

## A Cross-Sectional Study on Resistivity Index of Renal Vasculature in Patients with Cirrhosis of Liver in a Tertiary Care Centre

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Conflict of interest: Nil

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### Abstract:

**Aim of the Study:** To study resistivity Index of Renal Vasculature in Patients with Cirrhosis of Liver in A Tertiary Care Centre.

**Material & Methods:** A total of 92 patients in which there were 75 cases which included cirrhosis with ascites, cirrhosis without ascites and 17 controls which included fatty liver and healthy individuals formed the study group.

**Results:** The study group is a total of 92 patients, 49 were cirrhosis with ascites patients, 26 were cirrhosis without ascites patients, 17 healthy which includes fatty liver. In our study, Resistivity index is increased in both cirrhosis with ascites and without ascites. So early phase itself shows increased Resistivity Index. Resistivity Index was significantly higher in ascitic patients compared to non-ascitic patients (0.74 vs. 0.67,  $p < 0.01$ ) and in non-ascitic patients with liver cirrhosis than in control subjects (0.67 vs. 0.62,  $p < 0.01$ ). In our study Resistivity Index was significantly higher in ascitic patients compared to non-ascitic patients (0.87 vs. 0.76,  $p < 0.01$ ) and in non-ascitic patients with liver cirrhosis than in control subjects (0.76 vs. 0.64,  $p < 0.001$ ).

**Conclusion:** Renal vasoconstriction evaluated by these indices is correlated with Child score which quantitatively measures the hepatic function in cirrhosis. The diagnosis of elevated Resistivity Index may be taken into account in the clinical management of these patients.

**Keywords:** Resistivity Index; Renal vasculature; Cirrhosis of Liver; Hepatorenal Syndrome; Model for End-Stage Liver Disease.

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### Introduction

Among the various complications of advanced cirrhosis, development of Hepatorenal Syndrome (HRS) has a devastating course and outcome in cirrhotic patients. HRS is usually an extended spectrum of pre-renal azotemia and therefore is potentially reversible [1].

But after the evolution of the disease, the survival is short without liver transplantation or management with vasoconstrictors. Hepatorenal Syndrome is a part of events occurring in the background of cirrhosis with portal hypertension or acute liver injury [2].

Type I HRS patients have a mortality of 50% two weeks after diagnosis, approaching up to 100% within months. The median survival of untreated Type I HRS was calculated to be approximately 11 days, with a survival probability of 25% after 30 days. Patients with type II HRS show a lower mortality rate with the median survival being approximately six months [3]. Usually HRS can be diagnosed only after the rise in blood urea nitrogen and serum creatinine. By then the disease has progressed so that it is no longer reversible and has a poor outcome. But the disease can be predicted in advance by the estimation of renal resistive index (RI) that increases before a considerable period of time by Doppler ultrasound and so measures can be implemented to prevent the disease progression by avoiding the excess use of diuretics and nephrotoxic agents, avoiding large volume paracentesis [4].

The correlation between the clinical profile of cirrhotic patients with normal renal parameters and their resistivity index is yet to be studied in a larger population to make this an important prognosticating factor in determining the probability of the patient to develop HRS.

### Aim of the Study

- To correlate resistivity index of renal vasculature with ascites, with CHILD PUGH score and with MELD score of the cirrhotic patients.
- To detect a subgroup of patients with a higher RI index (i.e. at risk of developing renal impairment)

### Material & Methods

A total of 92 patients in which there were 75 cases which included cirrhosis with ascites, cirrhosis without ascites and 17 controls which included fatty liver and healthy were carried out in Tertiary Care Centre during the period of July 2018 to June 2020 at Telangana State. This study group was selected on the basis of the following inclusion and exclusion criteria:

### Inclusion Criteria

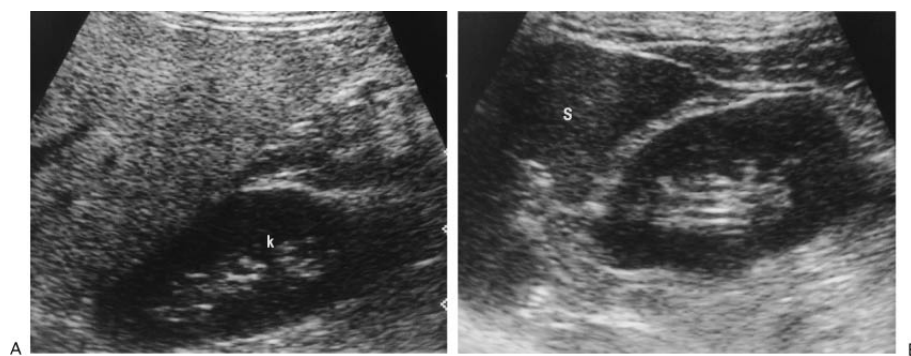
Patients attending Medical Gastroenterology Clinic & General Medicine Wards with Cirrhosis of liver with or without decompensation in the form of ascites.

### Exclusion Criteria

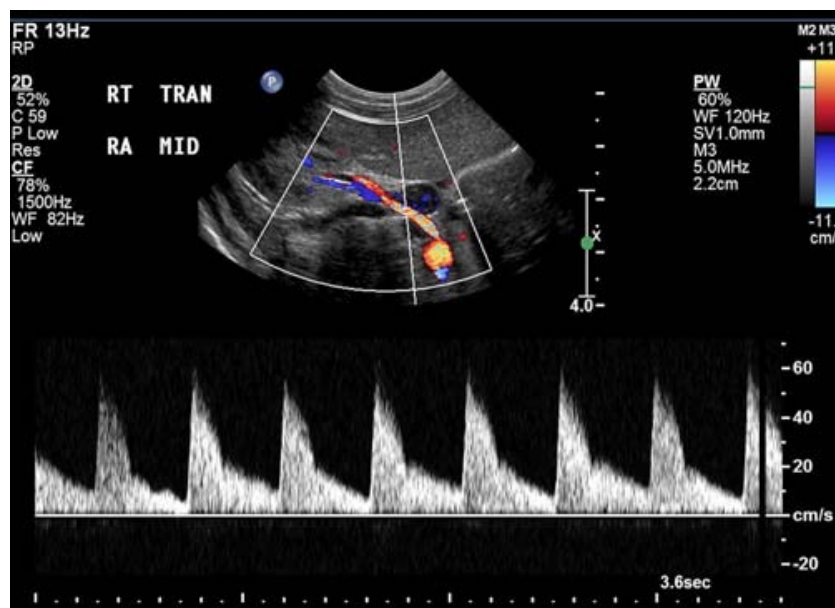
- Preexisting renal parenchymal disease
- Other causes of renal vasoconstriction
  - Drug-induced renal failure (e.g. amino-glycosides and NSAIDs)
  - Glomerulonephritis
  - Pre-renal failure
  - Sepsis
  - Acute tubular necrosis

### Methodology

- Detailed clinical history was taken from each of the patients.
- A complete clinical examination of the abdomen was done.
- Blood investigations were done (Liver Function Test, Renal Function Test, and Serum Sodium).
- USG abdomen to detect the liver echoes, Ascitic fluid, kidney size.
- Renal Doppler was done to measure the resistivity index. The RI of three renal vessels, obtained in three renal areas, was measured in each patient by using at least three Doppler spectra, and the mean value was calculated.

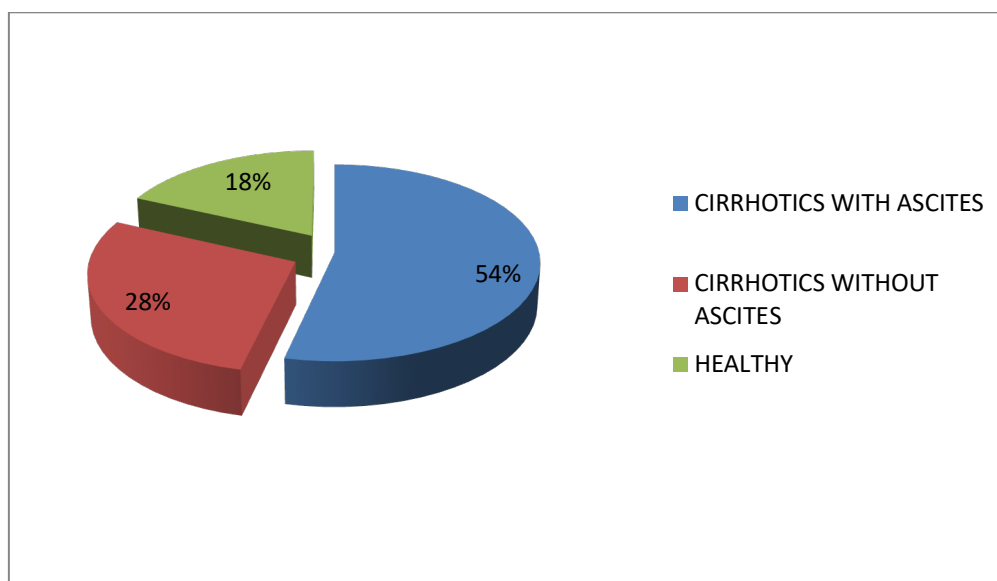


**Figure 1: USG abdomen showing both the Kidneys**



**Figure 2: Renal Doppler showing wave pattern**

## Results



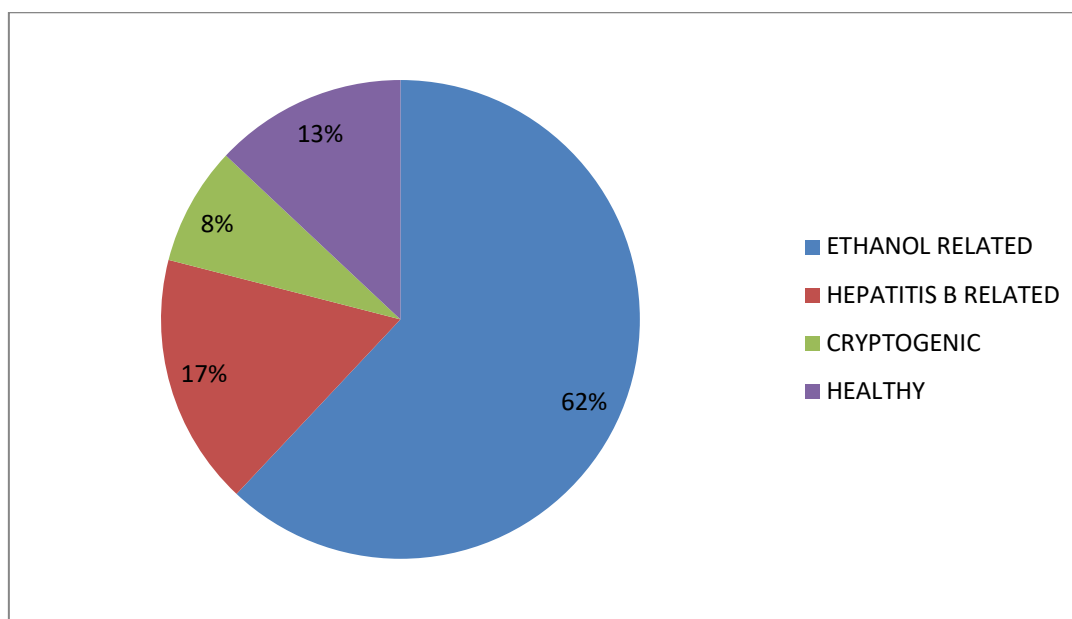
**Graph 1: Study Population**

**Table 1 : Alcoholics Vs. Non-Alcoholics**

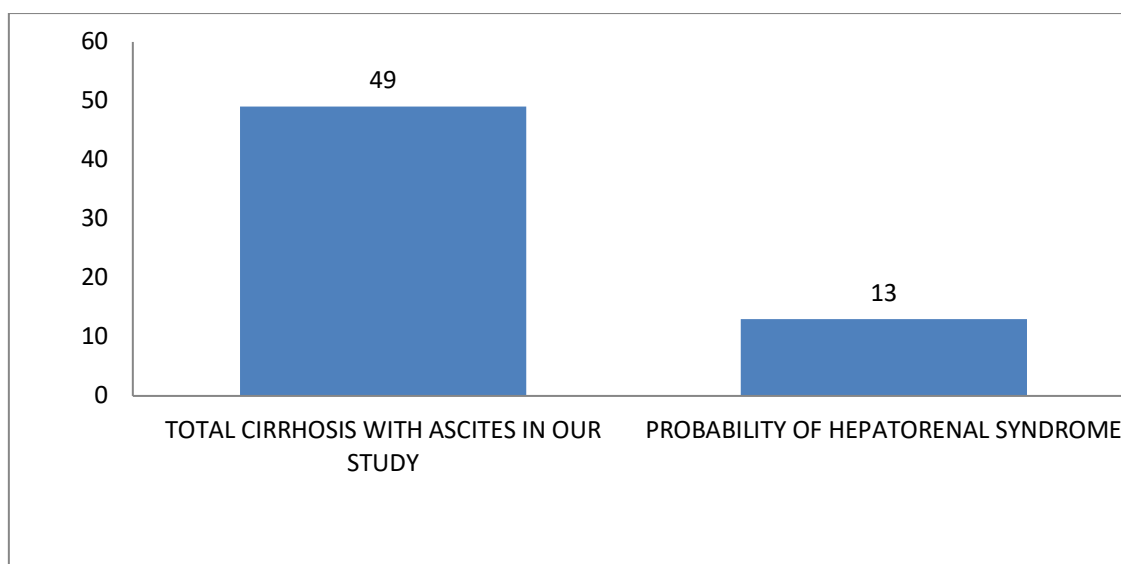
	<b>Males</b>	<b>Females</b>
Alcoholic	48 (52%)	7 (8%)
Non-alcoholic	19 (21%)	6 (6%)
Healthy	10 (11%)	2 (2%)

**Table 2 : Age-Wise Classification**

<b>Age in Years</b>	<b>Cirrhosis with Ascites</b>	<b>Cirrhosis without Ascites</b>	<b>Healthy</b>
<b>30-40</b>	1(1%)	1(1%)	0(0%)
<b>40-50</b>	21(23%)	10(12%)	6(5%)
<b>50-60</b>	23(25%)	14(18%)	9(8%)
<b>60-70</b>	4(4%)	1(1%)	2(2%)

**Graph 2: Classification based on Causes****Table 3: Comparison of Resistivity Indices**

	<b>Resistivity Index</b>
Cirrhosis with Ascites	>0.87
Cirrhosis with no Ascites	>0.76
Healthy	>0.64



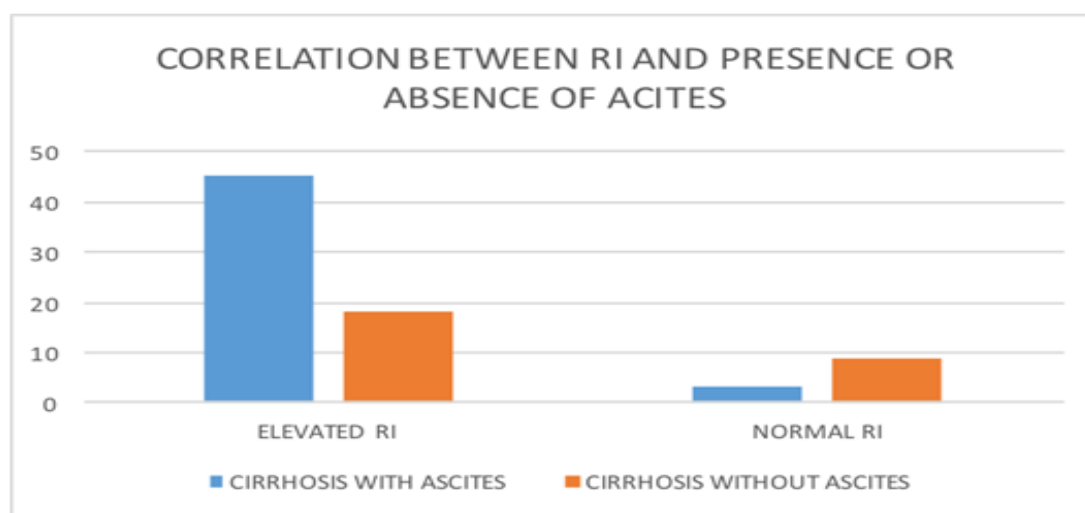
**Graph 3: Probability of HRS in Patients with Cirrhosis and Ascites**

**Table 4 : Expected mortality 1yr & 5yr in patients with cirrhosis and ascites**

<b>No of Patients with Cirrhosis and Ascites</b>	<b>49 (Total)</b>
<b>1 yr mortality</b>	10 (20%)
<b>5 yr mortality</b>	20 (40%)

**Table 5: 55% Cirrhotics with elevated RI and normal renal function develops subsequent Kidney Dysfunction**

<b>Total No. of Patients</b>	92
<b>Cirrhotics with Elevated Resistivity Index</b>	63
<b>Patients developing subsequent Kidney Dysfunction</b>	35(55%)



**Graph 4: Correlation between RI and Presence or Absence of Ascites**

**Table 6: Correlation between RI and Child Pugh Score**

Child Pugh score	RI index<0.7	RI index= $\geq$ 0.7	Total
Class A	3	2	5
Class B	6	20	26
Class C	3	41	44
Total	12	63	75

**Table 7: Correlation between RI and Meld Score**

MELD-Score	RI index<0.7	RI index= $\geq$ 0.7	Total
0-9	1	0	1
10-19	8	40	48
20-29	3	23	26
Total	12	63	75

## Discussion

As the majority of individuals with hepatorenal syndrome have cirrhosis, much of the epidemiological data on HRS comes from the cirrhotic population. The condition is quite common. Approximately 10% of individuals admitted to Tertiary Care Centre with ascites have HRS.

A retrospective case series of cirrhotic patients treated with terlipressin suggested that 20% of acute renal failure in cirrhotics was due to type 1 HRS, and 6.6% was due to type 2 hepatorenal syndrome. It is estimated that 18% of individuals with

cirrhosis and ascites will develop HRS within one year of their diagnosis with cirrhosis, and 39% of these individuals will develop hepatorenal syndrome within five years of diagnosis. The mean age was 51.8  $\pm$  12.1 yr, and 67% were male as per the study on Hepatorenal syndrome: diagnostic accuracy, clinical features, and outcome in a Tertiary Care Centre. Watt K, Uhanova J, Minuk GY. Liver Diseases Unit, University of Manitoba, Winnipeg, Canada. Comment in: Can J Gastroenterol. 2004 Feb;18 (2): 121-2. Am J Gastroenterol. 2002 Aug; 97 (8): 1868-70 [5].

Cirrhotics With Ascites	49 (53%)
Cirrhotics Without Ascites	26 (28%)
Healthy	17 (18%)

In our study 92 patients were studied including cirrhosis with ascites (49), without ascites (26), fatty liver and healthy individuals (17).

60% were alcoholic and 25% were non-alcoholic. Of the various causes apart from alcoholic, 17% were hepatitis B positive, 8% were cryptogenic, and 13% were healthy. Out of the total of 92 patients 77 were males, 15 were females. Males (84%) are more common than females (16%), whereas as per the study on Hepatorenal syndrome: diagnostic accuracy, clinical features, and outcome in a Tertiary Care Centre. Watt K, Uhanova J, Minuk GY.

Liver Diseases Unit, University of Manitoba, Winnipeg, Canada. Comment in: Can J Gastroenterol. 2004 Feb;18(2):121-2. Am J Gastroenterol. 2002 Aug; 97(8):1868-70, percentage of females was higher.

According to the study by "Recommendations available for managing ascites, SBP and hepatorenal syndrome. August 2010 05:53 "It is estimated that almost 60 percent of cirrhotic patients develop ascites within 10 years of their disease, which is a huge proportion of patient. In our study 75 patients were Cirrhotics and among them,



49 (65%) patients were cirrhosis with ascites, 26 (35%) patients were cirrhosis without ascites.

Doppler sonography is performed to determine the intrarenal arteriolar vascular resistance, defined as the resistive index (RI). The reference range for RI is lower than 0.7. The RI can be a more sensitive parameter than the creatinine clearance. Renal Duplex Doppler ultrasonography can non-invasively identify a subgroup of non-azotemic patients with liver disease that is at significantly higher risk for subsequent development of kidney dysfunction and the hepatorenal syndrome [6]. Out of the 49 cirrhosis with ascites patients 45 were showing elevated resistivity index, 3 were within normal range. Among 27 cirrhosis without ascites patients, 18 were showing elevated resistivity index, 9 were within normal range.

In our study RI was significantly higher in ascitic patients compared to non-ascitic patients (0.87 vs. 0.76,  $p < 0.01$ ) and in non-ascitic patients with liver cirrhosis than in control subjects (0.76 vs. 0.64,  $p < 0.001$ ). Resistivity indices were increased in both cirrhosis with and without ascites. Cirrhosis with ascites =  $>0.87$  Cirrhosis without ascites =  $>0.76$  Fatty liver and healthy =  $>0.64$ .

In the study by Eur J Med Res. 2008 Aug 18; 13(8):383-7, Intra renal resistance Index for the assessment of early Renal Function impairment in patients with liver cirrhosis.

The study group investigated the value of RI measurement in detection of renal function impairment in patients with different stages of chronic liver disease. Subjects were divided into 4 groups containing 21 patients with liver cirrhosis and ascites, 25 patients with liver cirrhosis without ascites, 35 patients with fatty liver disease and 78 control subjects. All patients underwent abdominal ultrasound examination with renal RI measurement

and correlation with laboratory results for renal function.

It was found that RI was significantly higher in ascitic patients compared to non-ascitic patients (0.74 vs. 0.67,  $p < 0.01$ ) and in non-ascitic patients with liver cirrhosis than in control subjects (0.67 vs. 0.62,  $p < 0.01$ ). 48% (19/40) of patients with liver cirrhosis and normal serum creatinine concentration showed elevated RI levels. There were no significant differences in RI levels between patients with fatty liver disease and controls (0.63 vs. 0.62) [7].

The pathogenesis of elevated RI and subsequent HRS that occurs in Cirrhotics. To summarize, Resistivity indices evaluated by duplex doppler ultrasonography are increased in the early phase of the disease. With development of ascites, a further increase in the resistivity indices occurs.

Early detection of renal vasoconstriction by Doppler predicts future development of HRS in patients with cirrhosis in a prospective study done by Platt et al [8]. According to the study, 55% cirrhosis with elevated RI and normal renal function develops subsequent kidney dysfunction.

We conclude that patients with cirrhosis are at risk of renal deterioration, which cannot be detected by serum urea, creatinine, and glomerular filtration rate. The increase of RI is not only associated with the progress of hepatocellular disease, the development of ascites, portal hypertension but also subsequent development of HRS. Hence, monitoring RI is a non-invasive means of studying early renal hemodynamic alteration in cirrhosis. 55% cirrhosis with elevated RI and normal renal function develops subsequent kidney dysfunction that is 35 patients out of 92 patients.

Development of hepatorenal syndrome in cirrhosis has so many clinical implications in the course of their disease as they carry a poor prognosis. Diagnosis of HRS needs a very high index of suspicion in cirrhotic

patients. Studies have shown that renal RIs are significantly increased in cirrhotic patients as compared with the healthy controls and are also higher in patients with ascites than in patients without ascites.

In our study, the RI values are more in patients with ascites and also in patients having elevated portal pressure. Renal vasoconstriction evaluated by resistivity index is correlated with Child score and MELD score which quantitatively measures the hepatic function in cirrhosis. The RI value was higher among patients under Child–Turcotte–Pugh Score (CTP) class C and with MELD 20-29 indicating as the severity disease increases RI also increases. There are also various studies demonstrating that the RI is not inferior to the MELD score in terms of sensitivity and specificity. At the present scenario, the MELD score is used mainly in the transplantation[9]. But MELD score also indicates the severity of liver disease. It is based on measured variables that include prothrombin time, serum bilirubin and creatinine [10].

Serum creatinine is a major indicator of impaired renal function; but it has disadvantages as it depends more on muscle mass and physical activity [11]. Therefore, renal function based only on the value of serum creatinine can be overestimated in patients with end stage cirrhosis as they have poor muscle mass [11]. Thus, it is still necessary to develop improved prognostic markers feasible in daily practice.

In the study, The Renal resistive index is a non-invasive indicator of hepatorenal syndrome in cirrhotics by Mohsin Aslam, S. Ananth Ram, Ajoy Krishnamurthy Patients with HRS ( $RI \leq 0.77$ ) had jaundice ( $P = 0.001$ ), encephalopathy ( $P = 0.038$ ), massive ascites ( $P = 0.02$ ), raised urea ( $P = 0.0003$ ), creatinine ( $P < 0.0001$ ), bilirubin ( $P = 0.01$ ), SGOT ( $P = 0.016$ ), and serum glutamic-pyruvic transaminase ( $P < 0.0001$ ) when compared to those without HRS ( $RI < 0.77$ ) in a statistically significant manner.

There is no doubt therefore of the usefulness of the RI in predicting HRS in cases of established cirrhosis and which can translate into the early initiation of treatment for impending HRS.

Both the Child–Turcotte–Pugh Score (CPT) and MELD scores were significantly related to the RI (0.03 and  $<0.029$ , respectively). This relationship implies that the RI could also be used to predict which patient is likely to worsen and can, therefore, be used as a prognostic indicator. A similar correlation was found in the study done Popov et al [12].

In our study, we found that RI index is significantly higher in Child Pugh C compared to Child Pugh B (p value-0.03 by Yates equation) and RI index is significantly higher in Child Pugh B when compared to Child Pugh a patients.

### Child Pugh Score

Measure	1 point	2 points	3 points
Total bilirubin, $\mu\text{mol/L}$ (mg/dL)	$<34$ ( $<2$ )	34–50 (2–3)	$>50$ ( $>3$ )
Serum albumin, g/dL	$>3.5$	2.8–3.5	$<2.8$
Prothrombin time, prolongation (s) OR INR	$<4.0$ $<1.7$	4.0–6.0 1.7-2.3	$> 6.0$ $>2.3$
Ascites	None	Mild (or suppressed with medication)	Moderate to severe (or refractory)
Hepatic encephalopathy	None	Grade I–II	Grade III–IV



## Meld Score

MELD=  $3.78 \times \ln [\text{serum bilirubin (mg/dL)}] + 11.2 \times \ln [\text{INR}] + 9.57 \times \ln [\text{serum creatinine (mg/dL)}] + 6.43$ .

## Conclusion

- We conclude that in cirrhotic, renal vascular resistance indices evaluated by duplex Doppler ultrasonography are already increased in the early phase of the disease.
- Development of ascites is associated with a further increase in the resistance indices.
- Renal vasoconstriction evaluated by these indices is correlated with Child score which quantitatively measures the hepatic function in cirrhosis.
- Intrarenal RI measurement is a predictor of renal vasoconstriction and serves to detect early renal function impairment in cirrhotic patients.
- The diagnosis of elevated RI may be taken into account in the clinical management of these patients.
- Patients having higher resistive index had normal creatinine suggesting that normal value of creatinine underestimates the actual scenario in cirrhotic patients.
- We confirm that RI is a non-invasive, economical test that gives useful information and it is used as a prognostic indicator and hence used in the management of cirrhotic patients.
- Elevated RIs even disclose the progress of liver disease before there are gross changes occurring in lab results. Therefore, RI may help in identifying a group of high-risk patients with poor prognosis who require special therapeutic care.
- According to the practice guidelines, cirrhotic undergo ultrasound examination every 6–12 months. Along with ultrasound screening of all cirrhotic patients especially with ascites and PHT to estimate the value of RI by Doppler ultrasound is essentially important as the degree of

intra-renal vasoconstriction can be predicted early before overt HRS develops and so preventive measures should be undertaken.

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