

## A Study of renal hemodynamics in chronic liver disease

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### Abstract

**Aim :** 1) To estimate renal resistive (RI) index and pulsatility (PI) index in chronic liver disease 2) To study the association between RI, PI and severity of liver disease, esophageal varices.

**Methods:** 57 consecutive CLD outpatients were included in study, detailed history and lab data was collected, all patient underwent Doppler study of renal artery to estimate RI and PI and gastroscopy Results: both mean RI and mean PI higher in CLD 0.72, 1.48 compared to normal 0.62, 1.00. RI and PI also showed a good correlation with severity of liver disease mean RI in child A 0.64 +/- 0.025, child B 0.71 +/- 0.019, child C 0.78 +/- 0.036 (Kruskal-wallis  $H=45.3, p<0.001$ . mean PI also showed a similar finding, mean PI in child A 1.15 +/- 0.086, Child B 1.38 +/- 0.086, Child C 1.83 +/- 0.180. Kruskal-wallis  $H=47.8, p<0.001$ . **Conclusion:** 1) RI and PI are higher in CLD. 2) RI and PI show a significant positive correlation with severity of liver disease 3) RI and PI may predict the presence of varices

**Keywords):** CLD, doppler study, PI, RI, severity

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### I. Introduction

Chronic liver disease with PHT causes generalized vasodilatation with renal vasoconstriction, which leads on to RAS activation and volume overload. Renal Doppler study using resistivity index and pulsatility index can be used to measure level of vasoconstriction. As the severity of liver disease increases, previous studies have shown RI and PI increases with increasing severity of liver disease. We wanted to study the same in south Indian population and investigate if the same could be used to predict presence of varices.

#### Aim

- 1) to estimate renal resistivity index (RI) and pulsatility index in chronic liver disease patients
- 2) to study the association between severity of liver disease and resistivity index.
- 3) to study the association between renal resistivity index and presence of esophageal varices

### II. Study and materials

#### Study design

prospective cross sectional study.

#### Inclusion criteria

Patients with who were diagnosed to have chronic liver disease (CLD) by combination of clinical, radiological, histological, and endoscopic features.

#### Exclusion criteria

Patient with elevated serum creatinine, intrinsic renal disease, diabetes mellitus, hypertension, active GI bleed, malignancy, infections not consented were excluded from study

#### Informed consent

All patients were briefed about study and written consent was taken from patients

#### Study period

August 2016 to July 2017

#### Study method

All eligible patients who were included in the study underwent a thorough physical examination following detail history elicitation. All patients had their basic metabolic panel tested. All of them underwent

gastroscopy followed by Doppler study of renal arteries. esophageal varices were graded according to modified packet classification. doppler was done by using 3.75Mhz convex transducer placed over intralobular artery along the border of medullary pyramid and recording blood velocity waveform. RI and PI was calculated using standard formulas  $RI = \frac{\text{mean systolic velocity} - \text{end diastolic minimum velocity}}{\text{end diastolic minimum velocity}}$  and  $PI = \frac{\text{mean systolic velocity} - \text{end distolic minimum velocity}}{\text{mean velocity}}$ . liver disease was graded using child grading system in to A,B, C grades, results were tabulated and stastiscal analysis done using epi info window software. RI of  $0.62 \pm 0.05$  and PI of  $1.00 \pm 0.12$  were taken as normal values in this study which was estimated from a previous study,

### III. Results

A total of 57 subjects participated in the study. The mean age of the patients was 44, with a range from 30-75 years. Of the 57 patients, 44 were male and 13 were female.

**Table 1 Demographic profile**

Age	(a) Mean	49
	Median	49
	Standard deviation	12.4
	Range	30 to 75
Sex	Male	44 (77%)
	Female	13 (23%)
Child	A	12 (21%)
	B	26 (46%)
	C	19 (33%)

Based on clinical and data from investigations 12 patients were categorized to Child A, 26 to child B, 19 to Child C. HBV (35%) infection was found to be the commonest cause found in 20 patients, alcohol abuse was seen in 18 (31%) patients, HCV (17.5%) were detected in 10 patients. Other causes include BCS, PBC, AIH, unknown causes.

**Table 2 etiology**

ALCOHOL	18 (31%)
HBV	20(35%)
HCV	10(17.5%)
OTHERS AND COMBINED	9(15%)

Resistive index and the Pulsatility index was found to be 0.72 with a standard deviation of 0.06, 1.48 with a standard deviation of 0.24 in cirrhosis patients which is higher than in normal population.

**Table 3 RI and PI in cirrhosis**

RI	(b) Mean	0.72
	Median	0.72
	Mode	0.73
	Standard deviation	0.06
	Range	0.60 to 0.85
	% normal ( $0.62 \pm 0.05$ )	13 (23%)
PI	Mean	1.48
	Median	1.40
	Mode	1.40
	Standard deviation	0.29
	Range	0.99 to 2.20
	% normal ( $1.00 \pm 0.12$ )	5 (9%)

Of these patients only 13(23%) patients had RI in normal range. while only 5(9%) patients have Pulsatility index in normal range. On subgroup analysis of patients in different grade of cirrhosis.

**Table 4 RI in different grades**

RI	A (n=12)	B (n=26)	C (n=19)
Mean	0.64	0.71	0.78
Median	0.65	0.71	0.78
Mode	0.65	0.73	0.76
Standard deviation	0.025	0.019	0.036
Range	0.60 to 0.68	0.67 to 0.73	0.71 to 0.85
% normal ( $0.62 \pm 0.05$ )	11 (92%)	2 (8%)	0 (0)

Kruskal-Wallis H (equivalent to Chi square) =45.3; p< 0.001

The mean value of RI was found to be as follows.

Child A 0.64 with SD of 0.025, child B 0.71 with standard deviation of 0.019 Child C 0.78 with standard deviation of 0.036.

Among those 12 patients in Childs A group it was found 11(92%) patients had RI in the normal Range. Only 2 out of 26 (8%) Grade B cirrheses, none of patients in Child C had RI in the normal range.

Resistive index showed a significant increase With increasing severity of cirrhosis. Kruskal- Wallis H value was calculated to study the correlation between resistive index and severity of cirrhosis. It was found to be 45.3 with a Pvalue< 0.0001 which is statistically significant. The mean Pulsatility index was 1.15 with standard deviation of 0.086 in child A cirrhosis, 1.38 with standard deviation of 0.086 in Child Cirrhosis, 1.83 with standard deviation of 0.180.

**Table 5 PI in grades of cirrhosis**

Mean	1.15	1.38	1.83
Median	1.16	1.38	1.78
Mode	1.20	1.40	1.69
Standard deviation	0.086	0.086	0.180
Range	0.99 to 1.30	1.29 to 1.55	1.60 to 1.69
% normal (1.00 ± 0.12)	5 (42%)	0 (0)	0(0)

Kruskal-Wallis H (equivalent to Chi square) =47.8; p < 0.001

Pulsatility index was within the normal range in 5 out of the 12 patients (42%) in Child A group while none of the 26 patients in ChildB, 19 in ChildC had PI in the normal range. Esophageal varices were seen in eight patients while 3 did not have varices in childA cirrhotic patients. All the 3 patients who did not have esophageal varices had a normal resistive index.

**Table 6 oesophageal varices and RI level**

RI level	Grade of varices					Total
	0	1	2	3	4	
Within normal range	3	6	3	0	1	13
Outside normal range	0	15	22	6	1	44
Total	3	21	25	6	2	57

RI value and presence of oesophageal varices among ChildA graded cirrhosis patients (N=8) are strongly and positively correlated (correlation coefficient is 0.67) However, this observation is based on just eight patients. This suggests a positive correlation between presence of esophageal varices and resistive index.

Out of the 57 patients in this study 45 patients were treated with diuretics. 40 (70%) patients responded to diuretics. while 5(9%) patients did not respond to diuretics.

**Table 7 response to diuretics by RI level**

RI level	Response to diuretics		Total
	Yes ; Respond to diuretics	Resistant to diuretics	
Within normal range	2	0	2
Outside normal range	38	5	43
Total	40	5	45

38 out of 40 patients who had adequate response had RI outside normal range. While only 2 patients had RI in the normal range. Among the non responder all the 5 patients RI were outside normal range.

**Table 8 Mean RI levels and diuretic response**

RI level	Mean (Standard deviation)
Respond to diuretics	0.73 (0.036)
Resistant to diuretics	0.83 (0.016)

Kruskal-Wallis H = 13.2; p value=0.0003

The mean RI was 0.73 (standard deviation of 0.036) and 0.83 (Standard deviation of 0.010) in diuretic responsive and non responsive group. Krushal -Wallis H value for correlation between mean RI and diuretic response was 13.2 with p value of 0.0003 which is stastically significant

#### **IV. Discussion**

This study was carried out in a tertiary level hospital. Most of the patients are from north Tamilnadu and few from Andrapradesh. Mean age of the patients in this study was 49 +/- 12. Mean age of patients with cirrhosis in study by Joshi et al<sup>1</sup> was 45 which is similar to this study. Out of 57 patients in this study 44(77%) were male and 13 (23%) were female. Male female ratio is 3:1. S.K.Sarin et al<sup>24</sup> reported a similar sex distribution in their study. The causes of cirrhosis vary in different places.

The most common cause of cirrhosis in this study was Hepatitis B Virus (35%) infection followed by ethanol and Hepatitis C Virus. Joshi et al<sup>1</sup> have reported similar figure in their study HBV (30%), alcohol (20%), HCV (14%). The higher number of patients in this study in alcohol group could be due to referral bias. As all patients with history of alcohol abuse are referred from Institute of mental health for evaluation of hepatocellular function to our hospital. Prevalence of HCV is comparable in both studies.

Marota et al<sup>2</sup> and Platt et al<sup>3</sup> were among first authors to show RI is increased in patients with nonazotemic functional renal failure in addition to other causes like ATN, renal arterial thrombosis<sup>1,15,16</sup>.

Renal arterial vasoconstriction is said to be the main pathophysiology in volume overload. This was ascribed to high levels of vasoconstrictors. N.Ljubcic et al<sup>20</sup> showed that RI is increased in cirrhosis. Further studies by Masohika Koda<sup>19</sup> have shown that RI also increases with progressive grading of cirrhosis. This study also shows a similar finding. The mean RI value is 0.72 +/- 0.06 and PI is 1.48 +/- 0.29 which is higher than normal values (0.57-0.67, 0.88-1.12). Masohika Koda et al have also showed that this increasing value of RI is associated with increasing level of serum vasoconstrictors rennin, aldosterone, and epinephrine. This study also shows mean RI & PI to increase with increasing grade of cirrhosis. Mean RI in Child A, Child B, Child C are 0.64 +/- 0.025, 0.71 +/- 0.019, 0.78 +/- 0.036 respectively, mean PI are 1.15 +/- 0.086, 1.38 +/- 0.086, 1.38 +/- 0.180.

Kruskal-Wallis N value for correlation between severity of cirrhosis and RI & PI values was significant with a p value of < 0.001. Out of the 57 patients in this study 45 patients were treated with diuretics. 70% responded adequately to diuretics, 9 percent of patients were non responders according to definition of Ljubcic<sup>20</sup>. The prevalence of diuretic resistant ascites is accepted to be around 10%. Gatta et al<sup>11</sup> have reported a prevalence of 9%. A study by Perez -Ayuso<sup>25</sup> also report a prevalence of 10%. Definition used in this study is not same as International ascites club definition. Sungaila et al<sup>10</sup> have showed patients who do not respond to 200mg of spironolactone, and 120mg of furosemide are unlikely to respond to dose escalation. Ljubcic has based his definition on this study. Further studies are needed to know if patients with inadequate response represent the classical diuretic resistant ascites.

This study also shows that a high value of RI is noninvasive predictor of inadequate response to ascites. However this observation is based on a small cohort. Studies involving larger sample is needed to confirm this finding.

Analysis of Child A cirrhosis subgroup shows that an elevated RI value is seen in patients with esophageal varices. Agostino Colli et al<sup>21</sup> have reported this association in their study. This is an important observation as this indicates renal vasoconstriction precede development of ascites in cases of portal hypertension. RI could also correlate with portal hypertension. Levy et al<sup>26</sup> and Schrier<sup>27</sup> et al have also reported an similar observation in their studies

#### **V. Conclusion**

- 1) RI and PI are abnormal in most patients with cirrhosis.
- 2) RI and PI show positive correlation with increasing severity of liver disease.
- 3) RI and PI are non invasive predictors of esophageal varices.
- 4) RI and PI may help in predicting response to diuretics

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