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Hepatology

Value of Renal Artery Resistive Index in Nonazotaemic Cirrhotic Patients with Ascites

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Abstract **Original Research Article**

Background: Renal dysfunction is a common complication in patients with liver cirrhosis, with hepatorenal syndrome (HRS) being the most severe form. HRS is characterized by disturbances in both circulatory and kidney functions and is diagnosed by excluding other causes of renal failure. ***Objective:*** This study aimed to measure the renal artery resistive index (RI) in non-azotaemic cirrhotic patients with ascites to predict early renal haemodynamic dysfunction. ***Methodology:*** A prospective study was conducted involving 30 cirrhotic patients with ascites and 15 healthy controls. Renal artery RI was measured using Duplex Doppler ultrasonography. Inclusion criteria for patients included normal renal function, as indicated by serum creatinine ≤ 1.2 mg/dl and creatinine clearance rate ≥ 50 ml/min. ***Results:*** The mean renal artery RI was significantly higher in cirrhotic patients with ascites (70% had RI ≥ 0.70) compared to controls (all had RI < 0.70). Significant differences were observed in serum bilirubin, SGPT, SGOT, and prothrombin time between cases and controls ($p < 0.05$). ***Conclusion:*** Renal Doppler ultrasonography is a valuable noninvasive method for detecting early renal haemodynamic dysfunction in cirrhotic patients with ascites. Elevated renal artery RI can serve as an indicator of renal dysfunction, aiding in early diagnosis and management.

Keywords: Renal dysfunction, Resistive index, Doppler ultrasonography, Ascites.

INTRODUCTION

Renal dysfunction commonly develops in patients with cirrhosis of liver [1]. The most serious form of renal dysfunction in these patients is known as hepatorenal syndrome (HRS). Hepatorenal syndrome is a clinical condition that usually occurs in patients with advanced liver disease and portal hypertension that is characterized by a combination of disturbances in circulatory and kidney function [2].

It is diagnosed following exclusion of other causes of renal failure in patients with liver disease such as hypovoluaemia, drug nephrotoxicity, sepsis or glomerulonephritis [3]. The exact basis for the syndrome is not clear, but altered renal haemodynamic changes appear to be involved.

Clinically, it is difficult to diagnose this functional renal insufficiency initially, as increases in plasma creatinine levels and decreases in creatinine clearance occur in the late phase of hepatorenal syndrome [4]. Detection of severe renal vasoconstriction seems to be the only key of demonstrating this functional renal insufficiency.

Duplex Doppler ultrasonography is a widely used noninvasive method to assess vascular structures and to evaluate vascular patency and blood flow in many sites [5]. Duplex Doppler ultrasonography can be used to assess vascular resistance in renal arteries through simple analysis of the Doppler waveform by a parameter termed as the Resistive Index (RI) [6].

Measurement of renal artery resistive index (RI) by Doppler ultrasonography is not routinely done in

cirrhotic patients. From above discussion it seems that detection of renal artery resistive index (RI) can be a useful predictor of early renal haemodynamic dysfunction in nonazotaemic cirrhotic patients and thus help to guide or modify further management.

OBJECTIVE

To measure value of renal artery resistive index in Nonazotaemic Cirrhotic patients with ascites.

METHODOLOGY

Type of study

This was a prospective study involving a total of 30 (thirty) cirrhotic patients with ascites having biochemical evidence normal of renal function and 15 (fifteen) healthy age matched subjects were enrolled as control group.

Period of study: The study was carried out during the period of January 2005 to December 2005.

Study place: Department of Hepatology, BSMMU, Dhaka.

Patient selection:

The study was done on 30(thirty) patients having cirrhosis of liver with ascites, age range 15-70 years, irrespective of sexes, seeking treatment in inpatient and outpatient department of hepatology, BSMMU. Diagnosis of cirrhosis and ascites was based on clinical features, liver function and other biochemical tests, viral markers, upper GI endoscopy and ultrasonographic findings.

Selection of control subjects:

A total number of 15(fifteen) normal healthy persons, age range 15-70 years, irrespective of sexes, were enrolled as control group. Other than cirrhosis with ascites, all inclusion and exclusion criteria were same as the patient group. Relevant liver function and other biochemical tests, viral markers and ultrasound scan were done to all of them.

Inclusion criteria:

Cirrhotic patients with ascites having normal renal function (Here biochemical parameters of normal renal function are serum creatinine ≤ 1.2 mg/dl and creatinine clearance rate ≥50 ml/min respectively).

Exclusion criteria:

1. Patients with renal, cardiac or respiratory diseases.
2. Patients with systemic hypertension or diabetes mellitus.
3. Patients receiving nephrotoxic or nonsteroidal anti-inflammatory drugs.
4. Patients with spontaneous bacterial peritonitis.
5. Patients with a history of haematemesis and melaena within 1 (one) month of the study.
6. Patients with serum creatinine level >1.2 mg/dl and/or creatinine clearance rate <50 ml/min.

Ethical consideration

Prior to commencement of this study, the thesis protocol was approved by the protocol review committee of the Department of Hepatology, BSMMU. The aims and objectives of the study along with its procedure, risks and benefits were explained to every individual patient and also to each control subject by an easily understandable local language. Then informed written consent was taken from each patient and control subject. It was assured that all information and records would be kept confidential.

Study Procedure and data collection

i. A patient presenting with the suspected features of cirrhosis of liver and ascites, was asked for detail history and was examined systematically for evidences of cirrhosis of liver and ascites. Diagnosis of cirrhosis was established on the basis of clinical, biochemical, serological, ultrasonographic and endoscopic findings and the correlation of these features.

   Presence of ascites was detected clinically by positive shifting dullness and/or positive fluid thrill examination. This was further confirmed by abdominal ultrasound results.

ii. If the patient had features of cirrhosis and ascites, he or she would be undergone relevant kidney function tests (serum creatinine and creatinine clearance rate).

iii. If the serum creatinine level and creatinine clearance rate were within normal range and there is no exclusion criteria, then the patient was finally included in the study.

iv. There after the patient was taken by the investigator himself to the Radiology and Imaging Department of BIRDEM Hospital, Dhaka for Colour Doppler Study of Renal Arteries and to measure Renal Artery Resistive Index (RI).

v. *Doppler measurement*: Each selected patient was studied after overnight fasting from food, liquids and cigarettes. All studies were performed by the same sonologist using a Colour Doppler apparatus with 2.5-5 MHz transducer (Acuson 128 XP/4, USA). The person who performed the Doppler Ultrasound examinations and renal artery RI measurements was blinded to the patients' clinical status and laboratory results.

   The transducer of the imaging system was placed below the costal margin in

the dorsolateral area of the flanks. Doppler signals were obtained from renal arteries in three different regions from each kidney.

vi. *Calculation and statistical analysis*: The renal artery resistive index (RI) for each kidney was calculated as the average of three measurements. For each measurement, peak systolic flow velocity (max) and end diastolic flow velocity (min) were determined (all measured in meters/second). Measurements were performed by using a built-in measurement analysis software package. The renal artery resistive index (RI) was calculated accordingly to the following formula:

$$RI = \frac{\text{(Peak systolic velocity – End diastolic velocity)}}{\text{Peak systolic velocity}}$$

Subsequently a mean renal artery resistive index was determined from the average of both kidneys for each patient. In addition to the actual RI value being recorded, it was classified as normal or high in comparison with a threshold RI values. On the basis of multiple prior studies, [5-6] a RI value of 0.70 or more was considered high indicating elevated renal vascular resistance and renal vasoconstriction.

Data Processing, Analysis

Individual patient was given a code number. All data collected from each patient by a questionnaire were entered into a personal computer. It was thoroughly checked for any possible error and was analyzed by SPSS programme. Significance of the test was tested by Student's t-test and Chi-squared Test (χ^2). Level of significance was 0.05(p-value of < 0.05 taken as statistically significant). Results of data analysis were considered against the hypothesis and the thesis was made.

RESULTS

Table I shows that highest frequency of cases (30%) were found in the age range 30 – 40 years, followed by 26.7% in 40 – 50 years and another 26.7% in age 50 years or above. More than half of the cases (16 cases) were of 40 years and above. The least frequency was observed below 20 years. In the control group nearly half (46.7%) were in the age range 30 – 40 years. The cases and controls were almost identical with respect to age (p > 0.05).

Table I: Comparison of age between groups:

Age (yrs)	Group		p-value[#]
	Case (n = 30)	Control (n = 15)	
< 20	2(6.7)*	1(6.7)	0.536
20 – 30	3(10.0)	3(20.0)	
30 – 40	9(30.0)	7(46.7)	
40 – 50	8(26.7)	2(13.3)	
≥ 50	8(26.7)	2(13.3)	
Median ± SEM	**40.0 ± 2.60**	**36.0 ± 3.41**	

Over three-quarter (76.7%) of the cases were males and the rest were females giving rise a male female ratio of about 3:1. In the control group, however, a female preponderance (60%) was observed.

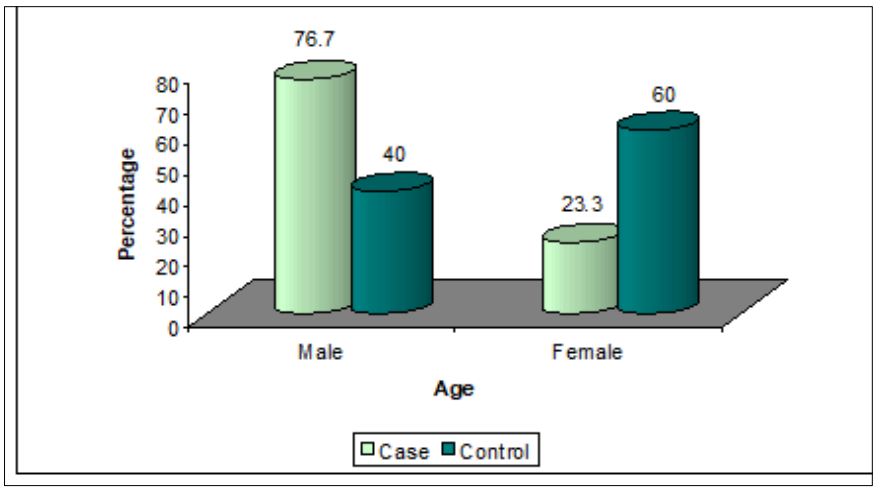

Figure-1: Gender Distribution of the Study Group

Table-2 demonstrates that the commonest presenting feature was swelling of abdomen (100%). Two-third (66.7%) of the cases exhibited yellow eyes and yellow colouration of urine, while 56.7% had swelling of legs and 40% experienced loss of appetite.

Table-II: Distribution of cases by their presenting features (N = 30*):

Presenting features	No	%
Yellow eyes and urine	20	66.7
Swelling of abdomen	30	100
Swelling of legs	17	56.7
Loss of appetite	12	40.0

* Total will not correspond to **N(100%),** because of multiple involvement.

Table depicts that jaundice (66.7%), leuconychia (76.7%), spider naevi (63.3%), testicular atrophy (70%), palmer erythema (53.3%) and ankle oedema (56.7%)were common clinical signs compared to anaemia (36.7%), gynaecomastia (30%), K-F ring(6.7%)and clubbing(6.7%).

Table III: Distribution of cases by their clinical signs (N = 30*):

Clinical signs	No	%
Jaundice	20	66.7
Anaemia	11	36.7
Leuconychia	23	76.7
Clubbing	02	6.7
Spider naevi	19	63.3
Palmer erythema	16	53.3
K-F ring	02	6.7
Testicular atrophy	21	70.0
Gynaecomastia	09	30.0
Ankle oedema	17	56.7

* Total will not correspond to **N(100%),** because of multiple involvement.

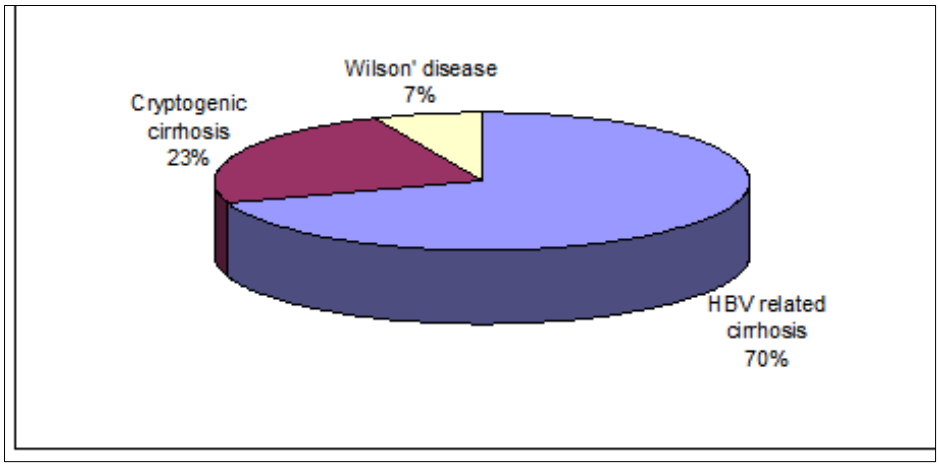

Figure-2: Distribution of cases by their diagnosis

Table demonstrates that serum bilirubin, SGPT, SGOT and prothrombin time were found to be significantly higher in case groups compared to their control counterpart ($p < 0.05$, $p < 0.005$, $p < 0.001$ and $p < 0.001$ respectively). Serum total protein and serum albumin, on the other hand, were observed to be significantly lower in cases than those in controls ($p < 0.001$ and $p < 0.001$ respectively).

Table IV: Comparison of biochemical variables between groups:

Biochemical variables#	Group		p-values
	Case (n = 30)	Control (n = 15)	
Serum billirubin (μ-mol/L)	77.66 ± 14.71	16.13 ± 0.72	0.005
ALT/SGPT (U/L)	96.40 ± 15.05	26.93 ± 0.72	0.002
AST/SGOT (U/L)	64.50 ± 7.18	21.27 ± 0.61	< 0.001
Prothrombin time (sec.)	18.85 ± 0.61	12.18 ± 0.09	< 0.001
Serum total protein (gm/L)	56.58 ± 1.27	72.80 ± 0.69	< 0.001
Serum albumin (gm/L)	28.05 ± 1.08	41.47 ± 0.70	< 0.001
Serum creatinine (mg/dl)	0.81 ± 0.02	0.76 ± 0.02	0.289
CCR (ml/minute)	99.90 ± 4.23	113.73 ± 1.26	0.028

Data were analysed using **Student's t-test** and presented as **mean ± SEM**.

Table demonstrates that Renal Artery Resistive Index (RI) of cases was not significantly associated with the levels of serum creatinine and CCR values ($p > 0.05$).

Table V: Association of Resistive Index with biochemical variables of kidney function in cases:

Biochemical variables#	Resistive Index (RI)		p-values
	< 0.7 (n = 9)	≥ 0.7 (n = 21)	
Serum creatinine (mg/dl)	0.80 ± 0.03	0.81 ± 0.03	0.809
CCR (ml/minute)	105.78 ± 9.23	97.38 ± 4.62	0.372

Data were analysed using **Student's t-test** and presented as **mean ± SEM**.

Table VI demonstrates that 100% of cases had different grades of oesophageal varices as revealed by upper GI endoscopy. But no significant association was found between the size of the varices and Resistive Index (RI) values ($p > 0.05$).

Table VI: Association between oesophageal varices and RI in cases:

Oesophageal varix	Group		p-value
	< 0.7 (n = 9)	≥ 0.7 (n = 21)	
Small	2(22.2)*	4(19.0)	0.989
Medium	2(22.2)	4(19.0)	
Small & Medium	4(44.4)*	10(47.6)	
Small, Medium & large	1(11.0)	3(14.3)	

***** Figures in the parentheses indicate corresponding **%;**

Chi-squared Test (χ^2) Test was used to analyse the data and the **level of significance** was **0.05**.

21(70%) of the cases had renal artery Resistive Index (RI) values of 0.7 or above, while none of the control's RI values reached to that level ($p < 0.001$).

Table VII: Comparison of Renal Artery Resistive Index (RI) values between groups:

Resistive Index (RI)	Group		p-values
	Case (n = 30)	Control (n = 15)	
RI of right renal artery			
< 0.7	9(30.0)*	15(100.0)	< 0.001
≥ 0.7	21(70.0)	00	
RI of left renal artery			
< 0.7	9(30.0)*	15(100.0)	< 0.001
≥ 0.7	21(70.0)	00	
Mean RI of Renal arteries			
< 0.7	9(30.0)*	15(100.0)	< 0.001
≥ 0.7	21(70.0)	00	

*Figures in the parentheses indicate corresponding **%;**

DISCUSSION

Time-velocity wave-form analysis of Doppler signals from intrarenal arteries allows estimations of renal arteriolar vascular resistance [7]. Among the various indexes proposed, the Resistive Index (RI) is the most widely used for this estimations. Therefore Duplex-Doppler ultrasonography may also be of value in the diagnosis of functional kidney failure in cirrhotic ascites, which is due to renal arteriolar vasoconstriction.

In this study, we measured renal artery RI in cirrhotic patients with ascites and in healthy persons both having normal kidney function. The aim of the study was to see whether renal artery RI is high in cirrhotic patients with ascites as increased renal artery vascular resistance due to arteriolar constriction is the earliest manifestations of Renal dysfunction or hepatorenal syndrome in cirrhotic ascites [8].

The study included 30(thirty) cirrhotic patients with ascites as Cases (23 men and 7 women; mean age, 40.0±2.60) and 15(fifteen) normal healthy persons enrolled as Controls (6 men and 9 women; mean age,36.0±3.41). The mean age of our study population

was similar to the study done by two other studies 5-6 but different from other reports [7-8].

Both groups had biochemical evidence of normal kidney function as inclusion criteria (serum creatinine ≤ 1.2 mg/dl and creatinine clearance rate ≥50 ml/min respectively). No patient with systemic hypertension; respiratory, renal or cardiac disease; or diabetes mellitus was included. Patients with encephalopathy, spontaneous bacterial peritonitis or gastrointestinal haemorrhage within one month of the study or those who had received nephrotoxic drugs were also excluded. Two studies had followed the same inclusion and exclusion criteria. 5-6 However other studies included a group of cirrhotic patients who had biochemical evidence of established kidney failure (hepatorenal syndrome) at the time of study [7-8].

In this study, serum bilirubin, SGPT, SGOT and prothrombin time were found to be significantly higher in case groups compared to their control counterpart ($p < 0.05$, $p < 0.005$, $p < 0.001$ and $p < 0.001$ respectively). Serum total protein and serum albumin, on the other hand, were observed to be significantly lower in cases than those in controls ($p < 0.001$ and $p < 0.001$ respectively). Values of biochemical parameters to assess liver disease in patient group were similar to the research works done by other studies [5-6].

Other study had done his study on 180 cirrhotic patients with normal kidney function and had demonstrated that elevated renal artery RI(≥0.70) was present in 76(42%) of the 180 patients. 6 Kidney dysfunction (doubling of initial creatinine level to 1.5 mg/dl or more) developed in 55% (42/76) of the patients with an elevated renal artery RI(≥0.70) and 6% (6/104) of those with normal results of Doppler study (P<0.00005). Hepatorenal syndrome developed in 26% (20/76) of subjects with an elevated resistive index and 1% (1/104) of those with a normal resistive index (P<0.00005).

Another study performed a research work including 20 cirrhotic patients with ascites 11 cirrhotic patients without ascites and 23 healthy control subjects [5]. All of them had normal kidney function during the research work. Renal artery resistive index values (RI) were significantly higher in cirrhotic patients with ascites (P<0.001 for all) than those of cirrhotic patients without ascites and control group (P<0.0007 for all).

Other study included 32 cirrhotic patents with ascites, 12 cirrhotic patients without ascites and 10 healthy subjects. [7] Renal artery resistive index (RI) measured by Duplex Doppler study was significantly higher in cirrhotic patients with ascites (0.74±0.01) compared with those of other two groups (0.64±0.02 and 0.64±0.02 respectively). They have concluded that, hepatorenal risk is higher in patients whose renal artery resistive index (RI) is 0.70 or more than in patients whose resistive index is less than 0.70.

In this study, among 30 cirrhotic patients with ascites, 21(70%) cases had renal artery RI value of 0.70 or above while all of the control had RI value of less than 0.70. Both groups had biochemical evidence of normal renal function. The results of this study are compatible with those of other study done earlier. Comparison between groups was done by Student's t-test and Chi-squared Test (χ^2). Here the p-value is < 0.001 which is statistically significant. So hypothesis is accepted and null hypothesis is rejected.

CONCLUSION

It was found that among 30 cirrhotic patients with ascites, renal artery RI value was ≥ 0.70(high) in 21(70%) cases while all of the control had RI value of ≤ 0.70.

We conclude that, renal Doppler US is a simple and noninvasive method for the detection of renal haemodynamic dysfunction in cirrhotic patients with ascites. Measurement of renal artery RI could be a useful noninvasive parameter of subsequent kidney status in nonazotaemic cirrhotic ascites.

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