ORIGINAL ARTICLE

RENAL DOPPLER ULTRASOUND AS PREDICTOR OF RENAL IMPAIRMENT IN PATIENTS WITH HEPATITIS C AND ITS CORRELATION WITH SERUM CREATININE

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Background: In patients with liver cirrhosis due to Hepatitis C virus, impaired renal haemodynamics leads to disturbance of glomerular filtration rate, real time estimation of renal haemodynamics can be assisted using renal Doppler. The aim of this study was to determine the correlation between renal resistive index (RI) and serum creatinine for evaluation of renal function in patients with Hepatitis C infection. **Methods:** This cross-sectional research was done from 22nd November 2013 to 5th November 2018 at Radiology Department, Mayo Hospital, Lahore. A total of 158 Hepatitis C positive patients divided to four groups (A, B, C, and D) according to disease stages and 79 healthy individuals were included as control group (group E). Serum creatinine was estimated and renal resistive index studied on colour Doppler, and correlation between serum creatinine and renal resistive index was studied. **Results:** Serum creatinine levels were considerably higher among diseased groups as compared to the control group. The highest creatinine level was observed in Group-D (1.05±0.20), followed by group C, B and A. Similarly, mean renal resistive index was significantly higher in diseased groups (highest: Group-D; 0.78 and 0.81 in right and left kidneys respectively). **Conclusion:** Renal resistive index has positive correlation with serum creatinine level. Resistive index taken on Doppler ultrasound can predict disease progression at an early stage, even before establishment of clinical symptoms and derangement of serum creatinine.

Keywords: Renal Doppler, resistive index, creatinine, hepatitis c, cirrhosis, mixed cryoglobulinemia

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INTRODUCTION

Hepatitis C does not only affect the liver, but also has extrahepatic manifestations. It has renal, neurological and dermatological complications due to a chronic immune complex-mediated process known as mixed cryoglobulinemia (MC). It has a strong association with mixed cryoglobulinemia in which vasculitis of small and medium sized arteries and veins occurs due to deposition of complexes of complement, cryoglobulin and antigen in vessel walls. It clinically presents as glomerulonephritis when kidneys are involved.[1] Type-I membranoproliferative glomerulonephritis (MPGN) associated with type II cryoglobulinemia is the most frequent association when kidneys of HCV infected patients are involved. Among all, 30–36% patients with cryoglobulinemia develop MPGN and it is the most relevant clinical manifestation.[2]

Renal Duplex Doppler Ultrasound is a simple, effective and non-invasive method and enables the detection of altered renal haemodynamics even before the renal dysfunction becomes clinically evident.[3] Renal Resistive Index (RI) is a useful parameter for quantifying the alternation in renal blood flow that may occur with renal impairment and has significant correlation relation with serum creatinine levels.[4]

Creatinine overestimates the renal function and results can be biased in case of liver disease. Therefore in HCV patients serum creatinine levels are affected by altered liver function and it may not correctly determine the renal function.[5] Renal Doppler Duplex Ultrasound may be useful for early identification of patients at high risk for developing impaired renal function. It can also be used to predict further disease course and outcomes.[6] The aim of this study was to assess the clinical validity of renal resistive index to diagnose renal impairment and correlate it with serum creatinine in patients having Hepatitis C infection.

MATERIAL AND METHODS

It was an analytic, cross-sectional study, conducted at Department of Diagnostic Radiology, Mayo Hospital Lahore, from 22nd November 2013 to 5th November 2018. The sample size was 158, calculated at 90% confidence level taking expected percentage of renal impairment in patients with Hepatitis C as 30%[7], margin of error at 6%, (α=0.06). Non-probability purposive sampling technique was used for data collection. The study was approved by the Institutional Review Board/Ethical Review Committee at King Edward Medical University. Written informed consent was taken from all individuals.

A total of 158 patients having Hepatitis C infection were selected as diseased population and 79 healthy individuals visiting hospital for routine physical examination were selected as control group.

First encounter was considered as Screening Stage where History, Clinical Examination, Serum Creatinine was performed. Patients already diagnosed with Hepato-renal Syndrome, Diabetes Mellitus, systemic hypertension, nephrolithiasis, renal vascular disease or malignancies were excluded from the study.

Included patients were divided into groups according to the stage of disease and ascites: Patients without liver cirrhosis (group A), patients at compensation stage of liver cirrhosis (no ascites) (group B), patients at decompensation stage of liver cirrhosis with non-refractory ascites (group C), patients with liver cirrhosis with refractory ascites (group D) and healthy individuals serving as control (group E).

Using real time ultrasound equipment (Toshiba Nemio XG) with standard 3.5–5.0 MHz curvilinear transducer, Colour Doppler Ultrasonography was performed in all patients and healthy controls to localize vessels and for calculation of Resistive Index (RI). RI value of inter lobar or segmental intra-renal arteries was calculated in each kidney using standard formula (RI=A-B/A). A mean RI value for each kidney was taken after obtaining three reproducible waveforms. RI value of ≤0.6 was considered as normal and RI value of 0.7 was taken as an upper limit. Values above 0.7 were noted as high Resistive Index (RI). RI values were co-related with serum creatinine levels. Value of serum creatinine was noted while keeping the standard reference range (0.84–1.21 mg/dl) and any deranged values were taken as abnormal.

Data was analysed on SPSS-20. One-way ANOVA was used to compare resistive index and serum creatinine value in relation to hepatitis C severity. Independent sample *t*-test was used to compare the resistive index and serum creatinine in hepatitis C positive cases and controls if data held the assumption of normality otherwise nonparametric test was applied. Spearman correlation coefficient was used to assess the correlation between resistive index and serum creatinine, and $p<0.05$ was taken as significant.

RESULTS

Mean age of Hepatitis C patients was 44.39±8.60 years. Males were 57.3% and females were 42.6%. Among these patients 20 patients were without cirrhosis (group A), 14 patients were with compensated cirrhosis without ascites (group B), 97 patients were with decompensated cirrhosis with non-refractory ascites (group C) and 27 patients were with decompensated cirrhosis with refractory ascites (group D). In the control group (group E) mean age of patients was 38.22±10.54 years, males were 74.6% and female were 25.3%.

Mean creatinine level in Hepatitis C patients and in controls was 0.83±0.16 and 0.73±0.08 respectively (Table-1).

Mean RI in both kidneys of patients included in Group-D and Group-C was significantly higher when compared with other groups, i.e., Highest Mean RI in right kidney (Group-D): 0.78, and in left kidney (Group-D): 0.81. After Group-D, highest mean resistive index was seen in Group-C (Right Kidney: 0.73 and Left Kidney: 0.72) followed by Group-B (Right Kidney: 0.55 and Left Kidney: 0.56) and Group-A (Right Kidney: 0.53 and Left Kidney: 0.51). Patients in Group-D and Group-C had significantly increased mean RI values than all others groups. Resistive Index in Hepatitis C patients and Controls respective of groups and site of kidney is shown in (Table-2).

Correlation between resistive index in the both right and kidneys and serum creatinine level in all groups is illustrated in (Figure-1 and 2).

Table-1: Creatinine level among groups (Mean±SD)

Study groups	N	Creatinine
Group-A	20	0.74±0.09
Group-B	14	0.75±0.09
Group-C	97	0.80±0.10
Group-D	27	1.05±0.20
Group-E	79	0.73±0.08
	F-test	42.6
	p	0.001

Table-2: Resistive Index among groups (Mean±SD)

Study Groups	n	Right Kidney	Left Kidney
Group-A	20	0.53±0.07	0.51±0.06
Group-B	14	0.55±0.06	0.56±0.06
Group-C	97	0.73±0.03	0.72±0.03
Group-D	27	0.78±0.05	0.81±0.07
Group-E	79	0.55±0.04	0.52±0.04
	F-test	238.8	297.6
	p	0.001	0.001

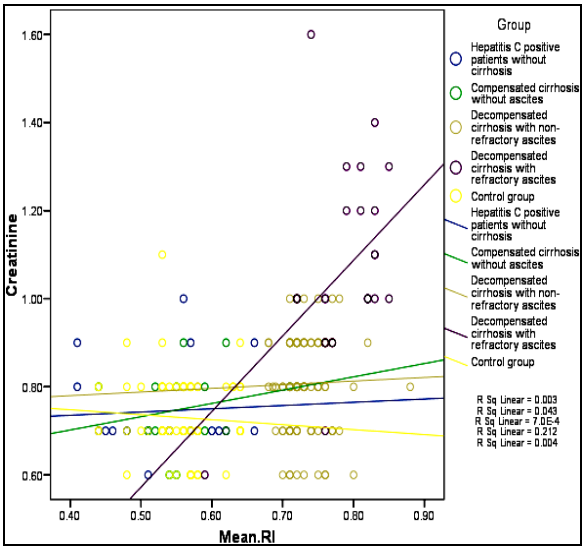

Figure-1: Correlation between Resistive Index (Right Kidney) and Serum Creatinine

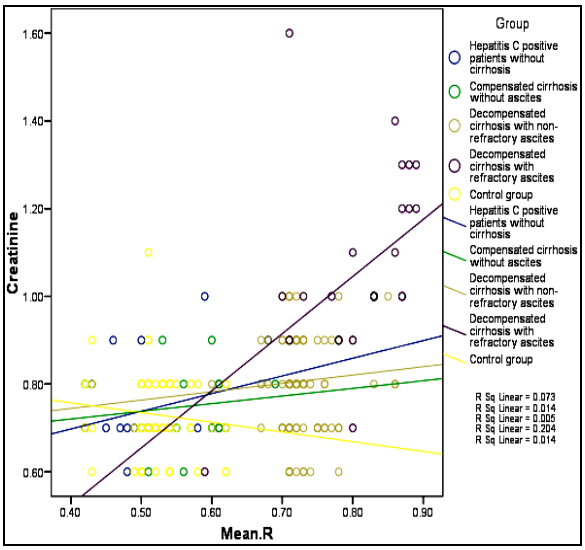

Figure-2: Correlation between Resistive Index (Left Kidney) and Serum Creatinine

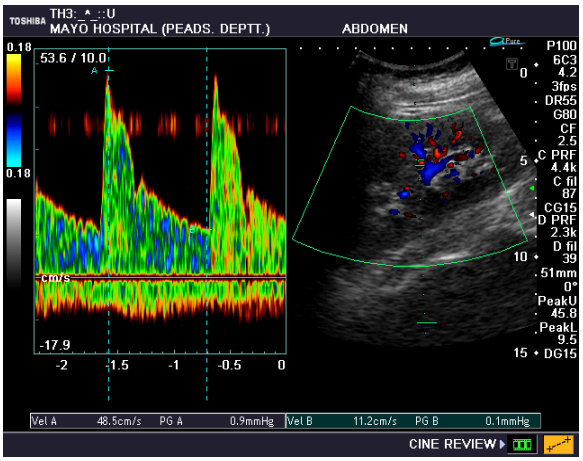

Figure-3: Colour and Pulse Wave Doppler analysis of inter-lobar renal artery showing increased Resistive Index in Group D case (RI= 0.76)

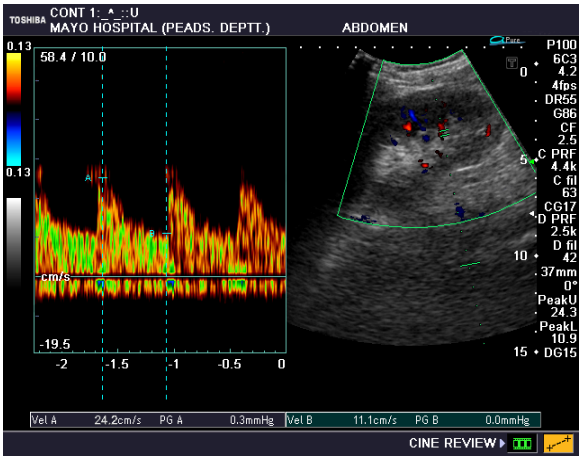

Figure-4: Colour and Pulse Wave Doppler analysis of inter-lobar renal Artery showing normal Resistive Index in Group E control case (RI= 0.54)

DISCUSSION

Doppler ultrasound serves as method for renal haemodynamic assessment and resistive index which is calculated from peak systolic and end diastolic renal arterial volumes helps in detection of alteration in blood flow to the kidneys.[3,6]

Previous studies have highlighted the importance of RI in order to assess renal blood flow in various pathological conditions of the kidneys. It is well known that in comparison to healthy population, generally there is increased RI in cirrhotic patients. Furthermore, RI is observed to be higher in cirrhotic population with ascites in contrast to those without ascites. It has been shown that patients with refractory type of ascites show further increase in RI values as compared to those with non-refractory ascites. Hence, it would be safe to say that value of renal RI varies with the degree of decompensation and type of ascites.[6,8,9]

Hamdy *et al*[10] have described importance of measuring resistive index using renal Doppler in early detection of alteration in haemodynamics in cirrhotic patients even before derangement of renal function clinically sets in. Furthermore, RI taken on renal Doppler was shown to be capable of identification of high-risk patients developing hepatorenal syndrome.

In this study mean creatinine level in Hepatitis C patients was significantly higher when compared with control group yet creatinine was still found within reference range in majority of the patients. The highest creatinine level was observed in Group-D (Decompensated cirrhosis with refractory ascites) patients followed by Group-C (Decompensated cirrhosis with non-refractory ascites) and Group-B (Compensated cirrhosis without ascites).

Study by Fouad *et al*[11] constituted of 60 patients with liver cirrhosis due to HCV and their distribution into 5 groups according to stage of disease was done. Adequately increased values of PI and RI were found by the authors in all groups in comparison with control group. Maroto *et al*[12] in their study observed significantly increased RI in cirrhotic patients at decompensated stage as compared to RI in patients with compensated liver cirrhosis which in turn was also higher than in healthy group. They also concluded high sensitivity and specificity of resistive index for detection of HRS. The findings of this study are consistent with the findings of Maroto *et al*[12] that patients with decompensated cirrhosis had significantly higher RI value in comparison to that of other study groups.

In a study conducted by Chen *et al*[4] renal Doppler indices were shown to be higher in cirrhotic patients when compared to values in non-cirrhotic and control population. They also demonstrated positive correlation of RI with severity of liver cirrhosis. Results of this study also support the findings of Chen *et al*[4] in

regard that values of RI correlated well with severity and stage of disease. A positive correlation between RI values and serum creatinine values was reported by Gamal *et al*[13]. However, in our study, serum creatinine was found increased above normal range in only 5 patients and all of them belonged to Group-D.

The results of various studies conducted by different research teams at different times and places including study by Macherla *et al*[6], Aslam *et al*[9], Fouad *et al*[11], Vlasov *et al*[14] and Mahmoud *et al*[15] support each other in conclusion that RI is significantly higher in patients with advanced liver disease as compared to healthy subjects. This study also concludes the same observation about renal resistive index.

Clinical significance of RI has enabled physicians to include renal Doppler in routine nephrological workup of patients as it provides reliable estimation of renal function even in challenging clinical settings like renal impairment due to advanced liver disease where renal function assessment by serum creatinine is doubtful.

CONCLUSION

Renal Doppler ultrasound is a reliable non-invasive method for evaluation of renal haemodynamics in cirrhotic patients with Hepatitis C. It can indicate renal impairment and disease progression towards hepatorenal syndrome even before development of clinical symptoms and derangement of serum creatinine.

LIMITATIONS OF STUDY

Renal Doppler ultrasound is equipment and operator dependent investigations which may result in inter observer variabilities. It requires breath hold, patient preparation and may take more time than routine ultrasound examination.

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SR: Intellectual content review, study design, ethical issues
AHAR: Data analysis, drafting, literature review, bibliography
FM: Methodology, selection criteria

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