females (14.7%). Mean age of patients in the study group was 50.49 years (\pm 13.70). The most common etiology of cirrhosis was found to be Alcohol, aggregating to 74.5%. 19 patients had more than 1 etiology for cirrhosis, the most common of which was combined Alcohol and NASH (Non Alcoholic SteatoHepatitis) related, seen in 7 patients. Etiology of cirrhosis is depicted in Table I. Only 2.9% of the population belong to CTP class A. Median value of MELD was 21. Other parameters of patients are depicted in table II.

Renal failure was observed in 45.1% of the total population. Among various causes of renal failure, Prerenal azotemia accounting for 47.8% of all the cases of renal failure. Hepatorenal syndrome was seen in 28.2%, ATN in 17.4%, while chronic kidney disease/Acute on chronic kidney

Etiological factor for cirrhosis**	N (%)
Alcohol (%)	76 (74.5%)
HBV related (%)	15 (14.7%)
HCV related (%)	12 (11.8%)
NASH related (%)	15 (14.7%)
Others (%)	4 (3.9%)
** 19 Patients had more than one etiology (alcohol and nash was the commonest seen in 7 patients)	

Table-1: Etiological factors for cirrhosis

Parameters	n(%)
SBP	12 (11.7%)
Infection	33 (32.35%)
Renal dysfunction	46 (45.1%)
Hepatic encephalopathy	36(35.3%)
ASCITIS	86 (84.3%)
CTP score	
CTP class A	3 (2.9%)
CTP class B	37 (36.3%)
CTP class C	62 (60.8%)

Table-2: Various Parameters in the cirrhotic patients (N- 102)

		Renal failure	Normal renal function	Odds ratio (OR) (95%C.I.)	p value
Gender	Male	42	45	2.56(0.75-8.68)	0.12
	Female	4	11		
Alcohol	Alcoholic	35	41	1.16(0.47-2.86)	0.74
	Nonalcoholic	11	15		
HBV	Positive	4	11	0.39(0.11-1.31)	0.12
	Negative	42	45		
HCV	Positive	5	7	0.85(0.25-2.89)	0.79
	Negative	41	49		
NASH	Positive	9	6	2.02(0.66-6.19)	0.21
	Negative	37	50		
ASCITIS	Present	40	46	1.44(0.48-4.34)	0.50
	Absent	6	10		
SBP	Present	9	3	4.29(1.08-16.95)	0.03
	Absent	37	53		
HE	Present	20	16	1.92(0.84-4.37)	0.11
	Absent	26	40		
Infections	Present	20	13	2.54(1.08-5.96)	0.03
	Absent	26	43		

Table-3: OR for renal dysfunction and various factors

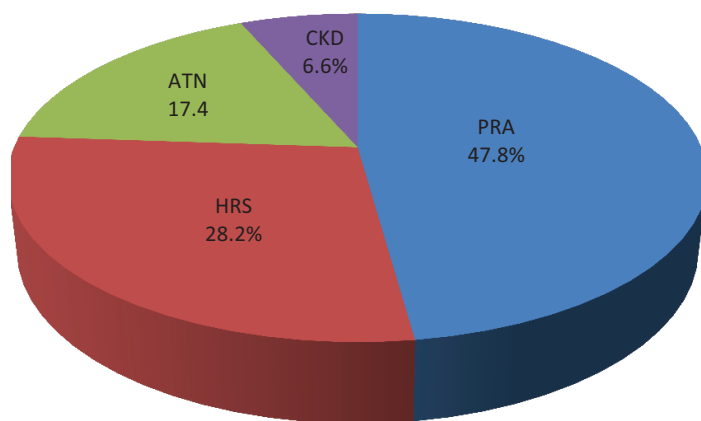


Figure-1: Spectrum of renal dysfunction seen in study group

disease was detected among 6.6% of all cases (Figure A). All patients with prerenal azotemia were using diuretics and lactulose therapy.

The Odds ratio was calculated for various parameters (Table III) and the ratio was significant for Spontaneous bacterial peritonitis and renal failure with the odds ratio of 4.29 (1.08-4.37) and p value <.05. Also, it depicted significant association for infections and renal failure with OR value 2.54 (1.08-5.96) at p value <.05.

A moderate positive correlation (Pearson correlation r 0.199) was seen between CTP Score and renal failure, this positive correlation was significant at p value <.05 level.

DISCUSSION

The demographic characteristics of the patients included in our study closely matches with the data seen in other studies from India. In a study by Rathi et al (conducted across multiple centers in India), 1114 cirrhotic patients were analyzed. Their mean age was found to be 49.5 years and male constituted 81% of the total population.⁷ In another single-center study of India done by Sethu Raman et al the mean age of patients was 49.58 years. This study had 92.23% male and 7.77% females. Mean age (50.49yrs \pm 13.70) and male predominance (85.3%) was nearly replicated in our study. Alcohol was the commonest etiology in a study, constituting 88.35% of all etiologies this was followed by hepatitis B which constituted only at 4.85%.⁸ Study by A Jhajharia et al acknowledged that alcohol followed by viral etiology is the commonest cause among Indian population.⁹ Alcohol related liver disease was the most common etiology involving 43.27% patients, in a multicentre Indian study.⁷ In a study by Brij Sharma et al, while alcohol was the leading cause of cirrhosis, NASH accounted for 7.9% of all cases.¹⁰ A Swedish population cohort study observed that men had a higher incidence rate of cirrhosis when compared to women. Also, Alcohol was the most common etiology (50.5%), while NASH was the offender in 5.7%.¹¹ Our study shows similar data, with alcohol as the commonest culprit followed by viral etiology and NASH respectively. According to one study alcohol related diseases are on the rise, and they comprise up to 21.5% of all gastroenterology admissions.¹² The peculiar point is the rising cases due to NASH, which has been observed in various national and

international studies.^{2,13} With the rise in the burden of NASH related cirrhosis, the liver related mortality is expected to rise because of associated risk factors like diabetes mellitus and CKD. Also, it is predicted that the etiology of hepatocellular carcinoma will see a rise in NASH cases, which currently is dominated by viral etiology.²

In a study by R Keshav et al, it was seen that only 4% percent of all patients belongs to child A CTP class while the rest 96% belong to class B and class C.¹⁴ In a large national study from India, 99% of patients with cirrhosis presented with decompensation.¹⁵ Similar to these data, our population included 97.1% decompensated cirrhosis patients. In the author's opinion, patients in India seek help / are diagnosed only once decompensations sets in. Multiple factors can be attributed for this behavior eg illiteracy, poverty, lack of universal health insurance and poor health facilities at some places etc.

In a recent hospital based study from India, Renal disease was present in 28% of all cirrhotic patients. Author established that an acute kidney injury (16%) was the commonest type of renal dysfunction among cirrhotic, this was followed by HRS (8%) and least common was CKD (14). In a study by Jaiprakash et al, it appeared that renal diseases were present in significant proportion (44%) in cirrhotic patients. Acute kidney injury was seen in 24.5% of the patients (ATN, HRS and Pre renal failure constituting 44.4%, 36.4% and 19.2% respectively). The prevalence of CKD was 15.6% in their cirrhotic patients (16). Also, occurrence of Acute on Chronic renal failure, Nephrotic and Nephritic syndrome was less than 5%.¹⁶ In study by M Arora et al, the prevalence of AKI was 40.6%. Prerenal and HRS were the most usual type of AKI constituting 67.6% and 23.8% of the all AKI respectively.¹⁷ In study by S Shetty et al, Acute Tubular Necrosis and Hepato Renal Syndrome were the predominant types of AKI constituting 42.3% and 43.9% of all cases of respectively.¹⁸ In their study Prerenal azotemia constituted 13.8% of all cases of AKI.¹⁸ Study from Brazil had 57.79% cirrhotic patients with AKI, PRA was the main etiology (59.55%) while HRS was in 10.11%.¹⁹ Studies have shown that more than a quarter to half of cirrhotic patients have renal involvement in one or the other form. Our study demonstrated a high percentage of cirrhotics having renal dysfunction (45%). The type of AKI varies with different studies, as in our study the PRA formed the majority (47.8% of all renal dysfunction), followed by HRS (28%) and ATN (17.4%). This pattern of renal disorder was different from what was observed by Jaiprakash et al and S Shetty et al. However the trend was supported by the data given by M Arora and R Keshav et al. The high prevalence of renal disorder can be attributed to the very high number of decompensated cirrhosis patients in the study group and rising number of NASH related cirrhosis each year. It is very difficult to pinpoint the single cause of PRA in any case and in the majority it is multifactorial. As seen in our study, all patients who had prerenal azotemia were on diuretics and lactulose therapy.

In a study by Rohit Keshav et al, statistically significant relationship was found between Child Pugh score and Serum

creatinine, suggesting that patients with higher severity of cirrhosis develop renal dysfunction much more commonly.¹⁴ Similarly, a study by Jaiprakash et al, added that renal diseases were more frequent with class B and Class C cirrhosis.¹⁶ Study by Manjot S et al also concluded that AKI had a significant association with CTP score, alcohol, spontaneous bacterial peritonitis, sepsis and shock.¹⁷ In our study, a positive correlation was seen between CTP Score and renal failure, predicting that more the patient is decompensated higher is the chances to get renal involvement. An odds ratio of 4.29 (p value - 0.03) was derived for SBP and renal failure, suggesting that patients with spontaneous bacterial peritonitis are more susceptible to renal failure. Similarly OR suggested an association for infections and renal failure with significant p value. However, no significant association was seen with alcohol, as demonstrated by M Arora et al in their study.

The percentage of the population who develop renal failure might not be true percentage as only hospitalized cirrhotic were included in our study. Also, since the majority of the patients belong to decompensated group i.e. class B and C CTP, this subgroup of patients is expected to have more complications.

This was an observational study done over a short period of time. A Prospective study over a longer period of time involving more number of patients will further validate the trends shown in this study. Also follow up of such patients over months to years will determine the prognosis of the disease. Few Studies from very limited centers in India have been done to show the spectrum of renal injury among cirrhotic. As per the author's knowledge this is first study of this region showing the spectrum of renal injury among cirrhotic. Prerenal azotemia was found to be the commonest cause of AKI among cirrhotic in this region. Among prerenal azotemia diuretic use was found to be the commonest culprit.

CONCLUSION

Renal dysfunction is a frequent complication among cirrhotic patients. The Authors suggest that cirrhotic patients who are decompensated and have any evidence of SBP / infection should have a more frequent monitoring of their renal parameters so that AKI can be diagnosed early or prevented.

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