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Association of chronic liver disease with resistive index of intra-renal artery

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Abstract

Background: Cirrhosis of the liver is characterized by a profound disarrangement of the parenchyma and intrahepatic circulation, which leads to portal hypertension. Several vascular changes occur in the course of hepatic cirrhosis leading eventually to renal vascular changes with consequent renal function affection. Renal hemodynamic changes with intense intrarenal vasoconstriction begin early in the course of liver disease before changes in the level of serum urea and serum creatinine. Resistive Index (RI) is the most widely used index for estimation of intrarenal vascular resistance and simple, effective, and non-invasive method that enables the early detection of renal hemodynamic disturbances in patients with liver cirrhosis even before renal dysfunction becomes clinically evident.

Materials and methodology: Seventy subjects, 50 with Chronic Liver Disease (CLD) and 20 healthy control were examined and RI was calculated with color and spectral doppler sonography analysis. The mean RI among healthy controls was compared with patients with CLD. Further comparison of RI was made among CLD patients with different grades according to Child Turcotte Pugh's classification and asities.

Result: The mean RI value in patients with CLD was significantly higher than in healthy controls (0.71 ± 0.05 vs 0.55 ± 0.28). The RI values of patients with no ascites, Grade I, Grade II, and Grade III ascites were 0.65 ± 0.08, 0.68 ± 0.26, 0.75 ± 0.28, and 0.79 ± 0.09 respectively. (p<0.01). Similarly, the RI value of patients with CLD also increased with an increase in the grading of CLD according to the Child Turcotte-Pugh classification (0.67 ± 0.05, 0.74 ± 0.30, 0.79 ± 0.50 for Child Turcotte-Pugh A, B and C groups respectively <0.01).

Conclusion: Renal duplex Doppler ultrasound is useful as a non-invasive method for the evaluation of renal hemodynamic changes in cirrhotic patients with a good correlation to the severity of the liver disease.

Keywords: Chronic liver disease; Resistive index; Ultrasonography; Color doppler.

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Introduction

Hepatic cirrhosis is defined histologically as a diffuse hepatic process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules that may occur over weeks to years [1]. Cirrhosis of the liver is characterized by a profound disarrangement of the parenchyma and intrahepatic circulation, which leads to portal hypertension. Several vascular changes involving the splanchnic and systemic circulatory beds occur in the course of hepatic cirrhosis leading eventually to renal vascular changes with consequent renal function affection [2,3].

Hepato-Renal Syndrome (HRS) is the development of renal failure in patients with advanced chronic liver disease in the absence of any identifiable causes of renal pathology that develop in at least 40% of the patients [4,5]. The first detailed description of HRS was made by Hecker and Sherlock in 1956 [6].

Renal Resistive Index (RI) which is a ratio of peak systolic and end diastolic velocity can test arterial stiffness and endothelial renal dysfunction. Renal hemodynamic changes begin early in the course of liver disease and the hallmark change is intense intrarenal vasoconstriction. Duplex Doppler Ultra-sonography is a widely used noninvasive method to assess vascular patency and blood flow in many sites in the small renal intraparenchymal vessels through simple analysis of the Doppler wave form by a parameter termed the RI. The renal RI is a nonspecific prognostic marker in vascular diseases that affect the kidney. High RI (>0.8) in native kidneys is associated with renal dysfunction and adverse cardiovascular events [4-7]. Early identification of those patients with established liver disease who are at particular risk for the development of the HRS may be benefited by avoiding other nephrotoxins and overt kidney failure is an independent risk factor for unfavorable liver transplantation [4-9].

Materials and methods

This cross-sectional study was performed from 1st January 2020 to 31st December 2020 at the department of Radiodiagnosis of National Academy of Medical Sciences (NAMS), Kathmandu, Nepal after approval from the Institutional Review Board (Ref. no. 154/2077/78).

Seventy subjects above 18 years were enrolled in our study, 50 were patients with Chronic Liver Disease (CLD) being evaluated at out and in patient departments of medicine at our institution, and 20 were healthy controls visiting the hospital. Subjects with hypertension, diabetes mellitus, reno-vascular kidney disease, thyroid dysfunction, gastrointestinal bleeding, history of chronic alcohol use, along with subjects receiving corticosteroids, angiotensin II receptor blockers, angiotensin converting enzyme inhibitors, or nonsteroidal anti-inflammatory drugs and patients with azotemia were excluded from the study. Diagnosis of CLD/cirrhosis was made either with routine laboratory tests like serum markers, liver functions test, and radiological evaluation of liver included (volume, redistribution, coarse-echotexture, nodular-surface, findings suggestive of portal hypertension: ascites, splenomegaly and varices).

Patients with CLD were further subdivided into grades A, B, and C according to Child Turcotte Pugh classification [5]. Patients with ascites were graded into 1, 2 and 3 according to the International Ascites Club grading 2003 [10].

In our study, we examined intrarenal arteries in the upper, mid, and lower poles of both kidneys for the measurement of Resistive Index (RI) values via renal duplex doppler ultrasonography in the morning after at least 10 hours of overnight fasting. The influences of respiratory and cardiac cycles on RI were removed as per the standard guidelines. All the patients and healthy subjects were examined by a single radiologist using a color Doppler ultrasonography Aloka Hitachi ultrasound system machine with curvilinear probe frequency of 3.5-5.0 MHz. Using color Doppler flow imaging, the renal artery in the renal hilum, the interlobar artery in the bertin's column and the interlobular artery in the middle portion of the renal cortex were identified. The sampling gate of the pulse Doppler machine was placed in the middle of these vessels. The angle between the sound beam and the direction of blood flow was corrected to < 30 degrees. Subjects were instructed to hold their breath when the Doppler flow spectrum was being obtained. The probe was rotated more posteriorly to improve the Doppler angle for the upper pole intrarenal arteries. For the mid pole kidney, the probe is centered in a coronal plane. The best Doppler angle for the lower pole intrarenal arteries was obtained by rotating the probe slightly anterior to the mid coronal line. Based on a clear spectrum image, the interlobar artery will be measured and the RI for each vessel will be calculated automatically or as (PSV-EDV)/PSV. Images from three successive cardiac cycles were obtained and mean RI was calculated. A train of atleast three similar, sequential time-velocity wave forms of Doppler signals were obtained at upper, middle and lower pole regions of kidney during suspended respiration. The RI was calculated on both diseased patients and healthy controls. The RI values were compared and correlated with healthy controls and different grades of CLD.

Statistical analysis was done by IBM SPSS windows version 26. Continuous variables were expressed as the mean or medians whereas categorical variables were expressed as number. The t test, Analysis Of Variance (ANOVA), spearman rank correlation were used to statistically analyze the data from the patient and control groups. The p-value of <0.05 was considered as significant.

Results

Seventy subjects were enrolled in our study. Out of them, 50 were cases of CLD, and 20 were healthy individuals. Among CLD patients, 26 were with grade A, 15 grade B, and 9 grade C as per Child Turcotte Pugh classification. On the evaluation of ascites among the cases, 5 had no ascites, 24 grade I, 13 grade II, and 8 grades III.

The mean RI values among patients with CLD and healthy controls were 0.71 (±0.05) and 0.55 (±0.28) respectively which was statistically significant ($p<0.01$). The RI of patients with ascites was higher than those without ascites and RI increased with increase in grade of ascites. Similarly, RI values increased in patients with CLD with increase in grades which was statistically significant (Table 1).

Table 1: Relationship between severity of ascites and the R.

Character	Category	RIright kidney (Mean)	RI left Kidney	RI both kidney (mean ±SD)	P value
Ascites Grading	No Ascites	0.65	0.65	0.65 ± 0.08	<0.001
	Grade 1	0.69	0.69	0.68 ± 0.02	
	Grade 2	0.74	0.74	0.75 ± 0.02	
	Grade 3	0.79	0.79	0.79 ± 0.09	
CLD Grading	Grade A	0.675	0.68	0.67 ± 0.01	<0.001
	Grade B	0.73	0.73	0.74 ± 0.03	
	Grade C	0.79	0.79	0.79 ± 0.01	

Spearman rank correlation was used to assess the strength of associations between variable variables with mean RI value of intrarenal artery. The spearman correlation (rho) for CLD grading and mean RI value of intrarenal artery was 0.863 with p value <0.01. Similarly, spearman's rho for ascites grading and mean RI value of intrarenal artery was 0.869 with p-value <0.01

Discussion

Cirrhosis refers to fibrosis or scarring of the liver with associated functional impairment. It has multiple etiologies, the most common of which include alcohol, viral hepatitis, nonalcoholic steatohepatitis, and chronic cholestatic diseases. Liver cirrhosis is associated with poor clinical outcomes. Therefore, assessment of prognosis is important in the management of these patients. The Child-Pugh score has long been the most widely used specific scoring system in liver disease. In 2002, the Model for End-Stage Liver Disease (MELD) was introduced for patients undergoing trans-jugular intrahepatic portosystemic shunt. It is currently used to predict survival in patients awaiting liver transplantation [3,4]. The MELD seems to be superior to the Child-Pugh score in prioritizing potential liver recipients according to mortality risk [5]. However, it is only based on three laboratory variables, and thus does not take into account all prognostic factors that will impact the survival of cirrhotic patients, notable complications due to portal hypertension [4].

HRS is the most serious complication of renal dysfunction in patients with end-stage liver cirrhosis [3,4]. It is characterized by a marked reduction in the Glomerular Filtration Rate (GFR) and renal plasma flow in the absence of other causes of renal failure [8]. The hallmark of HRS is hypo-perfusion of the kidney resulting from combined renal vasoconstriction and decreased total renal blood flow [9]. The earliest stages of this functional form of kidney failure often go unrecognized because creatinine elevation occurs late [11]. Therefore, better methods to diagnose this early stage of renal disease are needed.

Duplex ultrasonography is a widely used non-invasive method to assess vascular patency and blood flow in manysites. Duplex Doppler can be used to assess vascular resistance in the small intra-parenchymal vessels through a simple analysis of Doppler wave form by a parameter termed the Resistive Index (RI) [12]. An elevated renal RI has been observed in various conditions associated with elevated renal vascular resistance such as kidney obstruction, acute tubularnecrosis, and hemolytic uremic syndrome. However, in this study, we have excluded the other causes of elevated RI and have only included CLD related functional kidney failure. 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. In the current study, we prospectively investigated the course of intrarenal RIs and evaluated its role in patients with liver cirrhosis with special reference to ascites.

In this study, we found a significant increase in renal RI among all patient groups. The RI of patients with ascites was higher than those of patients without ascites. The increase in renal vascular RI in cirrhotic patients with ascites can be explained by a physiological homeostatic response to vascular underfilling occurring in ascitic patients. When the vascular underfilling is moderate, the renal vasoactive substances are effectively counter balanced by increased renal synthesis of prostaglandins so that renal blood flow and GFR remain normal. In contrast, when the vascular underfilling is severe, intense stimulation of endogenous vasoconstrictor systems occurs, producing renal vasoconstriction and impairment of renal blood flow and GFR. Pateron et al, concluded that intra-renal blood flow is preserved in cirrhotic patients by intra-renal mechanisms until the ascites becomes refractory. When this regulation fails renal ischemia causes tubular necrosis, azotemia and oliguric renal failure [13].

Similarly, RI value of patient with CLD also increases with increase in grading of CLD according to Child Turcotte-Pugh classification. J.S. Sikarwar et al, evaluated RI in various stages of liver cirrhosis and to determine its significance in developing hepatorenal syndrome in a study which included 60 cirrhotic patients divided into 4 groups (15 patients each): Compensated liver cirrhosis (group A), diuretic responsive ascites (group B), refractory ascites (group C), hepatorenal syndrome (group D) and ten healthy persons as control group (E). They demonstrated that the RI of interlobar and arcuate arteries were significantly higher in all patient groups than in control group (p < 0.05), in patient with hepatorenal syndrome than in patient with diuretic responsive ascites and patients with compensated cirrhosis (p<0.05). In patients with HRS than in patients with diuretic responsive ascites and patients with compensated cirrhosis (p<0.05) [14].

Vinodh V et al, demonstratedthat RI was significantly higher in patients when compared to healthy controls (0.63 vs 0.54, P<0.01).As compared to the controlled group without ascites RI was significantly greater in patients with ascites (0.63 vs 0.73, P <0.01) [15].

Götzberger M et al, demonstrated 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) [16].

Y M Fouad et al study revealed that RI of both interlobar and arcuate arteries was significantly higher in all patient groups than in the control group (p<0.01). The RI was significantly higher in patients with refractory ascites than in patients with diuretic responsive ascites, and also in patients with diuretic responsive ascites than in patients with compensated cirrhosis ($p<0.01$) [17].

Maroto et al, demonstrated that RI is significantly higher in decompensated cirrhotic patients with ascites than in compensated cirrhotic patients and that the RI of compensated cirrhotic patients is higher than in the controls [18]. They reported that these results were highly sensitive and specific for the diagnosis of HRS. Also, Masahiko et al, demonstrated that resistive indices were significantly higher in cirrhotic patients compared to controls and compared to patients with chronic hepatitis. RI indices measured color Doppler ultrasonography were closely related to the severity of cirrhosis and showed a significant correlation with increased Child-Pugh grade [19].

Kastelan et al, demonstrated that renal duplex Doppler of interlobar arteries was a simple effective, and non-invasive method that enables the early detection of renal hemodynamic disturbances in patients with liver cirrhosis even before renal dysfunction becomes clinically evident and makes possible the identification of a subgroup of patients with liver cirrhosis who are at higher risk for developing the hepatorenal syndrome [20].

In Italy, Sacerdoti et al, reported that the RI was significantly higher in nonascitic cirrhotic patients than in control patients, in ascitic patients than in nonascitic patients, in ascitic patients not treated with diuretics than in nonascitic ones, and in ascitic patients treated with diuretics than in those not treated. The RI was significantly higher in Child-Turcotte-Pugh class B and C patients than in class A patients. This non-invasive method may be applied to pathophysiological and clinical studies of renal functional impairment in cirrhosis [21]. In agreement with these studies/articles, this study also showed that there is also increase in resistive index of intrarenal artery in increasing severity of ascites in patients with cirrhosis. In overall this study showed that there is change in intrarenal artery hemodynamics with severity of chronic liver disease.

Conclusion

Assessment of the hemodynamics of intra- renal artery and its association in patients with CLD showed that there is significant difference in RI of intrarenal artery in patients with different stages of CLD in comparison to normal individuals. This study also observed a direct correlation between different grades of Child Pugh classification and ascites with RI values of intrarenal artery. Doppler examination in addition to the routine conventional USG examination in patients with chronic liver disease can provide contributory information about the hemodynamics of the intrarenal artery and renal dysfunction and development of HRS.

Limitations: Liver biopsy which is gold standard for diagnosis of CLD was not done. Gray scale imaging of CLD and Doppler examination of intrarenal arteries were examined and made subjectively by a single radiologist.

Declarations

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Ethical approval: Institutional Review Board of National Academy of Medical Sciences.

Conflicts of interest: The authors declare no conflicts of interest.

References

1. Wolf DC. Cirrhosis. Medscape 2008.
2. Roberto JG. Hyperdynamic circulation of liver disease 40 years later: pathophysiology and clinical consequences. Hepatology. 1994; 20: 1359–1363.
3. Arroyo V. Pathophysiology, diagnosis and treatment of ascites in cirrhosis. Ann Hepatol. 2002; 1: 72–79.
4. Sandeep M, Hemant K, Rowen K. Hepatorenal Syndrome. eMedicine, Article Last Updated. 2008.
5. Yeung E, Yong E, Wong F. Renal dysfunction in cirrhosis: Diagnosis, treatment, and prevention. Med Gen Med. 2004; 6: 9.
6. Hecker R, Sherlock S. Electrolyte and circulatory changes in terminal liver failure. Lancet. 1956; 2: 1221–1225.
7. Agostino C, Mirella F, Roberta P, Massimo C, Stefania V, et al. Renovascular impedance and esophageal varices in patients with Child-Pugh class A cirrhosis. Radiology. 2001; 219: 712–715.
8. Colli A, Cocciolo M, Riva C, Martinez E. Abnormal renovascular impedance in patients with hepatic cirrhosis: detection with duplex US. Radiology. 1993; 187: 561–563
9. Berzigotti A, Casadei A, Magalotti D, Castaldini N, Losinno F, Rossi C, et al. Renovascular impedance correlates with portal pressure in patients with liver cirrhosis. Radiology. 2006; 240: 581–586.
10. Møller S, Henriksen JH, Bendtsen F. Ascites: pathogenesis and therapeutic principles. Scandinavian journal of gastroenterology. 2009; 44: 902-911.
11. Tomas B, Scott W, Biggins S. In: Zakim, Boyer, editors. Hepatology a text book of liver disease. Philadelphia: Saunders; 2011; 837–852. Ch 47.
12. Francoz C, Glotz D, Moreau R, Durand F. The evaluation of renal function and disease in patients with cirrhosis. Hepatology. 2010; 52: 605–613 .
13. Pateron D, Barriere E, Condat B, Rassiat E, Heller J, Chagneau C, et al. Relationship between haemodynamic alternations and the development of ascites or refaractory ascites in patients with cirrhosis. Eur J Gastroentrol Hepatol. 2001; 13: 251–256.
14. Sikarwar JS, Muchhoria S, Singh R, Bhujade H, Ahirwar V. Study of resistive index in various stages of liver cirrhosis and its significance in calculating the risk for hepatorenal syndrome. Journal of Evolution of Medical and Dental Sciences. 2014; 3: 1195-1206.
15. Vinodh V, Shashidhar G, Krishnamurthy MS. A study of renal resistive index in hepatic cirrhosis. International Journal of Contemporary Medicine Surgery and Radiology. 2018; 3: C116-C120.
16. Götzberger M, Kaiser C, Landauer N, Dieterle C, Heldwein W, Schiemann U, et al. Intrarenal resistance index for the assessment of early renal function impairment in patients with liver cirrhosis. Eur J Med Res. 2008; 13: 383-387.
17. Fouad YM, Mokarrab H, Elgebaly AF, Amin HE, Raheem EM, et al. . Renal duplex doppler ultrasound in patients with HCV-related liver cirrhosis. Tropical Gastroenterology. 2010; 30: 213-218.
18. Maroto A, Gine A, Salo J. Diagnosis of functional renal failure of cirrhosis with Doppler sonography: Prognostic value of the resistive index. Hepatology 1994; 20: 839–844.
19. Masahiko K, Murawaki Y, Kawasaki H. Renovascular resistance assessed by color Doppler ultrasonography in patients with

chronic liver diseases Western Pacific Helicobacter Congress No3, pasar,Bali, INDONESIA. 2000; 15: 1424–1429.

20. Kastelan S, Ljubicic N, Kastelan Z, Ostojic R, Uravic M, et al. The role of duplex-doppler ultrasonography in the diagnosis of renal dysfunction and hepatorenal syndrome in patients with liver cirrhosis. Hepato-gastroenterology. 2004; 51: 1408-1412.

21. Sacerdoti D, Bolognesi M, Merkel C, Angeli P, Gatta A, et al. Renal vasoconstriction in cirrhosis evaluated by duplex Doppler ultrasonography. Hepatology. 1993; 17: 219-224.