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Original Research Article

Renal Resistive Index as an Early Predictor of Renal Involvement in Cirrhotic Patient

Dr. Prakash Chandra Mishra[1], Dr. Ujjwal Kumar[2], Dr.V.M. Dayal[3], Dr. S.K.Jha[4], Dr. Ravikant Kumar[5]

[1,2] Senior Resident, Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India
[3]Professor and Head, Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India
[4]Professor, Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India
[5]Associate Professor , Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India

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Corresponding author: Dr. Ujjwal Kumar
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Abstract:

Background: In India, cirrhosis and chronic liver disease (CLD) were responsible for 2.1% of all fatalities. One of the most significant clinical and prognostic consequences of liver cirrhosis is acute kidney Injury (AKI). In this context, renal progression of AKI is a warning indication of a significant risk of death. It has been noted that renal vascular constriction in cirrhosis patients increases the renal resistive index (RRI). The study aims to evaluate the predictive significance of duplex Doppler ultrasonography in a group of liver disease patients who are not azotemic.

Materials and Methods: It was a prospective observational cohort study that was conducted in the Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India. The study has been conducted from January 2022 to December 2023. The study included 136 participants in total. Ethical approval has been granted from the Institutional Ethics Committee (IEC), IGIMS, Patna, Bihar, India, under letter number 835/IEC/IGIMS/2022 dated 10 December 2022.

Results: The mean age of participants was 45.00 ± 11.92 years. 85.3% of the participants were Male, while 14.7% were Female. Creatinine at baseline and RRI at Baseline showed a weak positive connection, although this relationship was not statistically significant for those who developed AKI at one month. The outcomes of participants during follow-up tend to be uneventful in 71 (52.6%) patients, Readmitted patients 53 (39.3%), and expired patients 11 (8.1%) in number.

Conclusion: The study concluded that acute kidney injury has the highest clinical and prognostic significance and is a frequent consequence of liver cirrhosis. AKI is more likely to develop in patients with cirrhosis, particularly decompensated cirrhosis than in those without cirrhosis. Percentage change in creatinine versus RRI at one month, three months, and six months was found to be statistically significant. RRI may be used as a marker for AKI prediction and outcome in patients with cirrhosis.

Keywords: Acute Kidney Injury, Renal Resistive Index, Chronic liver disease, non-azotemic, Liver Diseases, Renal Impairment

Introduction

In India, liver problems are quickly becoming acknowledged as public health issues. India has a heavy burden of liver disease, which was responsible for 18.3% of the two million mortalities globally in 2015 from liver disease [1]. Cirrhosis and chronic liver disease (CLD) were responsible for 2.1% of all fatalities in India in 2016 [2].

Numerous complications that have a bad prognosis, such as varices, cirrhotic cardiomyopathy, hepatic encephalopathy, coagulopathy, hepatopulmonary syndrome, and hepatorenal syndrome, further change the course of the disease [2]. One of the most significant clinical and prognostic consequences of liver cirrhosis is acute kidney damage (AKI).

People who have cirrhosis are more prone to suffer AKI than people without the disease. Acute tubular necrosis (ATN) includes a variety of conditions in prerenal chronic liver disease, and the hepatorenal syndrome which is a type of AKI are the two most common causes of AKI in individuals with cirrhosis and chronic liver disease. Retention of water and sodium are two of the reasons linked to this illness [2].

It is observed generally that effective renal blood flow is reduced when peripheral vasodilatation occurs in advanced liver illness because it triggers a series of both hormonal and neurohormonal vasoconstrictors. Hepatorenal syndrome (HRS) is a syndrome of decreasing renal function that is mainly due to the systemic hemodynamic effects of severe portal hypertension. It is frequently used to elaborate renal failure in patients with advanced cirrhosis and ascites [3].

An alarming indication of a significant risk of death in this situation is the progression of AKI in the kidneys. When determining a patient's true GFR, traditional renal function tests are not always reliable. Chronic liver illness results in a decrease in the generation of creatine and creatinine. This causes blood creatinine to be erroneously "low" in these patients, leading to a correspondingly "low" estimated GFR by any formula [4]. Because creatinine can be influenced by liver failure, malnutrition, age, and a loss of muscle mass, thus, it cannot be accurately used as an appropriate marker for the evaluation of renal impairment, particularly in cirrhotic patients. As a result, it tends to be better to prevent early intervention to increase survival. There is ongoing research on new methods for identifying functional intrarenal hemodynamic alterations early on. Due to renal vascular constriction, patients with cirrhosis have been found to have higher renal resistive indexes (RRIs) [5]. In cirrhotic patients who are non-azotemic, RRI has been shown as a sensitive indicator of intrarenal hemodynamics [6]. Therefore, in some people, it may be a precursor to functional renal impairment.

The purpose of this study was to assess the predictive value of duplex Doppler ultrasonography in samples of adults without azotemic liver disease. Early identification of the patients with liver diseases who are especially at risk for developing hepatorenal syndrome may be beneficial because overt kidney failure has been identified as an independent risk factor for liver transplant outcome and because clinical management may be altered to avoid other nephrotoxins such as drugs and radiographic contrast.

Methodology

Study Design- This was a prospective observational cohort study conducted in the Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences

(IGIMS), Patna, Bihar, India. The study has been conducted from January 2022 to December 2023. The patients were fully explained that they were being enrolled in clinical research and had to sign a consent form written in their local language before enrollment. All the subjects were given standard medical therapy.

Study Population- A total of 136 participants were enrolled in the study. Patients with cirrhosis (both compensated and decompensated) (cirrhosis defined by biochemical, radiological, clinical, or/and by histological criteria) and NO AKI from baseline (documented normal baseline serum creatinine within 3 months before the study) presenting to the dept. of gastroenterology, IGIMS, Patna, and Bihar were included in the study. Participants between the ages of 18 and 80, have compensated or decompensated liver cirrhosis, and have no AKI at baseline (defined as a normal baseline serum creatinine within three months before the trial). Participants were excluded if they had a confirmed pregnancy, sepsis or recent gastrointestinal bleeding, HCC, underwent kidney or liver transplant, had hypertension or advanced chronic kidney disease (CKD), received renal replacement therapy, had diabetic nephropathy, glomerulonephritis, urinary tract obstruction, bladder tract infections, or had not given their consent.

Data Collection- Detailed history and clinical examination of the patients done. A routine biochemical test was performed using standard laboratory procedures. Liver Function tests were done in all the patients using an automatic biochemistry analyzer. Serum creatinine levels were measured using the modified Jaffe method. Special tests and radiological tests were done as needed. Duplex renal ultrasonography was performed to directly visualize the renal arteries from the origin to the interlobar arteries. Renal resistive index (RRI) was calculated from the renal arteries to the interlobar arteries. The system computed the RRI with help of various arteries' peak systolic and end-diastolic velocities. All individuals had baseline measurements of their serum creatinine and RRI. The patients were given standard medical therapy. Follow-up was done for six months further. The serum creatinine and serum RRI were repeated every 1, 3, and 6 months and on an SOS basis if required, and the development of AKI was observed for up to 6 months. The patients were still followed to judge the outcome.

Statistical Analysis- Statistical Package for Social Sciences (SPSS) version 21.0 was used for data analysis after the data was entered into a Microsoft Excel spreadsheet. Categorical variables were presented in numbers and percentages (%), while continuous variables were presented as mean ± SD and median. Spearman's correlation coefficient test has been used to establish a correlation between coefficients and obtain a p-value. A p-value of <0.05 was considered statistically significant.

Ethical Clearance- Ethical approval has been granted by the Institutional Ethics Committee (IEC), IGIMS, Patna, Bihar, India, under letter number 835/IEC/IGIMS/2022 dated 10 December 2022.

Results

The present study analyzed 136 patients. The mean age was 45.00 ± 11.92 years. 85.3% of the participants were Male, while 14.7% were Female. Table 1 represents the characteristics of enrolled participants.

Table 1: Patients Demographics

Characteristics	Value
Age (in years)	45.00 ± 11.92
Male	116 (85.3%)
Female	20 (14.7%)
Diabetes Mellitus	21 (15.4%)
Alcohol Use	96 (70.6%)
Heart Rate (bpm)	81.60 ± 10.91
Mean Arterial Pressure (mmHg)	81.36 ± 9.52
Icterus	107 (78.7%)
Pedal Edema	89 (65.4%)
Ascites	111 (81.6%)
HBsAg	15 (11.0%)
Hepatitis-C Virus	6 (4.4%)
Hemoglobin (g/dL)	8.57 ± 1.63
TLC (x10³/mm³)	6.37 ± 2.15
PLT (x10³/mm³)	83.92 ± 33.85
BUN (mg/dL)	20.35 ± 9.34
S. Na (mEq/L)	133.99 ± 5.72
Bilirubin (mg/dL)	3.78 ± 1.32
Albumin (g/dL)	2.71 ± 0.47
INR	1.59 ± 0.42
Ascites on USG	
Absent	26 (19.1%)
Mild	19 (14.0%)
Moderate	41 (30.1%)
Severe	50 (36.8%)

Data were presented as either mean±SD or n (%)

AKI developed in 59.66% cirrhotic patients at one month 73.3% at three months and 81.6% at six months. Table 2 represents the development of acute kidney injury at different time intervals.

Table 2: Presence of Acute Kidney Injury in Participants

Acute Kidney Injury	Percentage
At 1 Month	59.66%
At 3 Months	73.3%
At 6 Months	81.6%

There was a weak positive correlation between Creatinine (mg/dL) (Baseline) and RRI (Baseline), and this correlation was not statistically significant (rho = 0.12, p = 0.163) who developed AKI at 1 month. Table 3 shows correlation changes between creatinine versus RRI at different time intervals.

Table 3: Correlation changes between Creatinine versus RRI at different time intervals

Correlation	Spearman Correlation Coefficient	p-value
Creatinine (mg/dL) (Baseline) vs RRI (Baseline)	0.12 (95%CI: -0.05 to 0.28)	0.163
Percent Change in Creatinine (mg/dL) (1 Month) vs RRI (1 Month)	0.36 (95%CI: 0.2 to 0.52)	<0.001
Percent Change in Creatinine (mg/dL) >50% (3 Months) vs RRI (3 Months)	0.33 (95%CI: 0.16 to 0.48)	<0.001
Percent Change in Creatinine (mg/dL) (6 Months) vs RRI (6 Months)	0.27 (95%CI: 0.1 to 0.42)	0.002

Spearman correlation test was used to obtain the p-value

p-value was considered significant at <0.05

Outcome Of Patient Recorded Into 3 Group, Group with No Admission to Hospital During Follow-Up Period. Group With Readmission in the Hospital for Any Morbidity During Follow-up, Readmission Was Mainly for Severe Ascites, Hepatic Encephalopathy, Variceal Bleeding, and systolic blood pressure. Table 4 depicts the outcomes of participants during follow-up.

Table 4: Outcomes of Participants During Follow-up

Outcome	Value	95% CI
Uneventful	71 (52.6%)	43.9% - 61.2%
Readmitted	53 (39.3%)	31.1% - 48.1%
Expired	11 (8.1%)	4.3% - 14.4%

Data has been presented as n (%)

Discussion

In this study, we included 136 patients of chronic liver diseases (CLD) both compensated and decompensated, with no AKI at baseline fulfilling the International Club of Ascites work group. Serum creatinine and RRI by duplex ultrasound were measured at baseline and the patients were followed with standard medical therapy for 6 months, creatinine and RRI were measured at 1, 3, and 6 months, and the development of AKI, and the patient outcome was noted. Our study showed that the average age of CLD patients was 45±11.92 years with 85.3% males. The largest study from India by Asrani SK et al which included 1049 patients reported a median age of 45 years with 81.3% males [7].

AKI developed in 59.66% of cirrhotic patients at one month, 73.3% at three months, and 81.6% at six months, as per the International Club of Ascites group. The prevalence of AKI in liver cirrhosis ranges from 20 to 50%. Research conducted in India by Desai AP et al. found a prevalence of 40.6% of AKI among individuals with liver cirrhosis [1]. Gogoi N et al found 31.1% of patients were in stage 1, 38.5% of patients in stage 2, and 30.4% of patients were in stage 3 AKI at presentation [8].

It has been previously shown that serum creatinine is not a potential marker for renal injury in cirrhosis. According to Mogawer MS et al., duplex ultrasonography of the renal arteries is an easy, efficient, and non-invasive technique that allows the early identification of renal hemodynamic abnormalities in liver cirrhosis patients even before renal failure is manifested. Moreover, it enables the identification of a subset of liver cirrhosis patients who are more susceptible to hepatorenal syndrome [9]. Goyal et al. demonstrated that cirrhosis patients had a substantially higher RI than healthy controls. He determined that RI more than 0.70 was a significant predictor of the development of HRS later on with a p-value of 0.006 [10].

The study's limitations include a limited sample size and the fact that it was only conducted at one location, which would restrict how broadly our findings can be applied. We hope that more multicenter research with larger cohorts will validate and build on our findings. RRI also shows potential, but to fully evaluate renal function and HRS risk, it should be used in conjunction with other clinical and laboratory indicators. A larger cohort was needed to compare compensated and decompensated CLD because the maximum number of patients in our study were enrolled in the decompensated stage, resulting in a small cohort of compensated CLD.

Conclusion

The study concluded that the most clinically and prognostically significant consequence of liver cirrhosis is acute renal damage. Patients with liver cirrhosis, particularly those with decreasing cirrhosis, are more likely than those without cirrhosis to suffer AKI. At one, three, and six months, the percentage change in creatinine compared to RRI was determined to be statistically significant. RRI may be used as a marker for AKI prediction and outcome in patients with cirrhosis.

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