

# Cirrhosis Of Liver: How can Resistivity Index saves life ?

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DOI: 10.29322/IJSRP.10.07.2020.p10344  
<http://dx.doi.org/10.29322/IJSRP.10.07.2020.p10344>

**Abstract- Background :** Hepatorenal syndrome is a well recognized complication of liver cirrhosis . The intrarenal vasoconstriction is an early marker for functional renal failure . It can be assess using Renal artery blood flow test through colour Doppler .

**Aims :** To evaluate non -invasively renal arterial blood flow in patients with cirrhosis of liver by Doppler Ultrasonography .

**Methods :** Between May 2019 to April 2020 , we studied Renal artery blood flow test in 50 liver cirrhotic patients admitted in Rims Ranchi . It is an Observational and Hospital based Prospective study . All the patients underwent standard diagnostic protocol including Blood test and Renal colour Doppler test .

**Result :** Out of 50 patients , 36 were male and 14 were female . Alcohol is the most cause of liver cirrhosis . The resistivity index  $> 0.7$  was found in 17 decompensated and in 3 compensated liver cirrhotic patients with the significant P value  $< 0.001$  .

**Conclusion :** The resistivity index is not inferior in sensitivity and specificity to MELD Score .

**Index Terms-** Cirrhotic Liver Disease , Renal artery blood flow test , Resistivity Index ( RI )

## I. INTRODUCTION

Advanced liver cirrhosis is associated with a poor clinical outcome . Therefore , assessment of prognosis is important in the management of these patients .<sup>[1]</sup> In 2002 , the Model for End - Stage Liver Disease ( MELD ) was introduced for patients undergoing transjugular intrahepatic portosystemic shunt . It is currently used to predict survival in patients awaiting liver transplantation . Patients with liver cirrhosis frequently develop renal dysfunction . The hepatorenal syndrome ( HRS ) , the most serious renal complication , is associated with an extremely short survival time .

The HRS is characterized by renal arterial vasoconstriction, which may precede clinically manifest renal dysfunction . The intrarenal resistance index ( RI ) is the most frequently used parameter to assess intrarenal resistance and is calculated based on Doppler sonographic intrarenal measurements . It is routinely used to diagnose transplant rejection or renal artery stenosis . The RI is calculated as per the formula given below :

( peak systolic frequency shift - lowest diastolic frequency shift ) / peak systolic frequency shift .

On average , renal RI is higher in cirrhotic patients . The normal value of RI is 0.60 - 0.70 and is measured at the arcuate arteries ( corticomedullary junction ) or interlobar arteries ( adjacent to medullary pyramids ) . Increased intrarenal RIs in patients with liver cirrhosis , especially in the decompensated stage , have been described before as compared to healthy controls . Cirrhotic patients with elevated intrarenal RIs tend to develop the HRS leading to a poor prognosis .

## II. ANATOMY

Embryologically, the liver grows as a ventral diverticulum from the junction of foregut and the midgut into the ventral mesogastrium ( the caudal part of the septum transversum ; the cranial part forms the diaphragm ) . The same diverticulum forms the gallbladder and bile ducts as well . The ligamentum teres hepatis is the obliterated umbilical vein , which joins the left portal vein ; the ligamentum venosum is the obliterated ductus venosus , which joins the left portal vein to left hepatic vein . The upper surface of the liver is percussed at the level of the fifth intercostal space . Superior , anterior , posterior and right surfaces of the liver are continuous with each other and are related to the diaphragm and anterior abdominal wall .<sup>[2]</sup>

The anterior surface is separated from the inferior ( visceral ) surface by a sharp anterior ( inferior ) border that is clinically palpable on deep inspiration . The inferior surface is related to the hepatic flexure ( the area where the vertical ascending ( right ) colon takes a right - angle turn to become the horizontal transverse colon ) , right kidney , transverse colon , duodenum and stomach . The gallbladder straddles the undersurfaces of liver segments IVB and V .

There is an H - shaped fissure on the inferior surface of the liver . The right vertical arm of the H is formed by the gallbladder anteriorly and the inferior vena cava ( IVC ) posteriorly ; It is incomplete , with the caudate process between the two . The left vertical arm of the H is formed by the ligamentum teres hepatis in front and the ligamentum venosum behind . The transverse limb of the H is the porta hepatis ( hilum ) , a 5 - cm transverse fissure ( slit ) on the undersurface of the liver with the quadrate lobe in front and the caudate lobe behind . It contains the common hepatic duct ( CHD ) in front and to the right , the proper hepatic artery in front and to the left , and

the portal vein behind, enclosed in the hepatoduodenal ligament (HDL), composed of 2 layers of lesser omentum. [Figure 1]

### Blood Supply

The liver has a unique dual blood supply (about 1500 mL/min) both from the proper hepatic artery (20-40%) and from the portal vein. [3]

### Cirrhosis of liver

Cirrhosis of liver is a continuous, progressive and anatomically diffuse process characterized by fibrosis and distortion of the liver parenchyma with formation of nodules, resulting in decreased function of the liver and increased resistance to flow of portal venous blood. This process of cirrhosis is generally irreversible in the late stages and liver transplantation is the only treatment option in the advanced stage. But it is to be noted that certain conditions causing cirrhosis may respond to treatment of the underlying cause even resulting in reversal of the process in the early stages. This peculiarity is seen in cirrhosis caused by hepatitis C, alcohol, iron overload and obesity. [4] Cirrhosis is the end stage of chronic injury, inflammation and destruction and regeneration of the hepatocytes, inflicted by various conditions. The pathological features include the development of excessive fibrosis along with nodular regeneration of the parenchyma, finally culminating in complete alteration in the architecture, and blood flow through the liver. The induction of the process of fibrosis occurs with the "activation of hepatic stellate cells, leading to the formation of increased amounts of collagen and other extracellular matrix components"

As the function progressively decreases and portal hypertension develops secondary to the altered portal blood flow, various complications of cirrhosis set in and the survival of the patients is very much shortened

In India and most of the developing countries, the most common etiologies for development of cirrhosis are:

1. Alcoholic liver disease
2. Viral hepatitis.

Whereas in developed countries the common causes include: [5]

- Non alcoholic fatty liver disease
- Alcoholic cirrhosis
- Viral cirrhosis (hepatitis C)
- Other less frequent causes include:
- Primary and secondary biliary cirrhosis
- Autoimmune hepatitis

- Primary sclerosing cholangitis
- Wilson disease

### Pathogenesis

Induction of fibrosis occurs with activation of hepatic stellate cells to myofibroblasts resulting in the development of increased amounts of collagen and other components

of the extracellular matrix leading to architectural distortion in turn resulting in decrease in function and mass. [6]

### Clinical Features

Patients may present to the clinic for the first time with the complications of cirrhosis or may be asymptomatic and incidentally be identified during medical checkup for unrelated causes or because of abnormal liver function tests.

In clinical terms, cirrhosis is classified into: Compensated form and Decompensated form.

### Compensated Cirrhosis :

At this stage, the cirrhotic process of the liver is not severe enough to alter the function significantly and so the patients may be asymptomatic or present with non-localizing manifestations or may be picked incidentally due to alteration in biochemical parameters or imaging studies. [7] Patients may have fatigue, anorexia, weight loss, flatulence, dyspepsia, abdominal pain. On examination, palmar erythema, pedal edema, spider naevi, may point towards cirrhosis. Abdominal examination may reveal an epigastric mass which is the enlarged left lobe of the liver and splenomegaly. Biochemical tests are usually within normal limits in this group. The most common LFT abnormality in this group include mildly elevated transaminases, or gut. [8] Confirmation is by liver imaging or liver biopsy. Factors like bacterial infection, trauma, or medications, surgery may precipitate decompensation in compensated cirrhosis.

### Decompensated Cirrhosis :

These patients present with ascites, jaundice, altered sensorium, and bleeding manifestations.

### Symptoms :

Presentation in these patients may be with features of jaundice, pedal edema, abdominal distension, Upper GI bleed most commonly melena, hematemesis, pruritus, altered sensorium ranging from sleep disturbances to florid confusion and coma because of hepatic encephalopathy. [9] In women, menstrual irregularities are common due to anovulation. Men, may manifest hypogonadism in the form of impotence, loss of sexual drive, testicular atrophy and infertility.

### Hepatorenal Syndrome

Hepatorenal syndrome is the term attributed to the renal impairment which develops in patients with end stage liver cirrhosis or those with acute fulminant liver failure which is both reversible and only functional without any anatomical alteration. It is characterized by marked reduction in glomerular filtration rate and renal plasma flow (RPF), without any other contributing cause to renal failure. The pathophysiology behind HRS is severe vasoconstriction in the renal vascular bed with paradoxical peripheral arterial vasodilation. The function of the renal tubules is normal and there is no proteinuria or abnormal histology in the kidneys.

Type 1 HRS is defined as the “acute onset of rapidly progressive oliguric renal failure unresponsive to volume expansion with the doubling of serum creatinine value to more than 2.5 mg/dl within 2 weeks duration”. However as recently proposed a diagnosis of type 1 HRS should be considered whenever there is fulfillment of criteria defining acute kidney injury by an abrupt increase in serum creatinine more than or equal to 0.3 mg/dl or an increase of more than 1.5 times from the baseline. This is to ensure that treatment is not delayed unnecessarily, as baseline creatinine is a predictor of HRS reversal with vasoconstrictors.

Type 2 HRS progresses more slowly and the cut off of serum creatinine is 1.5 mg/dl. A precipitating factor frequently is identified in type 1 HRS, whereas there are no such factors involved in development of type 2 HRS and it clinically manifests as refractory ascites.

### Investigation

1. Complete blood count
2. Liver Function Test
3. Ultrasound Abdomen - Renal artery blood flow test
4. Liver Fibroscan
5. Liver biopsy

### Renal Doppler Ultrasonography

Renal vasoconstriction is the major pathology behind HRS.

This renal vasoconstriction can be assessed using Doppler ultrasound of the renal arteries by using an index called renal resistive index (RI). This value is derived from the spectral waveforms corresponding to the flow at the renal arteries and is determined using the formula:

**Renal Resistive Index** =  $\frac{\text{Peak systolic frequency shift} - \text{Lowest diastolic frequency shift}}{\text{Peak systolic frequency shift}}$

Peak systolic frequency shift

RI in cirrhosis is increased when compared to the normal population. And studies have shown that a high RI value (more than 0.7) can be documented in cirrhotic patients even in whom RFT is normal.<sup>[9]</sup>

It has also been shown that normally RI exhibits a gradient decreasing from the hilum towards the outer cortex. In cirrhotic patients with diuretic responsive ascites this gradient is well maintained. Whereas as the severity increases and in cirrhotic patients with refractory ascites this gradient is lost and the RI at the level of the cortex measured in interlobular arteries is also high suggesting renal cortex vasoconstriction. This happens even before serum creatinine begins to raise. Thus in cirrhotic patients an increased RI in spite of normal values of serum creatinine, implicates that they are at a greater risk for development of renal dysfunction and elevation of serum creatinine. With treatment of first, RI value reduces. Similarly liver transplantation also decreases the RI. Thus renal RI assessed using Doppler ultrasound may be used as an early marker for renal impairment in cirrhosis patients.

### Complication :

Portal hypertension

Hepatopulmonary syndrome  
Portopulmonary hypertension  
Malnutrition  
Gastroesophageal varices  
Portal hypertensive gastropathy  
Splenomegaly, hypersplenism  
Ascites

Spontaneous bacterial peritonitis  
Hepatorenal syndrome  
Type 1

Type 2

Hepatic encephalopathy  
Hepatopulmonary syndrome  
Portopulmonary hypertension

### Material and Methods

#### Source of Data

The study was conducted on 50 consecutive patients admitted to Rajendra institute of medical sciences, Ranchi during the study period.

#### Inclusion criteria

Liver cirrhosis patients of any etiology as diagnosed by clinical, biochemical and imaging methods. Abdominal USG and Renal Doppler US, was performed and interpreted by single investigator according to standard protocol. Hepatic parameters like Child Pugh Score, MELD score was calculated according to standard formulas based on which degree of liver damage will be evaluated.

#### Exclusion criteria

1. Diabetes
2. Hypertension
3. Nephrotoxic medication intake
4. Acute GI bleeding and shock
5. Ultrasonographic evidence of obstruction or parenchymal renal disease
6. Sepsis and Autoimmune Hepatitis

#### Lab Investigation

- a) Complete blood count
- b) Liver function test (LFT)
- c) Renal function test (RFT)
- d) PT- INR
- e) Serum albumin
- f) Ultrasound abdomen
- g) Renal artery duplex Doppler

#### Design of Study

Hospital based Prospective study and Observational study

#### Period of Study

One Year Study : 1<sup>st</sup> May 2019 to 30<sup>th</sup> April 2020

**Consent** : Individual / caretakers written and informed consent.

**Participants** : 50 Liver cirrhotic patients admitted in Medicine ward at RIMS Ranchi

### Results

Our data found 35 patients were decompensated and 15 patients were compensated liver cirrhotic disease . [ Table 1 ] Out of which 17 Decompensated liver cirrhotic patients had RI more than 0.7 . [ Table 2 ] The P value is significant I. e <0.001 . And 42 patients were discharged and followed up well . Remaining 8 dead patients had RI more than 0.7 . [ Table 3 ] , [Table 4 ]

### Discussion

Our study confirms that the RI , based on sonographic measurements of intrarenal resistance , is an effective , noninvasive , economical functional test that provides useful information for the prognosis and management of cirrhotic patients .

Therefore , the RI may help identify a group of high - risk patients with a poor prognosis that require special therapeutic care .

### III. CONCLUSION

Liver cirrhosis is characterized by complex changes in systemic hemodynamics . Especially renal dysfunction frequently complicate the clinical course of this disease . Doppler Ultrasound measurement of intrarenal resistance can estimate renal blood flow . Serum creatine is an indicator of impaired renal function ; however , it has disadvantages as it depends on muscle mass and physical activity . The elevated RI may even disclose progress of the liver disease before changes in laboratory results . The cirrhotic patients should undergo Ultrasonography examination every 6 - 12 months .

### Financial Support And Sponsorship

### Tables :

#### 1. Compensated Vs Decompensated Form

Compensation Status	No. Of Cases	Percentages ( % )
Compensated	15	30
Decompensated	35	70
Total	50	100

**Comments** : Out of 50 Cirrhotic patients 35 patients were decompensated and rest were compensated liver cirrhotic disease .

#### 2. RI Vs Compensation Status

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<http://dx.doi.org/10.29322/IJSRP.10.07.2020.p10344>

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Nil

### Conflict Of Interest

There are no conflict of interest

### Abbreviation

1. RI - Resistivity Index
2. HRS - Hepatorenal Syndrome  
MELD Score - Model For End Stage Liver Disease

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RI Vs Compensation Status	Compensated	Decompensated
< 0.7 (30)	12	18
> 0.7 (20)	03	17
	3/30 Vs 12 / 30	
P Value	< 0.001	

**Comments :** RI was > 0.7 in 17 liver cirrhosis patients with Decompensated liver cirrhotic patients while RI > 0.7 in only 3 patients with Compensated liver cirrhotic patients . P value was < 0.001.

### 3. Death Vs Alive

Status	No. Of Cases	Percentages (%)
Death	08	16
Alive	42	84
Total	50	100

**Comments :** 42 liver cirrhotic patients were discharged and followed up well .

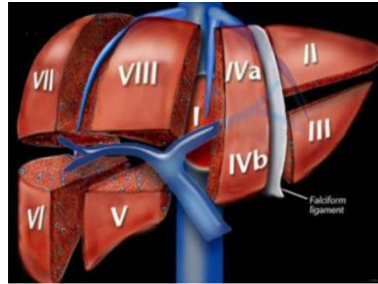
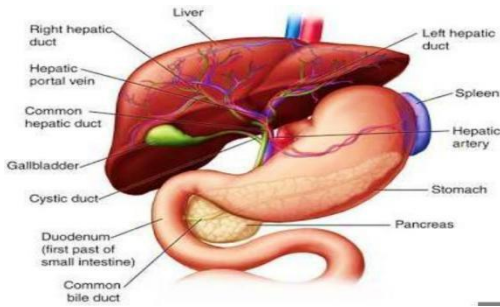
### 4. RI Vs Death Vs Alive

RI Vs Status	Death	Alive
< 0.7 (30)	00	30
> 0.7 (20)	08	12
	0 / 30 Vs 08 / 20	
P Value	< 0.001	

**Comments :** 8 patients were dead . All the 8 patients had RI > 0.7 .

P value was < 0.001 . Renal Resistivity Index correlated strongly with short term in - hospital mortality .

### Figure 1 Liver Anatomy and Its Segments



## Acknowledgement

We have been able to work on and complete this article, I would like to sincerely thank everyone who has been instrumental in making it a possible.

Words fail to express my deep sense of gratitude towards my guide Prof Dr. Umesh Prasad MD General Medicine, Ass. Prof Dr D K Jha MD Medicine and Ass. Prof Dr Gregory Minz MD Medicine for their unfailing belief in me. We have been blessed to work under his guidance and learnt lots of things from him. He encouraged and guided me from the inception of this project in 2020 till the very end and without whom it could not have come to fruition.

We want to thank our family for inspiring us to push our limit. Last but not the least I would thank all the patients of the study who served as the backbone and without their support the study would have been possible.

Thank you

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