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STUDY OF RENAL RESISTIVITY INDEX IN LIVER CIRRHOSIS IN PREDICITNG THE INCIDENCE OF HEPATORENAL SYNDROME

Radio Diagnosis

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ABSTRACT

Background: Cirrhosis of liver is the tenth leading cause of death in India. The Hepatorenal syndrome (HRS) is associated with a high mortality. The intra-renal resistivity index (RI) is considered one of the sensitive predictive markers of development of HRS. The present study is undertaken to compare RI in healthy controls versus patients with liver cirrhosis and assess its value for predicting subsequent renal and hepatic status. **Aim:** To Measure Renal Resistivity Index (RI) in patients having liver cirrhosis and estimate the incidence of Hepatorenal Syndrome. **Methods:** 50 patients of liver cirrhosis who met the inclusion criteria from Navodaya Medical College & Hospital, Raichur were studied from January 2021 to June 2022. Detailed examination was done. Ultrasound abdomen and renal artery doppler was done.Liver and renal function test,and other investigations were done. RRI was calculated. **Results:** This study included 50 subjects with liver cirrhosis. In our study, 10% of subjects developed HRS during the follow up period of 3 months. 6% of them showed increased RI (> 0.7), while 4% showed normal RI. ($p < 0.002$). In those subjects with a normal creatinine during follow up, RI was elevated in 8% of the subjects ($p = 0.002$). Mean RI in subjects who developed HRS was 0.77 ± 0.11. Mean RI in patients who did not have HRS was 0.61 ± 0.04. **Conclusion:** In our study, we noted that intrarenal RI values at the time of admission were significantly increased in cirrhotic patients who developed HRS during the 3 months follow up. But, 4% patients with normal RI also developed HRS, which calls for careful vigilance and repeat Doppler screening at intervals of all liver cirrhosis patients as an early warning tool and prognostic indicator for development of HRS.

KEYWORDS

Hepatorenal syndrome, Resistive index, Liver cirrhosis

INTRODUCTION

Cirrhosis of liver is the tenth leading cause of death in India and a major cause of disease burden among the population and is associated with a poor clinical outcome.[1] Therefore assessment of prognosis is important in the management of these patients.

Global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5% of the general population [2,3,4] Globally, alcohol, NASH and viral hepatitis currently are the most common causative factors.

According to WHO, about 46% of global diseases and 59% of the mortality is because of chronic diseases and almost 35 million people in the world die of chronic liver diseases[5] .

HRS is a reversible functional renal impairment that occurs in patients with advanced liver cirrhosis or those with fulminant hepatic failure. It is characterized by marked reduction in GFR and renal plasma flow (RPF) in the absence of other cause of renal failure.

According to Fede et al[6] approximately 20% of cirrhotic patients with diuretic-resistant ascites potentially develop HRS.The frequency of HRS in fulminant hepatic failure and severe acute alcohol-related hepatitis has been reported to be as high as 55% and 30%, respectively. Most patients with HRS are in their sixth or seventh decade with a male preponderance.

Type I HRS is characterized by acute onset and rapidly progressing kidney failure with a doubling of serum creatinine to > 2.5 mg/dL (corresponding to a 50% reduction in the creatinine clearance rate) in less than 2 weeks, usually associated with multiorgan damage. The prognosis is poor with only 10% of patients surviving longer than 90 days.[7]

This type of HRS can develop spontaneously but more often tends to follow a precipitating event, mostly spontaneous bacterial peritonitis or other infections like pneumonia, urinary tract infections or cellulitis. Other potential risk factors include viral, alcoholic, toxic or ischemic hepatitis (*e.g.*, TIPS), gastrointestinal bleeding and surgical procedures.

Type II HRS represents the final kidney response to hemodynamic impairments in cirrhosis. This type presents as a less severe and more gradual decline in renal function associated with refractory ascites. The increase in creatinine is gradual with mean values of 1.5-2.0 mg/dL. Type II HRS predisposes patients to the development of type I HRS after a precipitating event. The average survival rate is six to eight months after onset.

Diagnostic Criteria For Hepatorenal Syndrome[8]

- Cirrhosis with ascites
- Serum Creatinine > 1.5 mg/dL
- Absence of shock
- No improvement of serum creatinine (decrease to a level of 1.5 mg/dL or less) after at least 2 days of diuretic withdrawal and volume expansion with albumin (The recommended dose of albumin is 1 g/kg of body weight per day or up to a maximum of 100 g/d)
- No current or recent exposure to nephrotoxic drugs
- Absence of parenchymal disease as indicated by proteinuria > 500 mg/d, microscopic haematuria (50 red blood cells per high power field) and abnormal renal ultrasonography)

Renal Resisitivity Index

The Doppler-derived renal resistive index has been used for years in a variety of clinical settings such as the assessment of chronic renal allograft rejection, detection and management of renal artery stenosis, evaluation of progression risk in chronic kidney disease, differential diagnosis in acute and chronic obstructive renal disease, and more recently as a predictor of renal and global outcome in the critically ill patient.

To perform a correct measurement of RI, a standardized study protocol is required.

- The first phase is to detect the correct B-mode acoustic window with a precise regulation of focus and gain.
- The colour Doppler functions are set for a study focused on interlobar arteries, that is, the highest gains possible, the use of the lowest filters and a low pulse repetition frequency (PRF) of 1–1.5 kHz that must be preferred while always limiting the aliasing phenomenon.
- With the activation of the pulsed wave Doppler module, the sample volume is placed in the lumen of the vessel and the speed–time curve is recorded.
- The size of the sample volume must be set for interlobar arteries (approximately 1–2 mm) in order to avoid artefacts due to under or over sampling.

- As for the colour Doppler, a careful adjustment of pulsed wave Doppler functions (PRF 1.5–3 kHz, gain, depth, filter wall and Doppler frequency) is crucial to obtain a correct speed–time curve. As resistance to blood flow progressively increases from the hilar arteries toward the more peripheral parenchymal vessels, it is generally recommended that sampling for RRI should be done at the level of the arcuate or interlobar arteries, adjacent to medullary pyramids
- Multiple Doppler sampling in three different areas of the kidney (*i.e.* upper, mid or lower pole) at the interlobar or arcuate arteries level has been shown to be more effective than a single sampling: by increasing the number of samples, by minimizing the intra- and interoperator variability and considering the RI to be a highly reproducible test.
- The correct value of the RI is the arithmetic average obtained from the measurements.
- RRI = (peak systolic velocity—end diastolic velocity)/(peak systolic velocity).

Normal values are reported between 0.60 and 0.70 with the difference between both kidneys mostly being less than 5%.

RRI in HRS

Renal vasoconstriction occurs early and is a marked manifestation of HRS. Renal Doppler ultrasound can measure the renal resistive index (RRI), a sonographic index that reflects alterations in blood flow profile of the intrarenal arcuate or interlobar arteries. It reflects the relation between the decline in speed loss of flow ("flow velocity") between the peak of systole and the end of diastole in (renal) blood vessels:

Maroto et al.[9] investigated 32 cirrhotic with ascites. The subgroup of 17 cirrhotic patients with renal failure showed elevated RIs of 0.740.01.

In a study conducted by Vijayasundaram D et al[10], out of the 49 cirrhosis with ascites patients 45 were showing elevated RI, 4 were within normal range. Among 26 cirrhosis without ascites patients, 18 were showing elevated RI, 8 were within normal range. RI was increased in both cirrhosis with and without ascites.

Dorde C et al[11] studied a group of 41 Alcoholic cirrhosis (65.1%) and 22 Viral cirrhosis (34.9%) patients. RI was significantly higher in cirrhotic patients than in controls (P = 0.005).

METHODOLOGY

Study Design: Hospital based cross sectional study

Source Of Data:

Primary source of data includes 50 subjects >18 years admitted with liver cirrhosis in Navodaya Medical College ,Raichur from January 2021 to June 2022.

At the time of the baseline visit, all patients will undergo sonographic examination of the liver and kidneys, including Doppler evaluation of intrarenal resistance.

- Ascites will be graded as mild, moderate or severe based on sonography.
- Renal function tests will be done on D, D2, D3 and 3 months of follow up.
- RI will be calculated using the formula: peak systolic velocity – end diastolic velocity/peak systolic velocity, and the mean value of three measurements at each kidney will be considered. An RI value 0.60 ± 0.01 (mean ± SD) will be taken as normal with a value of 0.70 being considered the upper normal.

Secondary source of information from published articles, journals, books, related websites are used in planning, developing synopsis and dissertation as a supporting document.

Inclusion Criteria

Patients > 18 years admitted with liver cirrhosis.

Exclusion Criteria

Patients with:

- Ongoing HRS
- Overt malignant disease
- Spontaneous bacterial peritonitis
- GI bleeding
- Diabetic nephropathy
- Any acute illness at the time of baseline visit

Sample Size

With the prevalence of development of HRS in liver cirrhosis being 5%, level of significance 5% and allowable error of 10%, sample size is estimated to be 50.

Statistical Analysis

All the data will be expressed as mean standard deviation. Statistical analysis will be performed by using SPSS. Statistical significance will be shown by Chi-square test. Variables were considered to be significant if p<0.005.

RESULTS

- A total of 50 patients with liver cirrhosis were included in the study. Mean age in the study population was 46.6 ± 11.9 years.Mean age among males was 45.5 ± 10.8 years. Mean age among females was 56±18.5 years.
- Among the 50 subjects in the study, 45(90%) were males and 5(10%) were females. The ratio of male: female was 9:1
- In our study, CLD stigmata was present in 60% of the subjects. In 92% of the patients in our study, cirrhosis of liver was attributed to alcohol while the remaining 8% had other causes among which were - Hep B infection (4%), NAFLD (2%) and others (1%).

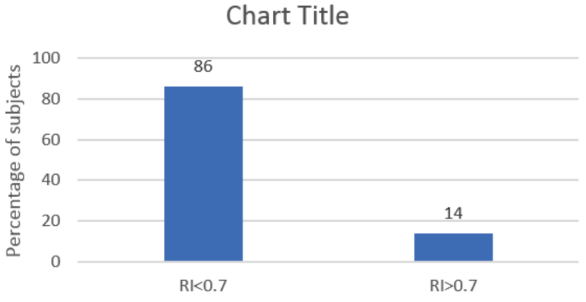

Figure 1: Distribution Of Subjects According To Ri

86% of subjects had an RI <0.7 and 14% had RI>0.7. This shows 14% of them had an abnormal RI in our study.
Mean RI in the total study population was 0.649 ± 0.065.

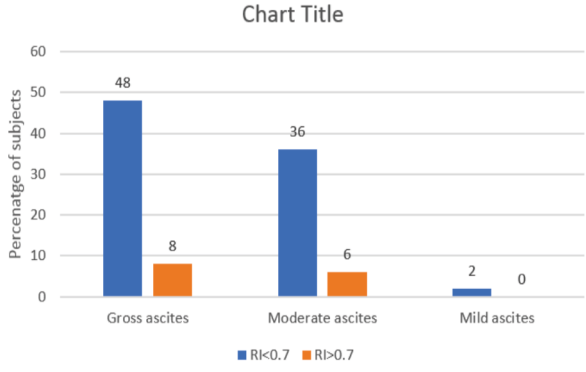

Figure 2: Correlation: Ri & Ascites

- In our study, out of 7 patients who had a RI of > 0.7, 4 (8%) of them had gross ascites, while 3 (6%) had moderate ascites.
- Among subjects having a RI<0.7, 24(48%) of them had gross ascites while 18(36%) of them had moderate ascites.

This shows that those who had greater degree of ascites had higher chance of developing hepatorenal syndrome, but this was statistically not significant(p<0.92).

- Among 10% subjects who developed HRS during the follow up period 4% of them had an RI of < 0.7, while 6% of them had an RI of > 0.7. This shows those subjects with higher RI had higher incidence of developing hepatorenal syndrome (p <0.002).
- In those subjects with a normal creatinine during follow up, RI was elevated in 8% of the subjects, this was statistically significant (p < 0.002).

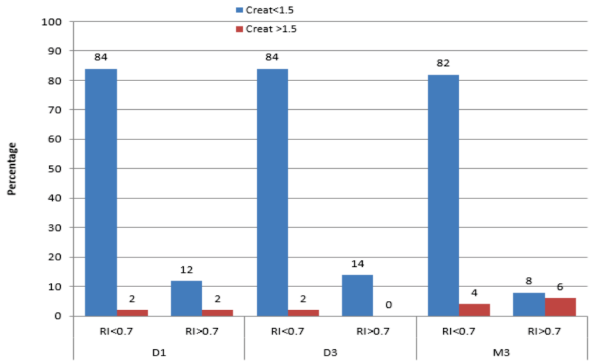

Figure 3: Correlation: Ri And Creatinine Follow-up – Development Of Renal Dysfunction – Hrs

DISCUSSION

Diagnosis of HRS needs a high degree of suspicion in cirrhotic patients. Cirrhotic patients with elevated RI have impaired short and long-term survival and are at risk of developing HRS.

Doppler ultrasound measurement of intra-renal resistance can quantify renal blood flow and it directly co-relates with portal pressure. Patients with decompensated liver disease but normal value of serum creatinine can have elevated RI.

In our study, patients who developed an elevated RI, 8% had gross ascites while 6% had moderate ascites (statistically not significant). In a study by Mohsin Aslam et al, patients who developed an elevated RI, 14.2% had moderate ascites while 37.5% had gross ascites and this had a positive correlation ($p = 0.02$).

In our study 5 of the patients (10%) developed HRS during the follow up period of 3 months. Mean RI in subjects who developed HRS was 0.77 ± 0.11. Mean RI in patients who did not have HRS was 0.61 ± 0.04. Three of them showed increased RI (> 0.7) while 2 of them showed normal RI. This value was statistically significant ($p < 0.002$).

In a study by Platt et al, out of 21 subjects who developed HRS, 20 had an elevated RI as compared to 1 who had a normal RI, which was statistically highly significant ($p < 0.001$). Mean RI in patients who did not develop HRS was 0.67 ± 0.07.

In our study, we noted that intrarenal RI values measured at the time of admission were significantly increased in cirrhotic patients who developed HRS during the 3 months follow up period. But, 2 patients with normal RI also developed HRS. This calls for careful vigilance and repeat Doppler screening at intervals of all end-stage chronic liver diseases as an early warning tool for development of HRS.

Limitations Of The Study

Since there is no definitive cut-off for RI in HRS, repeat renal Doppler was not done in all patients with raised RI but normal creatinine. This may have been indicated in patients who were progressing into HRS. Follow up period was only for 3 months.

CONCLUSION

Doppler ultrasound measurement of the RI is useful to quantify renovascular resistance in cirrhotic patients.

Renal Doppler RI is a useful non-invasive tool for indicating the presence of hepatorenal syndrome as well as acting as a prognostic indicator in patients with cirrhosis of the liver, hence should be done to all patients with cirrhosis.

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