

Original Research Article

Non-invasive evaluation of renal arterial blood flow in alcoholic cirrhosis of liver

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Abstract

Introduction: Studies of renal perfusion when kidney function tests are still normal could be useful in understanding the pathophysiology of functional kidney impairment in cirrhosis. Kidney functional failure in cirrhosis is considered as a consequence of active renal vasoconstriction. The same have been studied by invasive and non-invasive methods. The present study is aimed at non-invasive assessment of renal artery resistance in patients of cirrhosis of liver.

Materials and methods: The present study included 30 cases, patients with different stages of cirrhosis, who were clinically stable, while those with major complications like hepatic encephalopathy, major bleeding etc were excluded. All patients were evaluated clinically and a series of laboratory investigations were done. The resistance in the renal artery was calculated as Resistivity index, by using a color Doppler ultrasonography.

Results: In our study, we found the main resistivity index was higher in cases with MELD >20. There was further increase in resistivity index as a severity of the cirrhosis increases. Similarly the MDRD EGFR was decreasing as the severity of cirrhosis was increased.

Conclusion: Within limitations of the present study, we conclude that the estimation of the resistivity index in the kidney appears to be a sensitive and easy method for studying the early renal hemodynamic alterations in cirrhotic patients and thus by better understanding the Pathophysiology of hepatorenal syndrome.

Key words

Hepatic renal syndrome, Doppler ultrasonography, MELD, MDRD eGFR, Resistivity index.

Introduction

Alcohol is one of the most freely available and generally consumed mood altering substances causing serious medical, psychological and sociological problems.

According to WHO, nearly 2 billion people consume alcohol beverages and 76.3 million suffer with disorders arising out of alcohol abuse. In India 20 to 30% of adult males and 5% of adult females uses alcohol. Current concept is that alcoholism is a disease and alcohol is a disease agent [1].

Chronic and excessive alcohol ingestion is one of the major causes of liver disease, consists of three major lesions: fatty liver, alcoholic hepatitis, and cirrhosis. The threshold for developing alcoholic liver disease in men is an intake of > 60–80 g/d of alcohol for 10 years, while women are at increased risk for developing similar degrees of liver injury by consuming 20–40 g/d. Ingestion of 160 g/d is associated with a 25-fold increased risk of developing alcoholic cirrhosis (one beer, four ounces of wine, or one ounce of 80% spirits all contain 12 g of alcohol).

The complications of cirrhosis include portal hypertension and its sequelae, hepatic encephalopathy, spontaneous bacterial peritonitis, hepatorenal syndrome, and hepatocellular carcinoma. The hepatorenal syndrome (HRS) is a form of functional renal failure without renal pathology that occurs in patients with advanced cirrhosis or acute liver failure. This includes an increase in renal vascular resistance accompanied by a reduction in systemic vascular resistance. This renal vasoconstriction (increased renal vascular resistance) should be detectable noninvasively by Doppler ultrasonography [2].

Aim of the study

- To evaluate noninvasively renal arterial blood flow in patients with cirrhosis of liver by Doppler Ultrasonography.

- To study the alcoholic liver cirrhosis patients in relation to Child Pugh score, MELD score and their correlation with MDRD eGFR (6 variable) and Resistivity index by Renal Doppler Study.

Materials and methods

30 patients of alcoholic liver cirrhosis attending to Department of Gastroenterology of Gandhi Hospital during the period of 2014 to 2015 were included in the study.

Exclusion criteria

The patients with Viral hepatitis, Autoimmune hepatitis, Metabolic hepatitis, Gastrointestinal bleeding and or endoscopic band ligation or sclerotherapy in the last 8 weeks, Surgery, Thrombosis of portal veins, Liver tumors, Extra hepatic cholestasis, Acute alcoholic hepatitis, Hepatorenal syndrome, Therapy with vasoactive drugs, excluding beta-blockers and diuretics, Significant concomitant disease were excluded.

After informed consent, all selected patients underwent a detailed physical examination as per the proforma. The diagnosis of alcoholic liver cirrhosis was based on history, radiologically by using ultrasound abdomen and histopathologically using liver biopsy when indicated. After which a series of laboratory analysis of CBP, CUE, LFT, blood sugars, BUN, Serum creatinine, Serum electrolytes was done. Abdominal ultrasound and renal Doppler US, was performed and interpreted by single investigator according to standard protocol. Hepatic parameters like Child Pugh score (**Table – 1**), MELD score were calculated according to standard formulas based on which degree of liver damage was evaluated.

MDRD eGFR (6 variables) was calculated using standard formula and Resistivity index assessed by renal doppler study to evaluate the degree of kidney dysfunction. Statistical analysis was performed using ANOVA, Mann-Whitney, and correlation analyses (SPSS v.14). P value less

than 0.05 was considered as statistically significant.

MELD score

MELD uses the patient's values for serum bilirubin, serum creatinine, and

the international normalized ratio for prothrombin time (INR) to predict survival [4]. It is calculated according to the following formula:

$$\text{MELD} = 3.78[\text{Ln serum bilirubin (mg/dL)}] + 11.2[\text{Ln INR}] + 9.57[\text{Ln serum creatinine (mg/dL)}] + 6.43$$

Table - 1: Modified Child Pugh's classification.

PARAMETER	1 POINT	2 POINTS	3 POINTS
Sr Bilirubin (mg/dl)	<2.0	2.0 -3.0	>3.0
Sr Albumin (mg/dl)	>3.5	3.0 – 3.5	<3.0
Prothrombin time (no. of sec prolonged)	0 – 4.0	4.0 – 6.0	>6.0
Ascitis	None	Easily controlled	Poorly controlled
Hepatic encephalopathy	None	Minimal	Advanced encephalopathy

The Model for End Stage Liver Disease (MELD) score in patients with cirrhosis and ascites parallels the risk of developing HRS. In patients with MELD scores of about 10 is associated with an 8% and with a MELD score approaching 18, nearly 40% of patients develop HRS within 1 year.

MDRD eGFR (6 variable)

MDRD eGFR (6 variable) was calculated using standard formula which included creatinine, blood urea nitrogen and serum albumin levels of the patient.

$$\text{eGFR} = 170 \times \text{Serum Creatinine}^{-0.999} \times \text{Age}^{-0.176} \times \text{BUN}^{-0.170} \times \text{Albumin}^{+0.3189} \times 1.18 \text{ if Black} \times 0.762 \text{ if Female}$$

Equipment

US measurements were done by Aloka SSD 4000, convex probe 2.5–5.0 MHz, cut-off filter 100 Hz, with angle of insonation 50°, using a 2–3 mm, Doppler gate, as large as at least one-third of the vessel diameter. Doppler examination of the Renal Arteries requires an 8 hour fast, the patient was asked to drink 500 ml of water 30 minutes prior to the procedure. The Doppler signal was recorded from both kidneys from arcuate arteries at the level of corticomedullary junction and an average of 3 recordings was taken. The resistivity index (RI) measures the resistance of renal arterial flow to the kidney.

Resistivity index

The resistive index (RI) measures the resistance of renal arterial flow to the kidney [2]. In a normal situation, flow through the renal artery occurs throughout systole and diastole. However during renal vasoconstriction there will be reduced to possibly even reversed flow through the renal artery during diastole. When this happens, the resistive index which is calculated by measuring the arterial waveform throughout the cardiac cycle is elevated. Most radiologists consider 0.7 to be the normal RI [5].

Results

Table - 2 shows the characteristics of the patients included in the study. Out of the 30 patients there were 25 (80%) male patients and 5 (20%) female patients. Mean age of presentation was 42 years. 3 (10%) patients were falling into Child Pugh class A, 6 (20%) patients into Child Pugh class B, 21 (70%) patients into Child Pugh class C. Mean values of serum albumin was 2.37 ± 0.57 , of serum bilirubin was 6.24 ± 6.28 , of PT INR was 1.93 ± 0.68 , of serum creatinine was 1.19 ± 0.59 , of BUN was 20.85 ± 11.01 . 20 (66%) patients had esophageal varices, 25 (83%) patients had ascites and 17 (56%) patients had minimal hepatic encephalopathy. Mean values for MELD score was $19.3 + 18.54$, MDRD eGFR (6 variable) was $71.79 + 62.85$, and Resistivity index was $0.77 + 0.27$.

We observed that MELD score was increasing from class A to class C and there was inverse relation between MDRD eGFR (6 variable) and MELD and a direct relation between Resistivity index and MELD in all classes.

12 cases (40 %) were in the age group of 30 -40 years out of which 9 were males and 3 were females, 14 cases (46%) were in the age group of 41-50 years out of which 13 were males and 1 was female, 4 cases (14%) were of >50 years of age out of which 3 were males and 1 was female.

Table - 3 shows that out of the 30 cases, 25(80%) were males and 5 (20%) were females.

Table - 2: Characteristics of patients with alcoholic cirrhosis.

PARAMETERS	ALL PATIENTS (N=30)	CHILD A (N=3)	CLASS B (N=6)	CLASS C (N=21)
AGE (X ± SD)	42.7 ± 6.08	38.44 ± 3.44	40.08 ± 2.88	43.14 ± 5.69
SEX -M/F	25/5	3/0	5/1	17/4
LAB VALUES				
Serum albumin (GM/DL)	2.37 ± 0.57	2.38 + 0.50	2.45 + 0.45	2.35 + 0.57
Serum bilirubin (MG/DL)	6.24 ± 6.28	5.46 + 5.63	6.07 + 6.30	6.44 + 6.30
PT INR	1.93 ± 0.68	1.93 + 0.78	1.99 + 0.63	1.99 + 0.59
Serum creatinine (MG/DL)	1.19 ± 0.59	1.23 + 0.70	1.24 + 0.65	1.20 + 0.60
BUN(MG/DL)	20.85 ± 11.01	21.54 + 11.67	22.62 + 11.87	21.25 + 10.98
Esophageal varices (N)-Y/N	20/10	0/3	2/4	18/3
Hepatic encephalopathy- none/minimal	13/17	3/0	6/0	4/17
Ascites (N)-Y/N	25/5	0/3	4/2	21/0
MELD score (X ± SD)	19.9 ± 18.54	8.7 ± 5.68	19.3 ± 9.27	19.9 ± 8.97
MDRD EGFR 6 Variable (X ± SD)	71.79 ± 62.85	98.87 ± 11.15	70.53 ± 31.12	70.46 ± 30.99
DF score (X ± SD)	124.35 ± 77.54	11.66 ± 6.97	59.32 ± 42.0	63.68 ± 38.54
Resistivity index (X ± SD)	0.77 ± 0.27	0.56 ± 0.05	0.75 ± 0.09	0.77 ± 0.08

Table - 3: Age and sex distribution.

Age group (Years)	No. of patients	Males	Females
30-40	12	9	3
41-50	14	1	1
> 50	4	3	1

Table - 4: Mean MELD scores.

MEAN MELD IN TOTAL CASES (N=30)	CHILD A (N=3)	CHILD B (N=6)	CHILD C (N=21)
19.9 ± 18.54	8.7 ± 5.68	19.3 ± 9.27	19.9 ± 8.97

Table - 4 shows the mean MELD score was 19.9 ± 18.54 and as the severity of cirrhosis was increasing from child A to child C mean MELD

scores were increasing with little variation from class B to C.

$$\text{MELD} = 3.78[\text{Ln serum bilirubin (mg/dL)}] + 11.2[\text{Ln INR}] + 9.57[\text{Ln serum creatinine (mg/dL)}] + 6.43$$

increasing from child A to child C mean RI values were increasing but not much difference between class B to C.

Table - 5 shows the mean RI values was 0.77 ± 0.27 and as the severity of cirrhosis was

$$\text{Resistivity Index} = \frac{\text{Peak Systolic Velocity} - \text{Peak Diastolic Velocity}}{\text{Peak systolic Velocity}}$$

Table - 5: Mean RI values.

Mean RI in total cases (n=30)	CHILD A (n=3)	CHILD B (n=6)	CHILD C (n=21)
0.77 ± 0.27	0.56 ± 0.05	0.75 ± 0.09	0.77 ± 0.08

Table - 6: Mean MDRD EGFR 6 variable scores.

Mean MDRD EGFR 6 variable in total cases (n=30)	CHILD A (n=3)	CHILD B (n=6)	CHILD C (n=21)
71.79 ± 62.85	98.87 ± 11.15	70.53 ± 31.12	70.46 ± 30.99

Table - 7: MELD and RI.

CHILD CLASS	MELD <20 (N=19)	MELD >20 (N=11)	RI < 0.7 (N=7)	RI > 0.7 (N=23)
A	3	-	3	-
B	6	-	4	2
C	10	11	-	21

Figure - 1: Correlation between child class and MELD.

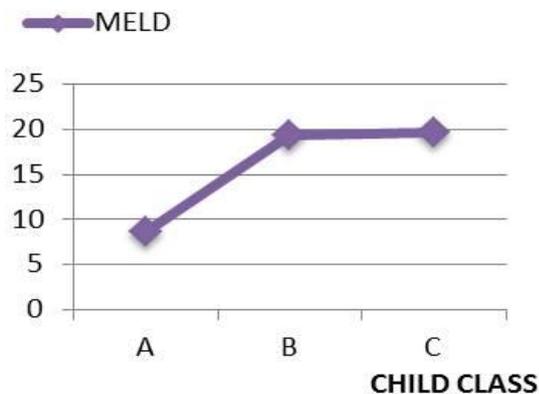


Figure - 3: Correlation between MDRD EGFR 6 variable and MELD.

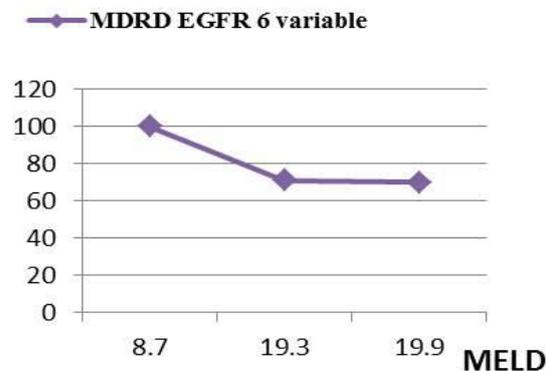


Figure - 2: Correlation between MELD and RI.

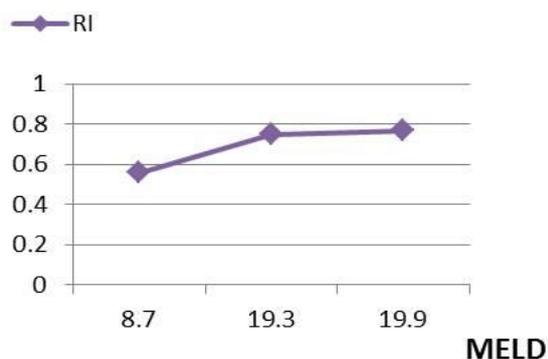


Figure - 4: Correlation between MDRD EGFR 6 variable and RI.

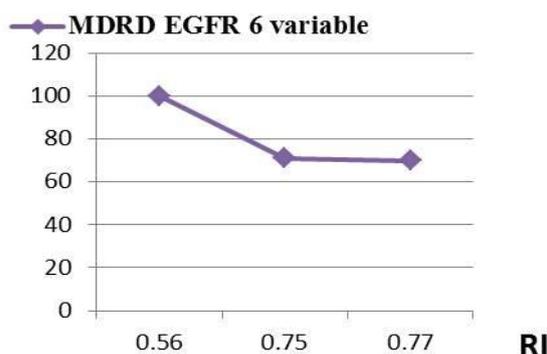


Table - 6 shows that Mean MDRD EGFR 6 variable value was 71.79 ± 62.85 and as the severity of cirrhosis was increasing from child A to child C mean MDRD EGFR 6 variable values were decreasing but not much difference from class B to C.

eGFR = $170 \times \text{Serum Creatinine}^{-0.999} \times \text{Age}^{-0.176} \times \text{BUN}^{-0.170} \times \text{Albumin}^{+0.3189} \times 1.18$ if Black $\times 0.762$ if Female

Figure – 1 graph shows the correlation between child class and MELD score, as severity of cirrhosis was increasing from child class A to class C, MELD scores were increasing with little difference between class B and C.

Figure - 2 graph is showing that MELD score was plotted against RI values there was a direct relationship.

Pearsons correlation between MELD score and RI was +0.55 which was statistically significant with p value of 0.001.

Graph (**Figure - 3**) is showing that when MELD score was plotted against MDRD EGFR 6 variable there was inverse relationship.

Pearsons correlation between MELD score and MDRD eGFR (6 variable) was -0.71, which was statistically significant with p value of 0.00001.

Graph (**Figure - 4**) is showing that when RI was plotted against MDRD EGFR 6 variable there was inverse relationship.

Pearsons correlation between RI and MDRD eGFR (6 variable) was -0.26 which was not statistically significant with p value of 0.16.

When MELD score of 20 was taken as cut off point all the cases were falling into CHILD class C whereas RI value of 0.7 was taken as cut off point majority were falling into CHILD class C (**Table – 7**).

Discussion

The hepatorenal syndrome is a well-recognized complication of liver failure that often appears to develop acutely in previously non-azotemic patients [6]. The earliest stages of this apparently functional form of kidney failure often go unrecognized because creatinine elevation is a late feature of the hepatorenal syndrome spectrum. Intense intrarenal vasoconstriction is an early hallmark of this functional kidney failure, although the precise causes are poorly defined and clinical assessment of the vasoconstriction has up to now been difficult [7-10].

Renal duplex Doppler ultrasonography is a widely available non-invasive modality, to the identification of this early kidney vasoconstriction in non-azotemic patients with established liver disease. Through use of a simply measured and easily obtained parameter, the RI, patients with probable kidney vasoconstriction can be quickly identified. In patients with refractory ascites, as well as in subjects with serum creatinine within the normal range, increased RI seems to be correlated with a higher risk of subsequent deterioration in renal function with eGFR.

In our study intrarenal blood flow Doppler parameters show a significant association with the severity of liver cirrhosis, evaluated by both CHILD's and MELD scores. In my study we found that the correlation between RI and the eGFR are inversely related.

Conclusion

- Resistivity index can be used as an early marker of kidney dysfunction in patients with cirrhosis.
- A MELD score > 20 was a poor prognostic indicator of cirrhosis.
- A Resistivity index of > 0.7 is significant predictor for hepatorenal syndrome hence necessary intervention can be initiated.

- Thus resistivity index is simple non-invasive parameter to assess the renal function.

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