

**Clinicopathological Profile of Patients Suffering from Hepatorenal Syndrome – an Observational Study in a Tertiary Care Centre**Bibhu Debbarma<sup>1</sup>, Rajesh Kishore Debbarma<sup>2</sup>, Swapan Sarkar<sup>3</sup><sup>1</sup>Post Graduate Trainee, Department of Medicine, Agartala Government Medical College, Tripura<sup>2</sup>Professor, Department of General Medicine, Agartala Government Medical College, Tripura<sup>3</sup>Associate Professor, Department of General Medicine, Agartala Government Medical College, Tripura

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Corresponding Author: Dr. Bibhu Debbarma

Conflict of interest: Nil

**Abstract:**

**Introduction:** Hepatorenal syndrome (HRS) is a clinical condition that occurs in patients with chronic liver disease, advanced hepatic failure and portal hypertension characterized by impaired renal function and marked abnormalities in the arterial circulation and activity of the endogenous vasoactive system. Chronic liver disease (CLD) continues to be a major public health problem especially in developing countries like India. In 2019, cirrhosis was associated with 2.4% of global deaths. Owing to the rising prevalence of obesity and increased alcohol consumption on the one hand, and improvements in the management of hepatitis B virus and hepatitis C virus infections on the other, the epidemiology and burden of cirrhosis are changing. This study is designed to observe the clinicopathological profile of HRS patients attending AGMC and GBP Hospital.

**Materials and Methodology:** This is an observational study done in 71 patients admitted with HRS in the department of medicine within the time period of one and half years. Patients were selected as per inclusion criteria and their various clinical profiles were observed.

**Results:** Out of 71 patients, 57(80.2%) were male and 14(19.7%) were female. Most of the patients were 50-59 years old. The mean age of the patient was 48.9 years. The most common etiology of HRS was found out to be alcohol related. Ascites being the most common clinical findings followed by pallor and pedal edema. Type 1 HRS consists of 53.5% and Type 2 consist of 46.4%. Child -Turcotte-Pugh (CTP) score was done to study the prognosis of the patient with HRS. It has been found that 37 patients were in CTP Class A, 35 patients in class B and 2 patients in class C.

**Conclusion:** Hepatorenal syndrome occurs in approximately 4% of patients with cirrhosis who are decompensated with a cumulative probability of 8% per year, which increases to 39% at 5 years. The study was aimed to evaluate clinical profile and to prognosticate as per CTP. HRS is not uncommon and with judicious treatment, especially using terlipressin and albumin a significant number of patients can be cured.

**Keywords:** Hepatorenal syndrome, chronic liver disease, Clinicopathological profile, CTP scores.

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**Introduction**

Hepatorenal syndrome is a clinical condition that occurs in patients with chronic liver disease, advanced hepatic failure and portal hypertension characterized by impaired renal function and marked abnormalities in the arterial circulation and activity of the endogenous vasoactive system. The distinctive hallmark feature of HRS is the intense renal vasoconstriction caused by interactions between systemic and portal hemodynamics.

This results in activation of vasoconstrictors and suppression of vasodilators in the renal circulation. [1] Histologically, kidneys are normal and kidney function is reversible with treatment. Although HRS usually occurs in patients with advanced cirrhosis, it has also been described in patients without ascites in the setting of acute fulminant hepatic

failure. [2] Hepatorenal syndrome occurs in approximately 4% of patients with cirrhosis who are decompensated with a cumulative probability of 8% per year, which increases to 39% at 5 years. In hospitalized patients with ascites, the incidence rate is 7-15%. The incidence of hepatorenal syndrome is similar globally. [3] People of all races and who have chronic liver disease are at a risk of Hepatorenal syndrome.

According to the International Ascites Club criteria, Hepatorenal syndrome has been classified into two different types, Type1 and Type2. [4] Moreau et al observed in 355 patients with cirrhosis and acute renal failure that 58% patients had pre-renal failure, one third of the patients had type 1 HRS, acute tubular necrosis in 41.7% and 1% had post

renal (obstructive) acute renal failure. Until the recent development of effective therapies, the median survival following the development of type 1 HRS was 1.7 weeks, with 10% of the patients surviving more than 10 weeks. Survival rates in type two HRS is 50% at five years and 20% at one year. The most important aspect in the management of HRS is to prevent its recurrence. The latter is achieved by avoidance, prophylaxis, early recognition and treatment of precipitating factor. [5]

There is paucity of studies related to HRS, and up-to our knowledge no study has been conducted in northeast and as well as in our state. So, we have planned to do this study in our institute to find the different types of HRS in CLD, and to find the epidemiological and clinical profile of HRS patients. This study also aims to prognosticate all cases of CLD with HRS as per CTP scoring system.

**Materials and Methodology**

This is an observational study done in 71 patients admitted with HRS in the department of medicine within the time period of one and half years.

Patients were selected as per inclusion criteria and their various clinical profiles were observed.

**Inclusion Criteria**

1. Chronic or acute liver disease with features of hepatic failure and portal hypertension.
2. Low GFR as indicated by creatinine clearance <40 ml/min.
3. No sustained improvement in renal function following volume expansion with 1.5 litre of isotonic saline.

**Exclusion Criteria**

1. Known case of chronic kidney disease.
2. Shock, ongoing bacterial infection and presence of excessive fluid losses including git bleeding.
3. Proteinuria >0.5g/day, and ultrasonographic evidence of renal parenchymal disease.
4. Patients treated with nephrotoxic drugs such as aminoglycosides, NSAIDS etc.
5. Patients who refused to give consent.

**Results**

**Table 1: Age distribution (along with mean, median, SD)**

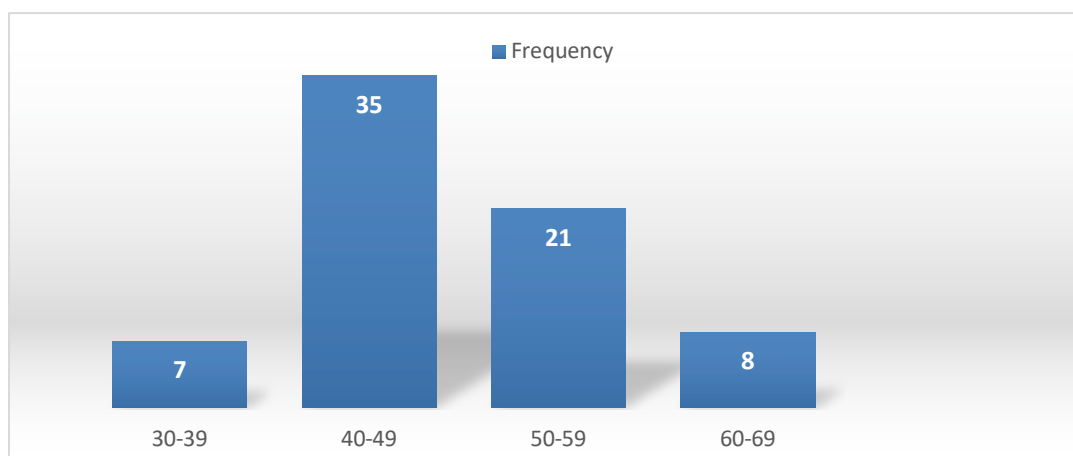
Parameters	Mean	SD	Median	Minimum	Maximum
Age (Years)	48.91	9.51	49	33	69

The age of the study population ranged from 33-69 years with the mean of 48.91 years and standard deviation of 9.51 i.e. 48.91±9.51.

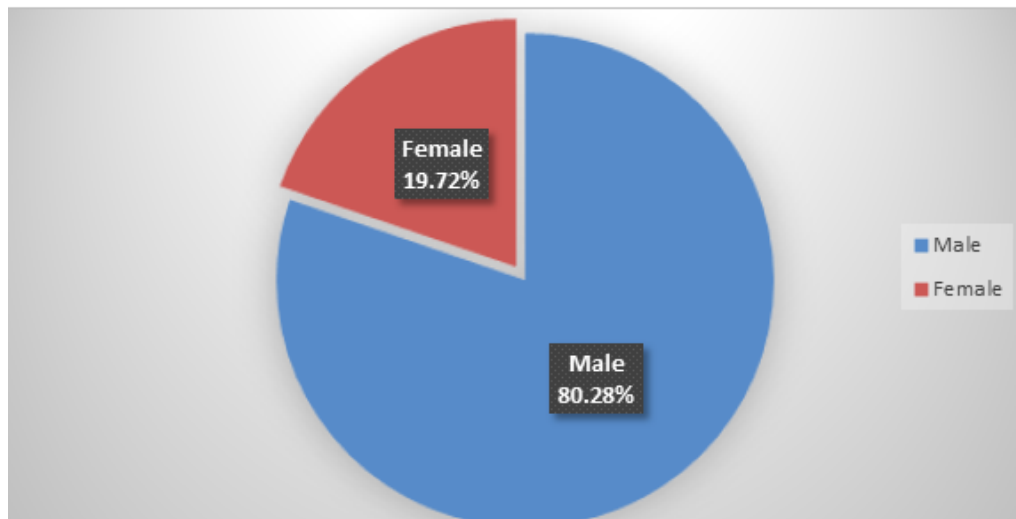
**Table 2: Age distribution along groups with the interval of 10 years**

Age (years)	Frequency	Percentage
30-39	07	9.86%
40-49	35	49.30%
50-59	21	29.57%
60-69	08	11.27%
Total	71	100%

Maximum number of the study participants belongs to the age group of 40-49 years with 35 participants out of 71 i.e. 49.30% belonging to this group. 21 participants (29.57%) belonged to 50-59 years, 08 participants (9.86%) belonged to 60-69 years, 07 participants (9.86%) belonged to 30-39 years.



**Figure 1: Distribution of participants by Age group**



**Figure 2: Distribution of participants by gender**

**Table 3: Distribution of Gender in the study population**

Gender	Number	Percentage
Male	57	80.28
Female	14	19.72
Total	71	100.0

Male population is 57 (80.28%) participants and the female population is 14 (19.72%).

**Table 4: Distribution of clinical and biochemical parameters in the study population**

Parameters	Mean	SD	Median	Minimum	Maximum
Hb (gm %)	7.73	2.23	7.4	4.1	12.8
Platelet count (Lakhs)	1.53	0.72	1.4	0.38	5.8
TLC (Per cmm)	9991.54	5145.44	9000	2000	29600
Na <sup>+</sup> (mmol/l)	132.95	5.63	132	120	155
K <sup>+</sup> (mmol/l)	3.98	0.77	4.0	2.3	5.6
Urea (mg/dl)	79	30.0	72	44	201
Creatinine (mg/dl)	2.7	1.233	2.7	1.5	7.9
RBS (mg/dl)	137.14	77.30	112	76	450
S.Bilirubin (mg/dl)	4.3	4.632	2.4	0.7	28.5
S.Albumin (g/dl)	2.78	0.637	2.9	1.5	3.8
AST (IU/L)	97.67	91.44	80	18	485
ALT (IU/L)	81.14	77.26	59	12	420
PT (sec)	19.08	5.373	18	11	44.9
INR	1.80	0.625	1.8	0.4	3.47
SBP (mmHg)	123.38	21.97	130	80	180
DBP (mmHg)	74.50	10.25	80	50	90

- Distribution of Complete blood count among participants: Hb 7.73±2.23, Platelet count 1.53±0.72, TLC 99991.54±5145.44
- Distribution of electrolytes among participants: Serum Na<sup>+</sup> 132.95±5.63, Serum K<sup>+</sup> 3.98±0.77
- Distribution of kidney function among participants: Urea 79±30.0, Creatinine 2.76±1.233
- Distribution of Random blood sugar among participants: RBS 137.14±77.30
- Distribution of Liver function test among participants: Serum Bilirubin 4.3±4.632, Serum albumin 2.78±0.637, AST 97.67±91.44, ALT 81.14±77.26, PT 19.08±5.373, INR 1.8±0.625
- Distribution of Blood pressure among participants: SBP 123.38±21.97, DBP 74.50±10.25

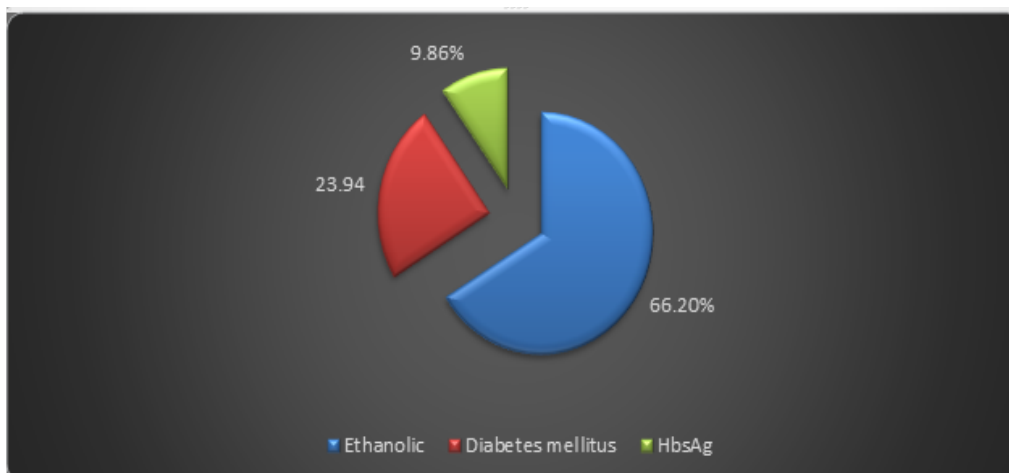


Figure 3: Etiology of Hepatorenal syndrome in the study population

Among 71 participants, 47 (66.20%) are ethanollic, 17 (23.94%) are Diabetes Mellitus and remaining 7 (9.86%) are HBSAg related disease.

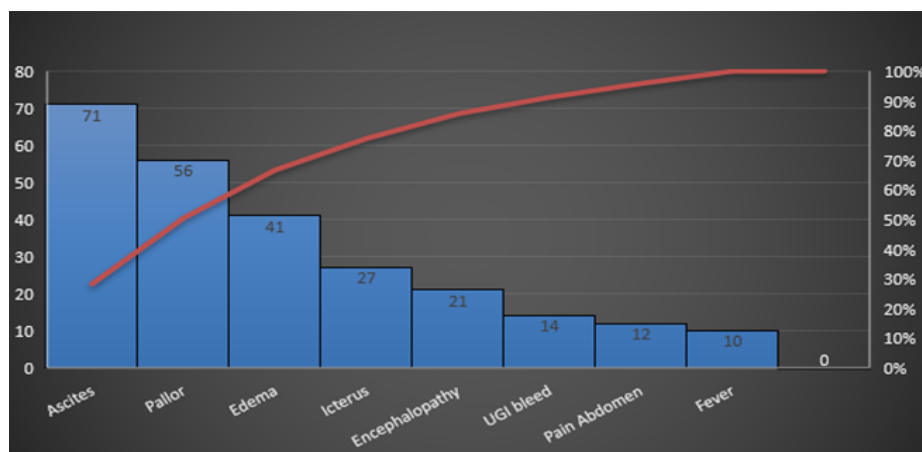


Figure 4: Distribution of clinical findings among the participants

The clinical findings among the study population includes Ascites 71 (100%), Pallor 56 (78.87%), Edema 41 (57.75%), Icterus 29 (40.85%), Encephalopathy 18 (25.35%), UGI bleed 14 (19.72%), Pain abdomen 12 (16.90%) and Fever 10 (14.08%).

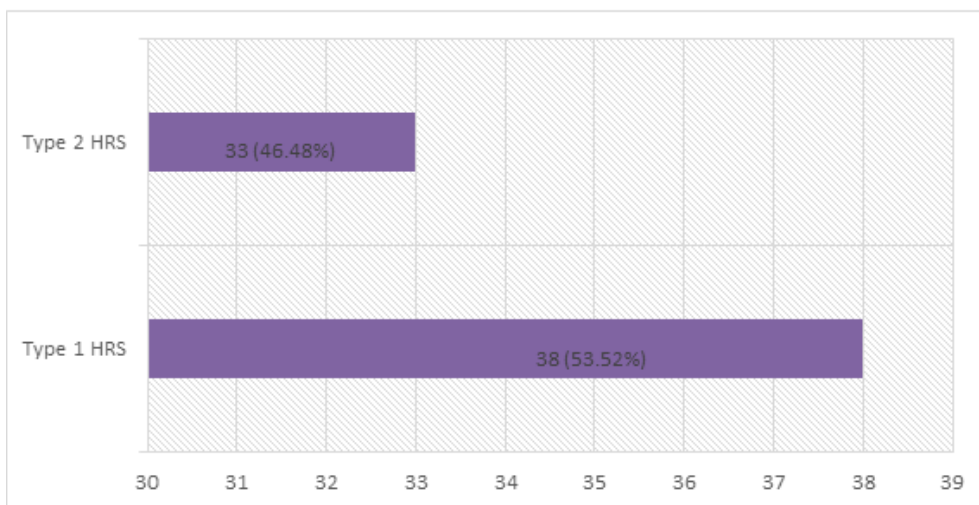


Figure 5: Distribution of Types of Hepatorenal syndrome (HRS) among the study population

Among 71 participants, 38 (53.52%) are Type 1 HRS and 33 (46.48%) are Type 2 HRS.

**Table- 5: Child – Turcotte – Pugh (CTP) Score among the study population**

CTP	A (5-6)	B (7-9)	C (10-15)	Total
Number	2	34	35	71

Among 71 participants, it is found that 34 patients are having CTP Class B, 35 patients are having CTP class C and 2 patients are having CTP class A. CTP class C is considered as poor prognosis and increase mortality.

**Table 6: Types of HRS and its relation with CTP score by Chi-square test**

	CTP <10	CTP ≥ 10	Marginal Row Totals
Type 1 HRS	8 (19.27) [6.59]	30 (18.73) [6.78]	38
Type 2 HRS	28 (16.73) [7.59]	5 (16.27) [7.8]	33
Marginal Column Totals	36	35	71 (Grand Total)

The chi-square statistic is 28.7588. The p-value is < 0.00001. Significant at  $p < .05$ .

The chi-square statistic with Yates correction is 26.2631. The p-value is < 0.00001. Significant at  $p < .05$ .

It is found that Type 1 HRS with CTP score of  $\geq 10$  consists of 85.71% of the total Type 1 HRS and most of the Type 2 HRS are associated with CTP < 10. The p value is significant which means that Type 1 HRS patients with CTP  $\geq 10$  are considered to have poor prognosis and increase mortality and Type 2 HRS patients with CTP < 10 are associated with good prognosis and outcome. So, it is statistically significant with significant p value < 0.05.

## Discussion

This Observational study has included 71 patients of Hepatorenal syndrome admitted in Tertiary care centre of Tripura.

Analysis of data from the study population shows that, mean age of the study population is  $48 \pm 9.51$  years and when distributed along the groups with the interval of 10, 49.30% of the participants belonged to the age group of 40-49 years, 29.57% belonged to the age group of 50-59 years, 11.27% belonged to the age group of 60-69 years and 9.86% belonged to the age group of 30-39 years. Maximum number of the participants belonged to the age group of 40-49 years.

In the study conducted by Rina et al [6] on Hepatorenal syndrome in cirrhotic patients in Madagascar showed that the median age group was  $49.8 \pm 11.3$  years which are similar to the study conducted by us.

Nearly 80.28% of the study populations were male and 19.72% were female. Maximum study has shown male preponderance which may be due to increased incidence of chronic liver disease among the males than females. As per Singh et al [6] a Punjab based study conducted in 42 patients of HRS, 95% of the study population were found to be male. Among 71 participants, 66.20% were found to be ethanolic, 23.94% were diabetic and 9.86% were found to be HbsAg related. As alcohol is widely consumed by the people globally, it became the commonest etiology of Chronic liver disease with hepatorenal syndrome.

The commonest clinical findings in my study population were ascites (100%), pallor (78.87%), edema (57.75%), icterus (40.85%), encephalopathy (25.35%), pain abdomen (16.90%), upper GI bleed (19.72%) and fever (14.08%). All the patients who were included in the study have ascites on clinical examination. As per study conducted by Singh et al [6] the commonest symptom was jaundice (92.8%), abdominal distension (71.4%), altered sensorium (61.9%), fever (40.9%), pain abdomen (33%) and gastrointestinal bleed was seen in 25% of the patients and patients had ascites on clinical examination. Icterus was present in 92.8% cases respectively.

The biochemical parameters were studied among the study population in which mean Hemoglobin was  $7.73 \pm 2.23$  gm%, platelet count  $53 \pm 0.72$  lakhs/cumm, Serum sodium  $132.95 \pm 5.63$  mmol/l, Serum potassium  $3.98 \pm 0.77$  mmol/l, blood Urea  $79 \pm 30.0$  mg/dl, Serum creatinine  $2.76 \pm 1.233$  mg/dl. Approximately 64.79% of the patient showed hyponatremia. According to Paolo Angeli et al [8] study on hyponatremia in cirrhosis they have found that low serum sodium levels were associated with greater frequency of hepatorenal syndrome, hepatic encephalopathy and spontaneous bacterial peritonitis.

The mean serum bilirubin was  $4.30 \pm 4.632$  mg/dl, serum albumin  $2.78 \pm 0.637$  g/dl, AST  $97 \pm 91.44$  IU/L, ALT  $81 \pm 77.26$  IU/L, PT  $19.08 \pm 5.37$  seconds and INR  $1.8 \pm 0.62$ . It is found that 84.51% of the patients have increased total serum bilirubin and 85% have hypoalbuminemia. Singh et al [7] studies have found raised bilirubin levels (mean value  $21.63 \pm 13.63$  mg/dL) and raised SGOT and SGPT in more than 90% of the patient. Almost all of the patients (97.6%) had hypoalbuminemia and coagulopathy was present in more than 90% of the patients. In our patients 92.96% were having coagulopathy.

In our study population we have found that Type 1 Hepatorenal syndrome (HRS) constitutes 53.52% and Type 2 constitutes 46.48%. The study

conducted by Khopde shweta et al [9] on 57 patients has found 75.4% of Type 1 HRS and 24.53% of Type 2. As per Anna Licata et al [10], 45.5% of the patients were found to have Type 1 HRS and 54.5% are Type 2 HRS. The study conducted by Rina et al [6] in Madagascar shows 88% of the patients is having CTP score of > 10. In my study we have found that 47.89% are having CTP class B, 49.30% are having CTP class C and 2.82% with CTP class A. CTP score predicts the one year and two-year mortality in the patients of Chronic liver disease.

So, we assume that 78.95% of the patients with Type 1 HRS having CTP class C and 15.51% of Type 2 HRS are suggestive of having poor outcomes with significant p value.

### Conclusion

The most common etiology of Hepatorenal syndrome in my study was found to be alcohol abuse. Hepatorenal syndrome is one of the complications of Chronic liver disease. It is seen when the renal blood supply is compromised. Early recognition and prompt treatment can prevent further progression of renal compromise as it a reversible condition.

The study aimed to evaluate clinical profile of the patients suffering from Hepatorenal syndrome and to prognosticate the patient as per CTP scoring system. The commonest clinical findings were ascites, pallor, edema, jaundice and encephalopathy. Coagulopathy, hyperbilirubinemia, hypoalbuminemia and hyponatremia constitutes the commonest abnormal biochemical test found in my study. Patients with Type 1 HRS are found to have high CTP score than Type 2 HRS. Type 1 HRS is found to be more common than Type 2 HRS.

Hepatorenal syndrome is not uncommon and with judicious treatment, especially using terlipressin with albumin a significant number of patients can be cured.

### Limitations

1. As this a hospital-based study, therefore it may not represent the actual incidence of HRS in general population.
2. The sample size was small.

3. The study has been conducted in a single centre.
4. Follow-up after discharge was not done in my study.

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