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A Study of Renal Indices in Liver Cirrhosis

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Abstract

Introduction: *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. Patients with liver cirrhosis and portal hypertension develop circulatory dysfunction characterized by disturbance in systemic and renal hemodynamics. Hepatorenal syndrome (HRS) is a "functional" and reversible form of renal failure that occurs in patients with advanced chronic liver disease.*

Aims and Objectives:

- *To evaluate renal indices values in various stages of liver cirrhosis.*
- *To determine their significance in developing hepatorenal syndrome.*

Material and Methods

Study Setting: *The study was conducted in the Department of Radio diagnosis (in association with departments of medicine and pathology) Gajra Raja Medical College and associated J.A. group of hospitals, Gwalior. The study was done during the period extending from October 2012 to October 2013.*

Summary & Conclusion: *The RI of both interlobar and arcuate arteries (renal intraparenchymal vessels) were significantly higher in all patient groups than in control group ($p < 0.05$), the RI was significantly higher in patients with refractory ascites than in patients with diuretic responsive ascitis, and also in patient of diuretic responsible ascitis than in patients with compensated cirrhosis ($p < 0.05$), in patient with hepatorenal syndrome than in patient with diuretic responsive ascitis and patients with compensated cirrhosis ($p<0.05$). Also, the PI was significantly higher in patients with hepatorenal syndrome than in patient with responsive ascitis and patient with compensated cirrhosis ($p<0.05$). Creatinine levels & blood urea levels in patients with the hepatorenal syndrome was significantly higher than that of other different groups ($p<0.05$) but there was no significant change in creatinine levels between patients with compensated cirrhosis and control group. While creatinine levels in patient with diuretic responsive ascitis was signicantly lower than that in patient with compensated cirrhosis ($p<0.05$) there was no significant change between patient with diuretic responsive ascitis and patient with refractory ascitis*

Keywords: *renal indices, liver cirrhosis*

1. Introduction

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. Patients with liver cirrhosis and portal hypertension develop circulatory dysfunction characterized by disturbance in systemic and renal hemodynamic.

Hepatorenal syndrome (HRS) is a "functional" and reversible form of renal failure that occurs in patients with advanced chronic liver disease.

The distinctive hallmark feature of HRS is the intense renal vasoconstriction caused by interactions between systemic and portal hemodynamic. This results in activation of vasoconstrictors and suppression of vasodilators in the renal circulation. Although the assessment of kidney function is of great clinical importance in patients with liver cirrhosis and ascites, serum creatinine and even creatinine clearance are not accurate indicators of renal impairment in patients with advanced liver cirrhosis.

2. Aims And Objectives

- To evaluate renal indices values in various stages of liver cirrhosis.
- To determine their significance in developing hepatorenal syndrome.

3. Material and Methods

3.1. Study Setting

The study was conducted in the Department of Radio diagnosis (in association with departments of medicine and pathology) Gajra Raja Medical College and associated J.A. group of hospitals, Gwalior. The study was done during the period extending from October 2012 to October 2013.

Ultrasonographic examination was performed at the Radiology Department using curvilinear and high frequency linear probes with a real time B mode imaging system with pulsed wave and colour Doppler facilities. All subjects were studied in the morning after overnight fasting. They underwent Abdominal and Pelvic Ultrasonography: The liver, spleen, kidneys, and ascites were evaluated and B mode-Renal duplex Doppler ultrasonography were done to assess Doppler indices. Patients were examined in the supine position as well as in the right and left lateral positions. The following parameters were calculated from each inter lobar artery and the arcuate artery:

1. Resistive and pulsatility index
2. Peak systolic velocity, which is the peak of the systolic waveform
3. End diastolic velocity, which is the velocity at the end of the diastolic phase
4. Mean velocity, which is the velocity throughout the cardiac cycle

A proforma was designed specially to capture the relevant information was used to tabulate the findings. The study was conducted strictly upon the guidelines issued by the Radiology department, and ethical committee.

The method of the study was direct ultrasonographic and Doppler examination examination of the the patient in the radiology department on first visit and then follow up ultrasonographic and Doppler examination after two months on next second visit .

The data was compilled in the formats and subjected to descriptive and statistical analysis.

3.2. Written Informed Consent

The patients were explained complete details about this study. An informed consent form in local language containing all information about this study was given to the patient. The consent was obtained from patient/ or his legal representative.

Study Design: prospective study

3.3. Study Population

The patients included in the study were those with various stages of liver cirrhosis presenting in the department, categorized under Group A included patients with compensated liver cirrhosis, Group B included patients with Responsive ascites, Group C: patients with refractory ascites and Group D: patients suffering from hepatorenal syndrome diagnosed clinically and by renal chemistry by keeping certain inclusion criterias based on a thorough workup of patients by history, clinical examination, laboratory investigations, gray scale sonography findings and clinical course on follow up.. A detailed medical history was recorded in each subject with particular attention to exclude evidence of diabetes, systemic infections, and renal disease, injury or stones, high blood pressure and physical examination was unremarkable in all. Another group of patient Group E were taken as control.

All patients were subjected to clinical assessment including detailed history of chronic liver disease especially bleeding tendency, ascites, jaundice, and encephalopathy.

4. Statistical Methods Applied

Data were checked, coded, entered and analyzed using SPSS(The Statistical Package for Social Sciences) version 10.0 software The results were collected, presented and analyzed using the 0.05 significance level and the 0.01 high significance level, p value of <0.05 was considered significant.

4.1. Statistical Methods Included

Descriptive methods such as mean, standard deviation, frequency distribution (minimal and maximal), independent t-test, one-way ANOVA, quantitative data to test the significance of differences between the mean values of the study variables for comparison between more than two groups and Pearson correlation, for determination of the correlation between the age, and sex of different groups and the resistive index and the correlation between urinary sodium and the resistive index in different groups.

4.2. Equipments Used

- NEMIO-30 Toshiba and ALOKA ultrasonography machines.

- High frequency linear probes 5 to 7 MHz and Curvilinear array transducer 3 to 6 MHz (multi frequency).
- Multi format camera for recording images.

5. Inclusion and Exclusion Criteria

5.1. Inclusion Criteria

1. All patients of age more than 15 years who have sonographic evidence of liver cirrhosis
2. Patients with chronic hepatic disorder with end stage liver disease
3. Patient willing to cooperate for the study.

5.2. Exclusion Criteria

1. Patients having history of diabetes mellitus, hypertension, and nephrotoxic drug intake.
2. Emergency, Trauma and post operative patients.
3. Patients unwilling to cooperate in the study.
4. Patients having other hepatic or renal comorbities.

6. Methods

Following history and clinical examination the patients and controls were subjected to following radiological examinations.

6.1. Gray Scale Ultrasonography

Ultrasound examination was performed on TOSHIBA Nemio-30 / ALOKA US SCANNER. The patients were examined in supine, oblique, both side lateral decubitus and occasionally prone position using a combination of subcostal and intercostals approaches. The kidneys were assessed in transverse and coronal planes. The sonographic features recorded included the size, shape, echotexture, corticomedullary differentiation of the kidneys, cortical thickness, pelvicalyceal, system. Grading of renal parenchymal echotexture was done as follows:

GRADE 1: Echotexture of kidney similar to adjacent liver/spleen

GRADE 2: Echotexture of kidney greater than adjacent liver/ spleen with preserved corticomedullary differentiation

GRADE 3: Echotexture of kidney greatly raised so as to result in diminished or absent corticomedullary differentiation)

6.2. Doppler Evaluation

First the kidneys were optimally visualized in the B mode image in the right and left lateral decubitus positions. After obtaining an optimum B mode, color flow and duplex Doppler were activated and the values of Doppler indices were measured in the proximal middle and distal thirds of at least three interlobar arteries (in the upper mid and lower poles respectively). A mean value is calculated for the Doppler indices for each kidney. Appropriate pulse repition frequency, color and Doppler gain settings and high pass filter were selected for each examination.

7. Observations

This study named "Study of Renal Doppler indices in various stages of liver cirrhosis and its significance in calculating the risk for hepatorenal syndrome" was conducted in department of radiodiagnosis, G.R. Medical College & J.A. Group of Hospitals, Gwalior between September 2012 to October 2013. This study was conducted among 60 patient of cirrhotic patients who were admitted in J.A. Hospitals. All 60 Cirrhotic patients under went clinical laboraterical, radiological examination. 10 normal subjects were taken as control group. On the basis of their clinical profile the patient were divided in 4 groups:

Group-A: Cirrhotic patient without any complication.

Group-B: Cirrhotic patient with complication responding to diuretics.

Group-C: Cirrhotic patient with complication non responding diuretics.

Group-D: Cirrhotic patient with established hepatorenal syndrome

Group-E: Control Group (n=10).

15 patients of each of A, B, C, & D groups were included in study in 10 control patients were also included which are normal subjects.

Data were collected and systematically analysis and statistical test were applied.

Table1. *Age Distribution of Controls (Group E)*

Age in Years	No. of Cases
15-25	1
26-35	1
36-45	3
46-55	2
56-65	2
65-75	1

The above table shows the age distribution among control group. Maximum number of controls groups were in between 36-45 years of age.

Table2. *Variation of Resistive Index with Age in Controls*

S. No.	Age Group	No. of Cases	Mean RI
1	15-25	1	0.51±0.02
2.	26-35	1	0.52±0.03
3.	36-45	3	0.57±0.04
4.	46-55	2	0.59±0.01
5.	56-65	2	0.62±0.02
6.	66-75	1	0.66±0.03

The above table shows variation of resistive index with age in controls. It is observed that resistive index increases with increasing age of the patients.

Table3. *Age Distribution of Cirrhotic Patients*

S. No.	Age Group	No. of Cases Total No. of patient (n)=60
1	15-25	6
2.	26-35	6
3.	36-45	10
4.	46-55	16
5.	56-65	14
6.	66-75	8

The above table shows age distribution of the patients. Maximum number of patients were in 46-55 years of age i.e. 26.68% (n=16). This was then followed by patients of age 56-65 years i.e. 23.37% (n=14).. This was followed by patient in age group 36-45 years of age i.e. 16.66% (n=10). Then the patient is in the age group of 66-75 years i.e. 13.33% (n=8). Then it is followed by age group 26-35 and then 15-25 years of age group i.e. 10% (n=6).

Table4. *Age Distribution among Groups*

S. No.	Age Group	Group A (n-15)	Group B (n-15)	Group C (n-15)	Group D (n-15)	Total (n=60)
1	15-25	3	2	1	0	6
2.	26-35	2	3	1	0	6
3.	36-45	4	3	2	1	10
4.	46-55	3	4	5	4	16
5.	56-65	2	1	4	7	14
6.	66-75	1	2	2	3	8

Among the group A maximum number of patient were of 36-45 years of age i.e. 4% and then 15-25 and 46-55 years of age i.e. 3%. Among the group B maximum no. of patient were 46-55 years of age which was followed by 26-35 & 36-45 years of age. Among the group C maximum number of patient were of 46-55 years of age (n=5) which was followed by 56-65 of age (n=4). Among the group B maximum number of patient were of 56-65 years of age (n=7) which was followed by 56-65 years of age (n=7) which was then followed by 46-55 years of age (n=4).

Table5. *Gray Scale Sonographic Finding in Various Stages*

		A	B	C	D
Liver Size	Normal	-	-	-	-
	Increased	14	6	4	2
	Decreased	1	9	11	3
Liver Echogenicity	Normal	-	-	-	-
	Hypoechoic	3	2	-	-
	Hyperechoic	12	13	15	15
Liver Ecotexture	Normal	2	-	-	-
	Coarsened	13	15	15	15
Irregular Liver Surface		15	15	15	15
Kidney Size	Normal	15	15	14	3
	Increased	-	-	-	2
	Decreased	-	-	1	1
Kidney Echogenicity	Normal	15	14	5	2
	Hypo	-	-	-	-
	Hyper	-	1	10	13
Renal Cortioco-medullary differentiation	Normal	15	14	13	-
	Accentuated	-	-	-	-
	Attenuated	-	1	1	6
	Lost	-	-	1	9

Ascitis	None	12	-	-	-
	Mild	3	9	-	-
	Moderate	-	5	11	3
	Gross	-	1	4	13
Splenomegaly	None	13	-	-	-
	Mild	2	10	2	-
	Moderate	-	3	9	7
	Massive	-	2	4	8

On comparison the Gray scale sonographic findings among the groups, it is observed that liver size increased in majority of the patients of group A (n=14). Where as in maximum number of patients the size of liver was decreased. Among the group A (n=1), Group B (n=9), Group C (n=11), Group D (n=3)

Liver Echogenicity

Liver was hyperechoic among the majority of patient Group A (n-12), Group B (n-13), Group C (n=10), Group D (n=15).

Liver Echotexture

In majority of the patient liver Echotexture coarsened Group A (n=13), Group B (n=15), Group C (n=15), Group D (n=15).

Irregular Liver Surface

It was observed in all cirrhotic patient.

Kidney Size

Kidney size was normal in Group A & B. Where as it is decreased in 1 patient of Group C & normal in 14 patient in Group C. Kidney size in decreased in 3 patient of Group D.

Kidney Echogenicity

Kidney echogenicity was normal in group A. In Group B normal in (n=14) patient and increase echogenicity in 1 patient. In group C normal in n=5 i.e. increase in majority of the patient. And in Group B Echogenicity b=5 and increase in (n=10) i.e. in majority of the patient.

Renal Corticomedullary Differentiation

In group A it was normal in all the patients, in Group B normal in 14 patients and attenuated in 1 patient. In group C normal in 13 patients and attenuated in 1 patient and lost in 1 patient. In group D attenuated in 6 patients and lost in 9 patient.

Ascitis

In group a no evidence of ascitis seen in 12 patient and mild ascitis was seen in 3 patients. In group B mild ascitis in 9 patients and moderate ascitis seen in 5 patient. Group C moderate ascitis seen in 11 patient and gross ascitis seen in 4 patient. In Group D moderate ascitis seen in 3 patient and gross ascitis in 12 patients.

Splenomegaly

In Group A spleen size was normal in 13 patients and there is mild splenomegaly was seen in 2 patient. In group B mild grade splenomegaly was seen in 10 patient moderate grade in 3 patient in massive splenomegaly in 2 patients i.e. majority patients has mild splenomegaly. In Group C mild splenomegaly seen in 2 patient moderate in 9 patient massive in 4 patient i.e. moderate grade splenomegaly seen in majority of patient. In Group D moderate ascitis seen in 7 patient, massive seen in 8 patient i.e. massive splenomegaly seen in majority of the patient.

Table6. *Doppler Indices in Various Stages*

Doppler Index		**A**	**B**	**C**	**D**	**E**
Ri	< 0.60	9	7	6	-	9
	0.61-0.70	6	6	4	-	1
	0.71-0.80	-	2	4	8	-
	>0.80	-	-	1	7	-
Pi	< 1.00	7	2	2	-	9
	1.01-1.40	8	10	10	-	1
	1.41-1.80	-	3	3	9	-
	> 1.80	-	-	1	6	-

In group A, R.I. value were < 0.60 in 9 patient, between 0.61 to 0.70 in 6 patient, in Group B < 0.60 seen in 7 patient ,in between 0.61 to 0.70 patient in 6 patient and 0.71 to 0.80 in 2 patient. In Group C < 0.60 in 6 patient, between 0.61 to 0.70 in 4 patient, in between 0.71 to 0.80 in 4 patient > 0.80 in 1 patient. In group D, R.I. indices between 0.71 to 0.80 in 8 patient, > 0.80 in 7 patients.

For P.I. Value in Various Group

In group A, PI value < in 7 patients and between 1.01 to 1.40 in 8 patients. In Group B < 1.00 in 2 patient, between 1.01 to 1.40 in 10 patients and 1.41 to 1.80 in 3 patients. In group C < 1.00 in 1 patient, between 1.01 to 1.40 in 10 patients, between 1.41 to 1.80 in 3 patients, > 1.80 in 1 patients. In Group D PI values were 1.41 to 1.80 in 9 patients, > 1.80 is 6 patients. Where as in control group E, PI value < 0.10 in 9 patients in between 1.01 to 1.40 in 1 patient.

Table7. *Urea and Creatinine Values In Various Stages*

Doppler Index		A	B	C	D	E
Creatinine	<1.15	15	14	12	-	10
	> 1.5	-	1	3	15	-
Urea	< 40	15	14	12	-	10
	> 40	-	1	3	15	-

In group A Blood urea levels < 40 in 15 patient, Serum creatinine level < 1.15 in 15 patient in Group B Blood Urea level < 40 in 14 patients > 40 in 1 patient. Serum Creatinine < 1.15 in 14 patient > 1.5 in 1 patient. In Group C Blood Urea level < 40 in 12 patients > 40 in 3 patient. Serum Creatinine < 1.15 in 12 patient > 1.5 in 3 patient. In Group D Blood Urea level > 40 in 15 patient. Serum Creatinine in < 1.5 in 15 patient. In Group E Blood Urea < 40 and Blood Serum Creatinine < 1.15 in all the patients.

Follow Up Tables

Table8. *Gray Scale Renal Sonographic Findings*

		A	B	C	D
Size	Normal	15	7	6	-
	Increase	-	1	2	-
	Decrease	-	7	7	15
Echogenicity	Normal	14	12	4	-
	Hypoechoic	-	-	-	-
	Hyperechoic	1	3	11	15
Echogenicity C.M. Differentiation	Normal	-	-	-	-
	Diminished	-	5	7	-
	Lost	-	3	5	15

Kidney Size

In Group A renal size was normal in all patients. Group B increase in 1 patient, normal in 7 patient, and decreased in 7 patient. Group C normal in 6 patient, increase in 2 patient, decreased in 7 patient. In Group D decreased in all patients.

Renal Ecogenicity

In group A normal in 14 patient, increase in 1. In Group B normal in 12 patient, increased in 3 patients. In group C normal in 4 patient, increased in 11. In Group D increased in all patients.

Corticomedullary Differentiation

In group B all patients had normal Corticomedullary differentiation. In Group B normal in 7, diminished in 5 and lost 3. In Group C normal in 3 patient, diminished in 7 patient and lost in 5 patient. In Group D lost in all patients.

Follow Up Tables

Table9. *Doppler Indices in Various Stages*

		A	B	C	D	E
Ri	< 0.60	7	6	4	-	9
	0.61-0.70	5	5	2	-	1
	0.71-0.80	3	3	6	6	-
	>0.80	-	1	3	9	-
Pi	< 1.00	7	6	4	-	9
	1.01-1.40	5	5	2	-	1
	1.41-1.80	3	3	6	6	-
	> 1.80	-	1	3	9	-

In group A R.I. < 0.60 in 7 patients, between 0.61 to 0.70 in 5 patients, and between 0.71-0.80 in 3 patients. In Group B < 0.60 in 6 patients, between 0.61 to 0.70 in 5 patients, between 0.71-0.80 in 3 patients and > 0.80 in 1 patient. In Group C <0.60 in 4 patients, between 0.61 to 0.70 in 2 patients, between 0.71-0.80 in 6 patients and < 0.80 in 3 patients. In Group D between 0.71 to 0.80 in 6 patients, > 0.80 in 9 patients. In Group E < 0.60 in 9 patients, between 0.61 to 0.70 in 1 patients.

For P.I.

In group A < 1.00 in 7 patients, between 1.01 to 1.40 in 5 patients, between 1.41 to 1.80 in 3 patients. In group B < 1.00 in 6 patients, between 1.01 to 1.40 in 5 patients, between 1.41 to 1.80 in 3 patients and > 1.80 in 1 patients. In Group C < 1.00 in 4 patients, between 1.01 to 1.40 in 2 patients, between 1.41 to 1.80 in 6 patients, and > 1.80 in 3 patients. In Group D 1.41 to 1.80 in 6 patients > 1.80 in 9 patients. Group E < 1.00 9 patient and between 1.01 to 1.40 in 1 patients.

Follow Up

Table10

		A	B	C	D	E
Creatinine	<1.15	15	13	9	-	10
	> 1.5	-	2	6	15	-
Urea	< 40	15	13	9	-	10
	> 40	-	2	6	15	-

About table shows the follow up status of Urea and Creatinine. In Group A Blood Urea < 40 in seen in 15 patients and Serum creatinine < 1.15 seen in 15 patients. In Group B Blood Urea < 40 in 13 patient, in > 40 in 2 patients. Serum Creatinine < 1.15 in 13 patient and > 1,5 in 2 patients. In Group C Blood Urea < 40 in 9 patients, > 40 in 6 patient, Serum creatinine < 1.15 in 9 patient and > 1.5 in 6 patients in Group D Blood Urea > 40 and Serum Creatinine > 1.5 seen in 15 patient. In Group E Blood Urea < 40 in 10 patient in Serum Creatinine > 1.15 in 10 patients.

Table11. *Group A*

	Na (meq/dl)	K (meq/dl)	Albumin	Creatinine (mg)	Urea (mg)	Bilirubin (total in mg/dl	SGOT (IU/L)	SGPT (IU/L)	Renal Doppler RI	Renal Doppler PI
Mean	138.47	4.18	3.68	0.90	23.60	2.46	55.33	52.67	0.5253	0.6413
SD	5.32	0.55	0.49	0.35	8.38	0.92	8.97	7.64	0.1488	0.4131
Corr.									**0.2073**	**0.2767**

In the above table which includes Group A i.e. patients of uncomplicated Cirrhosis. This group of 15 patients were showed that mean Na^+ in the group was 138.47 with SD of 5.32 which was in the normal range. Whereas mean K^+ value was 4.18 S.D. of 0.55 and albumin was 3.68 with SD 0.49 and Serum Bilirubin level was 2.46 with SD 0.92, Mean SGOT was 55.33 with SD 8.97, and Mean SGPT was 52.67 with SD 7.64. Mean Blood urea in the group was 23.60 with SD 8.38 and mean creatinine value 0.90 with SD 0.35 and Mean RI Value 0.53 with SD 0.15 and Mean PI value were 0.64 with SD 0.41.

Upon correlation, the values obtained in colour doppler parameters with those of hematological parameter, the coefficient of co-relation between blood urea & mean RI was 0.20 and the coefficient of co-relation of Blood urea and Mean PI was 0.27.

This indicates that positive correlation exists between the values of RI & PI & Blood Urea. It is observed that increased RI & PI value in cirrhotic patients of group A was associated with corresponding increased Blood urea level.

The quantitative estimation of level of increase in blood urea with level of increase in RI & PI could not be obtained because of the lack of sensitivity of laboratory investigations to correlate with small changes in RI & PI value.

Table12. *Group B*

	Na (meq/dl)	K (meq/dl)	Albumin	Creatinine (mg)	Urea (mg)	Bilirubin (total in mg/dl	SGOT (IU/L)	SGPT (IU/L)	Renal Doppler RI	Renal Doppler PI
Mean	144.93	4.18	3.75	1.25	34.47	3.86	111.27	70.20	0.62	1.20
SD	7.44	0.62	0.32	0.66	10.67	5.22	147.98	99.84	0.09	0.27
Corr.									**0.26**	**0.32**

In the above table which includes Group B i.e. Cirrhosis patients who are responding to treatment (diuretic etc).This group of 15 patients showed that mean Na^+ in the group was 144.93 with SD of 7.44. Whereas mean K^+ value was 4.18 S.D. of 0.62 and albumin was 3.75 with SD 0.32 and Serum Bilirubin level was 3.86 with SD 5.22, Mean SGOT was 111.27 with SD 147.98, and Mean SGPT was 70.20 with SD 99.84. These indices are raised as compared to Group A.

Mean Blood urea in the group was 34.47 with SD 10.67 and mean creatinine value 1.25 with SD 0.66 and Mean RI Value 0.62 with SD 0.09 and Mean PI value were 1.20 with SD 0.27 Upon correlation, the values obtained in colour doppler parameters with those of hematological parameter, the coefficient of co-relation between blood urea & mean RI was 0.26197 and the coefficient of co-relation of Blood urea and Mean PI was 0.317.

This indicates that positive correlation exists between the values of RI & PI & Blood Urea. It is observed that increased RI & PI value in cirrhotic patients of group B was associated with corresponding increased Blood urea level.

Table13. *Group C*

	Na (meq/dl)	K (meq/dl)	Albumin	Creatinine (mg)	Urea (mg)	Bilirubin (total in mg/dl	SGOT (IU/L)	SGPT (IU/L)	Renal Doppler RI	Renal Doppler PI
Mean	144.73	4.12	2.40	1.31	41.20	5.74	78.87	42.73	0.64	1.43
SD	7.64	0.53	0.53	0.61	19.07	4.76	36.26	19.72	0.14	0.24
Corr.									**0.2762**	**0.2202**

In the above table which includes Group C i.e. patients of complicated Cirrhosis non responding to treatment. In this group of 15 patients showed that mean Na^+ in the group was 144.73 with SD of 7.64. Whereas mean K^+ value was 4.12 S.D. of 0.53 and albumin was 2.40 with SD 0.53 and Serum Bilirubin level was 5.74 with SD 4.7, Mean SGOT was 78.87 with SD 36.26, and Mean SGPT was 42.73 with SD 19.72.

Mean Blood urea in the group was 41.20 with SD 19.07 and mean creatinine value 1.31 with SD 0.61 and Mean RI Value 0.64 with SD 0.14 and Mean PI value were 1.43 with SD 0.24.Upon correlation the values obtained in colour doppler parameters with those of hematological parameter, the coefficient of co-relation between blood urea & mean RI was 0.2762 and the coefficient of co-relation of Blood urea and Mean PI was 0.220159.

This indicates that positive correlation exists between the values of RI & PI & Blood Urea. It is observed that increased RI & PI value in cirrhotic patients of group C was associated with corresponding increased Blood urea level.

Table14. *Group D*

	Na (meq/dl)	K (meq/dl)	Albumin	Creatinine (mg)	Urea (mg)	Bilirubin (total in mg/dl	SGOT (IU/L)	SGPT (IU/L)	Renal Doppler RI	Renal Doppler PI
Mean	224.40	2.67	1.84	13.12	100.87	19.53	501.20	293.61	0.75	1.76
SD	55.27	0.61	0.58	2.85	14.78	8.23	395.12	180.31	0.07	0.06
Corr.									**0.31**	**0.12**

In the above table which includes Group D i.e. patients of hepatorenal syndrome. This group of 15 patients showed that mean Na^+ in the group was 224.40 with SD of 55.27. Whereas mean K^+ value was 2.67 S.D. of 0.61 and albumin was

1.84 with SD 0.58 and Serum Bilirubin level was 19.53 with SD 8.23, Mean SGOT was 501.20 with SD 395.12, and Mean SGPT was 293.61 with SD 180.31.

Mean Blood urea in the group was 100.87 with SD 14.78 and mean creatinine value 13.12 with SD 2.85 and Mean RI Value 0.75 with SD 0.07 and Mean PI value were 1.76 with SD 0.06. Upon correlation the values obtained in colour doppler parameters with those of hematological parameter, the coefficient of co-relation between blood urea & mean RI was 0.309 and the coefficient of co-relation of Blood urea and Mean PI was 0.119.

This indicates that positive correlation exists between the values of RI & PI & Blood Urea. It is observed that increased RI & PI value in cirrhotic patients of group D was associated with corresponding increased Blood urea level.

Table15. *Group E*

	Na (meq/dl)	K (meq/dl)	Albumin	Creatinine (mg)	Urea (mg)	Bilirubin (total in mg/dl	SGOT (IU/L)	SGPT (IU/L)	Renal Doppler RI	Renal Doppler PI
Mean	141.40	4.07	3.64	0.57	28.50	0.60	19.80	25.10	0.54	0.88
SD	9.59	0.60	0.57	0.29	6.62	0.23	8.89	5.70	0.08	0.42
Corr.									**0.53**	**0.11**

In the above table which includes Group E i.e. normal control group. This group of 15 patients showed that mean Na^+ in the group was 141.40 with SD of 9.59. Which was in the normal range? Whereas mean K^+ value was 4.07 S.D. of 0.60 and albumin was 3.64 with SD 0.57 and Serum Bilirubin level was 0.60 with SD 0.23, Mean SGOT was 19.80 with SD 8.89, and Mean SGPT was 25.10 with SD 5.70.all in normal range.

Mean Blood urea in the group was 28.50 with SD 6.63 and mean creatinine value 0.57 with SD 0.29 and Mean RI Value 0.54 with SD 0.08 and Mean PI value were 0.88 with SD 0.44. Upon correlation the values obtained in colour doppler parameters with those of hematological parameter, the coefficient of co-relation between blood urea & mean RI was 0.526 and the coefficient of co-relation of Blood urea and Mean PI was 0.109.

This indicates that positive correlation exists between the values of RI & PI & Blood Urea. It is observed that all the values of RI & PI & serum urea level were within normal limits among the subjects of control group.

Table16. *Group A Follow Up*

S.NO	UREA	CREATININE	RI	PI
Mean	25.33	0.91	0.64	0.95
SD	9.04	0.23	0.09	0.38
correl	0.245492	0.033592		

The mean blood urea values were 25.33 with SD 9.00, mean Serum creatinine values were 0.91 with SD 0.23.

The Mean RI values 0.64 with SD 0.09. Mean PI values 0.95 with SD 0.38.

This was higher than previously observed values.

Blood urea mean was 23.60 with S.D 8.38, Serum creatinine mean was 0.70 with SD 0.35. The mean RI 0.53 with SD 0.15, the mean PI value was 0.64 with SD 0.41.Upon correlation of the Renal Colour Doppler parameters (i.e. RI & PI) with observed haematological parameters i.e. Blood Urea, the following observation was found. The co-efficient of correlation between Blood urea & Mean RI was 0.24592. The coefficient of correlation between Blood urea & Renal PI 0.033. This indicates the positive correlation exist between the values of RI & PI with blood urea.

It is observed that increased levels of RI & PI values were associated with increased in blood urea level.

Table17. *Group B Follow Up*

S.NO	UREA	CREATININE	RI	PI
Mean	1.27	36.93	0.64	1.21
SD	0.89	14.41	0.12	0.41
correl	0.43959	0.378273		

The mean blood urea values were 36.93 with SD 14.41, mean Serum creatinine values were 1.27 with SD 0.89. The Mean RI values were 0.64 with SD 0.12. Mean PI values 1.21 with SD 0.41.

This was higher than previously observed values.

Blood urea mean 34.47 & S.D. 10.67, Serum creatinine mean 1.25 with SD 0.66. The mean RI 0.62 with SD 0.14, the mean PI value was 1.20 with SD 0.27.Upon correlation of the Renal Colour Doppler parameters (i.e. RI & PI) with observed hematological parameters i.e. Blood Urea. The following observation was found, the co-efficient of correlation between Blood urea & Mean RI was 0.43959. The coefficient of correlation between Blood urea & Renal PI 0.378. This indicates the positive correlation exist between the values of RI & PI with blood urea.

It is observed that increased levels of RI & PI values were associated with increased in blood urea level.

Table18. *Group C Follow Up*

S.NO	UREA	CREATININE	RI	PI
Mean	1.73	49.40	0.69	1.44
SD	0.79	22.62	0.19	0.42
correl	0.424796	0.320005		

The mean blood urea values were 49.40 with SD 22.62, mean Serum creatinine values were 1.73 with SD 0.79. The Mean RI values 0.69 with SD 0.19. Mean PI values 1.44 with SD 0.42.

This was higher than previously observed values.

Blood urea mean 41.20 & S.D. 19.01, Serum creatinine mean 1.31 with SD 0.61. The mean RI 0.64 with SD 0.14, the mean PI value was 1.43 with SD 0.24.

Upon correlation of the Renal Colour Doppler parameters (i.e. RI & PI) with observed hematological parameters i.e. Blood Urea. The following observation was found, the co-efficient of correlation between Blood urea & Mean RI was 0.424. The coefficient of correlation between Blood urea & Renal PI 0.320 this indicates the positive correlation exist between the values of RI & PI with blood urea.

It is observed that increased levels of RI & PI values were associated with increased in blood urea level.

Table19. *Anova Results*

For purpose of comparison of all the five groups i.e. A, B, C, D, E, the data were collected for systematically analyse by SPSS software for application of analysis of variance test i.e. ANOVA test.

Upon application of ANOVA the following results were obtained.

F-values	28.35	18.98	40.98	219.48	86.68	31.77	14.49	19.3	9.241	30.861
P-values	0	0	0	0	0	0	0	0	0	0

This result clearly interprets that since P~0 i.e. $p<0.05$ so there is significant difference exist among the various groups. i.e. the 5 different study groups having remarkable difference among each other and the study results of one study group cannot be applied to other group as well.

Table20. *Paired t-Test*

For the purpose of comparison of follow up status of patients with previous status Paired t-test was applied.

The paired t-test was applied for Group A was follow up data of Group A. In this the results were as follows.

Table20.1: *Group A vs Follow-up Group A*

	t-Value	p-Value
Urea	0.873	0.398
Creatinine	0.103	0.919
RI	2.413	0.03
PI	1.912	0.077

Since the $p>0.05$ for urea, creatinine & PI which shows that there was no any significant difference between these parameters in patient at presentation in OPD and in follow up. Renal RI values was ($P<0.05$) so there is significant difference in RI in initial presentation and in follow up of the patient. The paired t-test was applied for Group B was follow up data of Group B. In this the results were as follows.

Table20.2: *Group B vs Follow-up Group B*

	t-Value	p-Value
Urea	0.56	0.584
Creat	0.065	0.949
RI	0.441	0.666
PI	0.114	0.91

Since the $p>0.05$ for urea, creatinine, RI & PI which shows that there was no any significant difference between these parameters in patient at presentation in OPD and in follow up. The paired t-test was applied for Group C was follow up data of Group C. In this the results were as follows.

Table20.3: *Group C vs Follow-up Group C*

	t-Value	p-Value
Urea	1.416	0.179
Creat	2.033	0.061
RI	0.76	0.46
PI	0.151	0.882

Since the p>0.05 for urea, creatinine, RI & PI which shows that there was no any significant difference between these parameters in patient at presentation in OPD and in follow up.

8. DISCUSSION

The hepatorenal syndrome is a well recognized complication of liver failure that often appears to develop acutely in previously non azotemic patients. The earliest stages of this apperently functional form of kidney failure often go unrecognised because creatinine elevation is a late feature of the hepatorenal syndrome. Intense intrarenal vasoconstriction is an early hallmark of this functional kidney failure, although the precise causes are poorly defined & clinical assessment of the vasoconstruction has upto now been difficult. We have applied renal duplex Doppler ultrasonography a widely available noninvasive modality, to the identification of this early kidney vasoconstriction in non azotemic patients with established liver disease through use of simply measured and easily obtained parameter, the RI/PI in patients with probable kidney vaoconstriction can be quickly identified. We hypothesised that patients with an elevated RI/PI (presumbly reflecting intra renal vasoconstitution) would be at greater risk for development of overt hepatorenal syndrome. We found renal RI/PI be a useful non invasive predictor of subsequent kidney status is non-azotemic patient with liver disease.

In this study we tried to predict renal dyssfunction by monitoring the range of RI/PI values among the patient in various stage of cirrhosis and tried to correlate this with altered levels of Blood urea and serum creatinine levels which is itself is an indicator of Renal dysfunction is also studied to know the outcome.

In case of group A i.e. patient of uncomplicated cirrhosis. The initial RI & PI values of the patient was < 0.71 & 1.42 & none had raised blood urea and creatinine level. Whereas on follow up patient of group A 20.5% of them i.e. (n=3) have raised RI/PI values but still none of them have elevated blood urea/serum creatinine level.

In case of Group B initially only 13.5% (n=2) have RI value on higher side i.e. (> 0.70) & only 20% have raised PI value i.e. > 1.41 on hematological values only 6% (n=1) have raised blood urea /serum creatinine where as upon follow up of patient of group B 26.66% (n=4) patient have raised RI/PI values i.e. (RI > 0.70 & PI > 1.41) and on haematological examination 13.33% (n=2) have raised Blood Urea & Serum creatinine.

In case of Group C 33.33% (n=5) patient have RI/PI value on higher side i.e. (RI > 0.70 & P > 1.41) & on haematological examination 20% (n=3) of patient have raised blood urea & serum creatinine value i.e. (Blood urea > 40 & serum creatine > 1.5). On follow up of patient of group C 60% (n=15) have RI/PI value on higher side & on haematological examination 40% (n=5) have raised blood urea & serum creatinine values.

In case of group D all 100% have raised values of RI/PI values i.e. (RI > 0.70 & PI > 1.41) and raised Blood urea & serum creatinine (Blood Urea > 40 & Serum Creatinine > 1.5) and also in follow all the patient have raised RI/PI values and raised blood urea & serum creatinine level.

When the data collected from all the above groups it was then subjected to statistically analysis to correlate. The values of RI & PI & Blood Urea it was observed that patient with initially raised RI & PI values irrespective of blood urea & creatinine levels had subsequently showed raise in Blood urea & creatinine levels. This was also in accordance study of Joel et al.

Upon comparing the coefficient of correlation of Renal Doppler RI & PI values among the groups with blood urea levels it was observed that a positive correlation is present between the increase in RI, PI values & blood urea level. This shows that patient with raised RI/PI values will subsequently show raise in blood urea levels. This implies that patient with elevated RI/PI values may probably have intra renal vasoconstruction which can subsequently lead to renal dysfunction in cirrhosic patient and can lead to grave consequences like hepatorenal syndrome. This is also in accordance to finding in study of Fouad Y.M. et al.

Although almost all patient is when increase urea/hepatorenal syndrome developed & most in when kidney dysfunction developed had an elevated renal RI/PI values. Not all patient with an elevated RI/ PI values showed a poor kidney outcome. It is therefore presume that an additional insult such as sepsis, bleeding or nephrotoxic drugs administration is necessary to hasten the development of clinical hepatorenal syndrome among the group at risk patient i.e. those already with renal vasoconstiction reflexed by elevated Ri & PI.

Although the severity of liver disease is related to observed RI the elevation of RI/PI was much more common in Group C than Group A, it would be a mistake to consider the RI as merely providing repetitive information to traditional parameters.

However combining the clinical & doppler data allows identification of a sub group of patient at highest risk for kidney dysfunction and hepatorenal syndrome.

Several potential limitation of our study are important to come. We used serum creatinine & blood urea as an indicator of the patients initial kidney status. More sophisticated types of kidney evaluation such as glomerular filteration rate were not used.

Other pathological states of kidney besides hepatorenal syndrome & frank kidney failure are capable of elevating RI & PI.

Kidney obstruction, acute tubular necrosis, renal vein thrombsis in the hemolytic uremic syndrome etc. all can cause elevation in RI & PI values. Also acute GI bleeding, constipation etc can cause change in blood urea level.

Also the quantitative estimation of level of increase in Blood Urea with level of increase in RI & PI could not be established because of lack of sensitivity of laboratory investigation to correlate exactly the minute rise in blood urea level with small change in RI and PI values.

9. SUMMARY

The RI of both interlobar and arcuate arteries (renal intraparenchymal vessels) were significantly higher in all patient groups than in control group ($p < 0.05$), the RI was significantly higher in patients with refractory ascites than in patients with diuretic responsive ascitis, and also in patient of diuretic responsible ascitis than in patients with compensated cirrhosis ($p < 0.05$), in patient with hepatorenal syndrome than in patient with diuretic responsive ascitis and patients with compensated cirrhosis ($p<0.05$). Also, the PI was significantly higher in patients with hepatorenal syndrome than in patient with responsive ascitis and patient with compensated cirrhosis ($p<0.05$). Creatinine levels & blood urea levels in patients with the hepatorenal syndrome was significantly higher than that of other different groups ($p<0.05$) but there was no significant change in creatinine levels between patients with compensated cirrhosis and control group. While creatinine levels in patient with diuretic responsive ascitis was signicantly lower than that in patient with compensated cirrhosis ($p<0.05$) there was no significant change between patient with diuretic responsive ascitis and patient with refractory ascitis

10. CONCLUSION

Both renal resistive index & pulsatility index increases with degree of hepatic decompensation. Renal duplex ultrasound is a non invasive, simple and easy method to study intrarenal haemodynamics in patients with liver cirrhosis who are at higher risk for subsequent kidney dysfunction & hepatorenal syndrome by early detection of renal vasoconstruction, in which an elevated RI/PI are obtained.

Doppler information will be useful for prognosis and in the management of liver disease, in patients whenever they require paracentesis, diuretic therapy, potentially nephrotoxic medications or radiographic contents examination. In the future renal RI and PI measurements may prove to be valuable in assessing therapies designed to maintain normal renal vascular tone (26.271) and in recognising patient in when early liver transplant may be desirable.

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