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SPECTRUM OF RENAL DYSFUNCTION IN CIRRHOTIC PATIENTS OF JHARKHAND

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ABSTRACT Liver cirrhosis is a major health problem worldwide. Renal dysfunction is a common and serious complication in patients with decompensated cirrhosis. The study was undertaken to evaluate renal dysfunction in patients of cirrhosis of liver and find out the correlation between renal dysfunction with the graduation of liver disease (assessed by CPS and MELD score).This hospital based observational study was carried on 150 cirrhotic patients admitted in Rajendra Institute of Medical Sciences, Ranchi, Jharkhand. The mean age of cirrhotic patients was 51.38 ± 10.12 years.Of these, majority were males (78.66%). Renal diseases was found to be present in 28% of cirrhotic patients. Most common type of renal dysfunction in cirrhotic liver patients was AKI (16%) followed by HRS (8%) and CKD (4%). The most common etiology of cirrhosis was found to be alcoholism(84.66%) followed by Hepatitis B (10.66%) and C virus (4.66%). There was a statistically significant difference of the presentation of renal dysfunction between patients with different stages of liver cirrhosis according to MELD and Child-Pugh scoring system. This study highlights the fact that we should be more vigilant in treating chronic liver disease patients with regard to their renal function in order to reduce the mortality and morbidity of such patients.

KEYWORDS : Cirrhosis, Renal Dysfunction, Child – Pugh score

INTRODUCTION

Liver cirrhosis is a major health problem worldwide and has been associated with significant morbidity and mortality. According to the WHO, almost about 800,000 people die of cirrhosis annually. [1] The clinical course of patients with cirrhosis is often complicated by a number of important sequelae that occur regardless of the underlying cause of the liver disease [2]

Renal dysfunction is a common and serious complication in patients with decompensated cirrhosis.[3] A series of studies which evaluated the predictors of survival in cirrhosis have reported that parameters of renal dysfunction (creatinine and blood urea nitrogen) together with parameters of liver dysfunction (Child-Pugh score with its components) were important predictors of death in patients of decompensated cirrhosis.[4] The exact incidence of renal disorders in patients with cirrhosis is probably largely unknown and underestimated.[5]

Renal dysfunction has been heavily weighted in MELD calculation as it has a strong impact on survival before transplantation.[6] Identification of renal function is important because it is associated with a high morbidity and mortality.[7] Even moderate elevations of creatinine up to 2 mg/dl and more severe renal insufficiency of creatinine >2 mg/dl were associated with 1.7- and 2.7-fold increase, respectively, in the risk of death in cirrhotic patients.[8] Likewise, MELD estimates that a one-unit increase in loge (creatinine) is associated with a 2.6-fold increase in the risk of death in cirrhotic patients.[9]

The study was undertaken to evaluate the renal dysfunction in patients of cirrhosis of liver and find out the correlation between creatinine and glomerular filtration rate (GFR) as a marker of Renal dysfunction with the graduation of liver disease (assessed by CPS and MELD score).

1. MATERIALS AND METHODS.

This Hospital based observational study was carried on 150 cirrhotic patients admitted in RIMS,Ranchi a tertiary referral center in Jharkhand, from January 2018 to July 2018 after taking informed consent of the patient/attendant.

Inclusion criteria were inpatients with liver cirrhosis of any etiology and age >18 years. Mortality in patients with the effect of other diseases such as heart failure or coronary artery disease, malignancies (primary or metastatic) and patients with incomplete data were not included in this study.

A thorough clinical history of patients and details of complete clinical examination, pelvic-abdominal ultrasound, chest xray, and results of laboratory investigations like complete blood count, liver function test, blood urea, serum creatinine, urine analysis, ascetic fluid analysis, serum sodium, serum potassium and coagulation parameters were collected. Liver cirrhosis was confirmed by clinical, biochemical, and ultrasonographic findings. Staging was done using modified Child–Pugh and MELD scoring system. e. The estimated GFR was evaluated by Cockcroft-Gault formula.

Definitions used for the purpose of this study were:

- *Acute renal failure*: A reduction in the kidney function manifested by an absolute increase in serum creatinine of 0.3 mg/dL or more, equivalent to a percentage increase in serum creatinine of 50% or more (≥1.5-fold from baseline) without any evidence of preexisting kidney disease.
- *Chronic kidney disease*: (1) An evidence of kidney damage for ≥3 months with/ without a decreased glomerular filtration rate (GFR): persistent proteinuria (24-h excretion of protein >300 mg/day or spot protein-to-creatinine ratio >200 mg/g), abnormalities of urine sediment (RBCs, RBC casts, WBC), or abnormal imaging tests (hydronephrosis, cysts, masses, nephrocalcinosis or discrete stones); or a (2) GFR <60 mL/min/1.73 m^2 for ≥3 months, with/without kidney damage.
- *Hepatorenal syndrome*: A rise of serum creatinine of >1.5 mg/dL in patient with cirrhosis and ascites, with no improvement of serum creatinine even after 48 h of diuretic withdrawal and volume expansion in the absence of shock, nephrotoxic drug treatment, and renal parenchymal disease.

For descriptive statistical analysis, mean, standard deviation, and frequencies were calculated. All data were analyzed with statistical software SPSS 22.0 using univariate and bivariate analysis with 95% confidence interval. Bivariate analysis was carried out using Chi-square, Fisher exact, one way ANOVA, Kruskal Wallis test and Pearson coefficient of correlation with significance level set at p<0,05.

2. RESULTS

A total of 150 cases were enrolled in this study and renal diseases were present in 28% (42/150) of cirrhotic patients. The mean age of patients

was 51.38 ± 10.12 years. Of these, majority were male (78.66% (118/150)) and females were 21.33% (32/100).

Table 1 : Baseline Variables.

Variable	n (%)
Male	118/150 (78.66)
Female	32/150 (21.33)
Age	51.38 +/- 10.12
Serum Creatinine	1.71 +/- 0.64
MELD Score	20.88 +/- 7.42
ETIOLOGY OF CIRRHOSIS	
Hep. B	16/150 (10.66)
Hep. C	7/150 (4.66)
Alcoholism	127/150 (84.66)
Types	**n/150 (%)**
Normal	108 (72)
AKI	24 (16)
HRS	12 (8)
CKD	6 (4)

Ascites was found to be the most common clinical presentation, present in 103 (68.66%) of the patients. Hepatic encephalopathy (HE) was found in 21 (14%) patients. There was a statistically significant association between HE and reduction of kidney function meaning renal dysfunction was more frequent in patients with HE (OR: 5.45; p<0.038). However, gender and the presence of ascites had no significant effect on impairment of renal function (p = 0.991 and p = 0.336 respectively).

The most common etiology of cirrhosis was found to be alcoholism in 84.66% (127/150) followed by Hepatitis B (10.66% (16/150)) and C virus (4.66% (7/150)). Renal dysfunction was observed in 30.43% (7/23) of cirrhotic cases with viral etiology. There was no significant association between the etiologies of cirrhosis and renal disorders (P = 0.25)

Table 2 : Etiology of cirrhosis and renal dysfunction distribution.

Cirrhosis Etiology	Normal Renal Function n (%)	Renal Dysfunction n (%)	Odds RATIO (95 % confidence interval)	p - value
Viral (Hep B and Hep C)	16/23 (69.57)	7/23 (30.43)	0.5 (0.2 - 1.6)	0.25
Alcoholism	92/127 (72.44)	35/127 (27.56)		

The most common type of renal dysfunction in cirrhotic liver patients was AKI, present in 16% (24/150) of patients followed by HRS (8%, 12/150) and CKD (4%, 6/150).

Of the 150 patients, twenty four (16%, 24/150) corresponded to Child–Pugh C class, 80% (120/150) to B class, and only 4% (6/150) were class A.

There was a statistically significant difference of the presentation of renal dysfunction between patients with different stages of liver cirrhosis according to Child-Pugh scoring(CPS) system. In the cirrhotic patients with higher severity of cirrhosis (Child-Pugh class B and C), renal dysfunction was developed much more (OR: 1.59; P<0.012)

There was a statistically significant inverse correlation between GFR and CPS (p = 0.022; r = - 0.308). There was also a statistically significant correlation between the serum creatinine levels and CPS (p = 0.007; r = 0.382).

There was a statistically significant inverse correlation between GFR and MELD score (p = 0.04; r = - 0.278). There was also a statistically significant correlation between serum creatinine levels and MELD score (p = 0.004; r = 0.359).

Table 3 : Correlation of GFR and S. Creatinine with:

CHILD - PUGH SCORE		
Variable	Correlation Coefficient	p - value
GFR	-0.308	0.022
S. Creatinine	0.359	0.007
MELD SCORE		
Variable	Correlation Coefficient	p - value
GFR	-0.278	0.04
S. Creatinine	0.382	0.004

There was a statistically significant inverse correlation between GFR and MELD score (p = 0.04; r = - 0.278). There was also a statistically significant correlation between serum creatinine levels and MELD score (p = 0.004; r = 0.359)..

3. DISCUSSION

Liver cirrhosis has been a major health problem. The first reports of renal failure in the setting of cirrhosis of liver were described from Europe and the United States in the late 19th century. Since then, the relationship between the liver and kidney functions has always been an object of great research and study. Majority of clinical studies however have focused their attention on HRS, which is mostly present only in advanced stages of cirrhosis. Other forms of renal disorders in cirrhotic patients have equal importance in view of their incidence and prognostic impact in these patients. [10]

Cirrhosis of liver is often accompanied by a functional renal failure particularly in advanced stages of the disease. Hemodynamic alterations with reduced effective arterial blood volume and peripheral vasodilation are followed by an activation of vasoconstrictive hormones (rennin-aldosterone, vasopressin, endothelin) and neurohumoral systems (including an increased activity of the nervous system).[11] Also, infections, an aggressive use of diuretics, repeated large volume paracentesis and gastrointestinal hemorrhage often contributes to renal dysfunction in these patients causing a pronounced reduction in GFR.[12]

Cirrhotic patients with renal failure are at a high risk for mortality while awaiting transplantation and have an increased incidence of complications and to have a reduced survival post transplantation.[13-16]

In our study renal dysfunction was presnt in 28% of hospitalized patients with cirrhosis. The reported incidence of renal disease (28%) in our cirrhotic patients may not reflect the true incidence of renal disease, because we had included only indoor patients. A routine screening for evidence of renal disease in all cirrhotic patients attending the hospital (outdoor as well as indoor) may provide a better incidence of renal disease in this population.

We found that liver cirrhosis was more frequent in male then female (78.66%) with mean age is 51.38± 10.12 it is similar with Ira IY who also found that male was the majority (68.8%) with mean age 56.12 years.[17] . In the present study no statistically significant difference in renal parameters was observed in different etiologies of liver cirrhosis, which is in contrast with other study reports.[18-19]

Most common type of renal dysfunction observed was found to acute kidney injury (AKI), accounting for 57.1% (24//42) of the cases which is similar to a study report from North India.[20] AKI has been well documented to occur secondary to hypovolemia (gastrointestinal haemorrhage, aggressive diuresis, or diarrhoea), infection and drugs.[21,22] Our studies concluded that HRS constitutes for 28.57% of the cases with renal dysfunction and chronic kidney injury is seen in 14.28% of the cirrhotic patients with renal dysfunction which is similar to the study reports from India and Texas which have reported 15.6% and 13% respectively.[20,23]

Among the renal dysfunction cases studied 30.96 % (13/42) had hepatic encephalopathy and 57.1% (24/42) were under diuretic therapy. It has been well documented previously that diuretics are associated with a risk of renal injury and factors such as hepatic encephalopathy have been associated with the progression of AKI.[24,25]

Our study also found a statistically significant relationship between CPS and serum creatinine as a parameter of renal dysfunction and that in the cirrhosis patients with higher severity of cirrhosis, renal dysfunction was developed much more; findings which were similar to as found by Nupur Das et al. [26] and Yun Jung Choi, et al.[27] Both the CPS and the MELD score correlated positively with serum Creatinine as a marker of renal dysfunction.These results are confirmed by the research done by Amin et al. (CPS and serum Cr r = 0.556; p< 0.0001, MELD scores and serum Cr r = 0.849; p< 0.0001).

[28] Qureshi et al. found Child-Pugh and MELD scores were significantly higher in RD patients (11±2 vs. 9.4±2; p <0.001 and 19.6±5.7 vs. 16.3±4; p<0.001). [29] Both scores also showed a negative correlation with GFR.

These results contrast with Culavic D at al which detected no significant correlation between creatinine and MELD score (p = 0.091) and also no significant correlation between GFR and MELD score (p = 0.460).[30]

Table 6 : Renal Dysfunction and associated factors.

Column1	Factors	Renal Dysfunction (n (%))	Normal Renal Funcion (n (%))	p - value	Odd's Ratio (95 % CI)
Gender	Male	33/118 (27.96)	85/118 (72.03)	0.991	1.00 (0.71 - 1.41)
	Female	9/32 (28.12)	23/32 (71.87)		
Ascites	Yes	32/103 (31.06)	71/103 (68.93)	0.336	1.28 (0.91 - 1.72)
	No	10/47 (21.27)	37/47 (78.73)		
Hepatic Encephalopathy	Yes	13/21 (61.9)	8/21 (38.09)	0.038	5.45 (3.11 - 7.25)
	No	30/129 (23.26)	99/129 (76.74)		
Child - Pugh Score	Class A	0 (0)	6/6 (100)	0.012	1.593 (1.265 - 2.005)
	Class B - C	50/144 (34.72)	94/144 (65.28)		
Diuretic Drug Use	Yes	24/80 (30)	56/80 (70)	0.026	1.571 (1.272 - 1.986)
	No	15/70 (21.42)	55/70 (78.58)		

4. CONCLUSION

This study highlights the fact that we should take utmost care and should be more vigilant in treating chronic liver disease patients with regard to their renal function . This need for early diagnosis, prevention and treatment of renal dysfunction can significantly decrease the morbidity and mortality of such cirrhotic patients.

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