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Doppler Profiles of Renal and Hepatic Hemodynamics in Patients with Cirrhosis of Liver

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Abstract:Background: Renal dysfunction is a frequent problem in liver cirrhosis patients, that is linked with extended morbidity and death of patients, The severe complication of renal dysfunction in CLD patients is "hepatorenal syndrome" (HRS), which is linked with extremely limited survival time.
Objectives: Evaluating and comparing changes in liver and renal Doppler US parameters according to the severity of liver failure in liver cirrhosis patients.
Methodology:A prospective study will be conducted at "AcharyaVinobaBhave Rural Hospital, Sawangi", involving60 patients coming to Radiology department for Doppler of liver cirrhosis will be included in the study. Abdominal ultrasound (US) will be conducted in compliance with the normal protocol, as well as liver and renal doppler US. Near the point where it reaches the principal PV, the proper hepatic artery (HA) will be examined. Pulsatility is quantified by the PI.
Results: After statistical analysis, we expect to finda relation between hepatic and renal artery variables in Doppler US.
Conclusion: In this study, we expect,"renal Doppler US parameters" associate with liver cirrhosis severity and complications. Therefore follow up of these patients is necessary with Doppler US of the renal arteries
Keyword: Doppler, Renal, Hepatic, Hemodynamic, Cirrhosis, Liver.

INTRODUCTION:

Renal dysfunction is a frequent problem in liver cirrhosis patients that is linked with extended morbidity and death of patients, developing in one in five patients [1]. 20-50 per cent of patients admitted to the hospital with liver failure record renal dysfunction [2].
The most severe complication of renal dysfunction in CLD patients is "hepatorenal syndrome"(HRS), which is linked with extremely limited survival time [3]. Renal hemodynamic modifications start immediately in the functional renal failure process associated with liver disease, earlier than serum creatinine concentration modifications are observable [4, 5-8]. Intensive intrarenal vasoconstriction is the hallmark of HRS transition [6,7,9,]. "This vasoconstriction is associated with decreased renal plasma flow and increased renal arterial vascular resistance", which can be followed by weeks or months of clinically recognised kidney dysfunction .Although the true cause of renal vasoconstriction remains unclear and is multifactorial, many non-azotemic liver disease patients have elevated renal vascular resistance. [10]. These cirrhotic patients may be at greater risk of developing overt"hepatorenal syndrome" subsequently[4,5].

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Therefore, for assessing renal blood flow and predicting the development of HRS in patients with cirrhosis and portal hypertension, dynamic control of haemodynamic changes in the kidney is important.

We will analyse the variations in a wide range of hepatic and kidney Doppler US variables, evaluate concurrently in liver cirrhosis patients according to the severenessof hepatic cirrhosis as measured by both "MELD and Child's Pugh" rating.

We will perform the colour Doppler of liver and both kidneys, in hepatic part we will do colour Doppler of "Portal vein" (PV) and "hepatic artery" (HA) while for the colour Doppler of kidney, examine the intrarenal arteries (RAs) or inter lobar segmental branch of kidney. We will evaluate the hepatic and intrarenal blood flow Doppler parameters as in Annexure.

Rationale: In previous years many study were performed in patients with liver cirrhosis, in which hemodynamic changes of portal vein, hepatic artery and renal arteries were evaluated separately. There are very few reports of simultaneous analysis of hepatic and renal blood flow in cirrhotic patients using Doppler methods in real time according to the severity of hepatic disease. Prior identification of liver cirrhotic disease patients who are at specific risk of developing "hepatorenal" disorder can be helpful as it is possible to modify clinical management. This also underlines the importance of close co-operation in diagnosis and management with clinicians.

OBJECTIVES:

1. To evaluate "relationship between Liver and renal Doppler US Parameters and Severity, Complications of Liver Cirrhosis".
2. To evaluate "relationship between Liver and Renal Doppler US Parameter, surrogate Markers of Renal Function".
3. To evaluate "impact of Patient's Age on Liver and Renal Doppler US Parameters".

Methods:

Setting –"Department of Radio-diagnosis, AcharyaVinobaBhave Rural Hospital, DattaMegheInstitute of Medical Sciences, Sawangi (Meghe), Wardha".

Research design- Prospective study.

Inclusion criteria

Patients coming to Radiology department of AacharyaVinobaBhave Rural Hospital, Sawangi (Meghe), Wardha, for Doppler of liver cirrhosis will be included in the study.

Exclusion criteria

The patients with

- "Endoscopic band ligation or sclerotherapy" in the last 8 weeks for GI bleed
- Liver tumours,
- Hepatorenal syndrome
- Important concomitant illness and co-therapy that may intervene with the parameters of Doppler ultrasound and renal function will be removed.
- Patients not willing to give consent for the study.

Duration of study: 2020-2022

"Abdominal ultrasound (US), as well as liver and renal Doppler US", will be done as per protocol. US evaluation will be done by ALOKA HITACHI ARIETTA S70 , convex probe "1–5,0 MHz, cut-off filter 100 Hz", with an insonation angle of 50◦ with a Doppler gate of 2-3,5-5 mm, as wide as a minimum of one third of the vessel's diameter. Patient will fast overnight and rest for at least 10 minutes prior to the US measurements in bed in the supine position.

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Near the point where it reaches the principal PV, the proper hepatic artery (HA) will be examined. A rectilinear portion of the typical portal vein (PV) tract will be analysed as close to the bifurcation as possible for the portal vein Doppler and three Doppler waveform tracing for renal artery Doppler will be obtained from each kidney by sampling the renal arteries (intrarenal arteries, interlobar or segmental branch) of both kidneys in the upper, middle and lower portions of the kidneys. It will use the average parameter values for each kidney.

Method of collection of data (including sampling procedure):

All OPD/IPD patients will be referred for Doppler to the department of Radio diagnosis with liver cirrhosis.

Sample size: Formula

"N = $א^2$ *N *p(1-p)/ C ^{2}(N-1)+ $א^2$ p(1-p)"

Where,

$א^{2=}$ "chi square value for 1 degree of freedom at some desired probability level this is 3.84 at 5% level of significance"

"P = 50% proportion"

"C= confidence interval of one choice (95% CI)"

Sample size = **60** patients

Sample size: Calculated by formula.

Equipment: US measurements will be done by Aloka Hitachi Arietta S70, convex probe 1–5,0 MHz

Statistical analysis: Appropriate statistical method will be applied and analysis will be done accordingly.

Expected Outcomes: This study aims at finding a relation between hepatic and renal artery variables in Doppler US.Whether renal and hepatic Doppler US variables changing at advance stages of liver cirrhosis or not.

DISCUSSION:

Patients were divided into three categories in the 2004 study by SnijezanaKastelan et al[11].: Thirty one liver cirrhosis patients with normal kidney function , Nine liver cirrhosis patients with kidney failure but without hepatorenal syndrome development and six liver cirrhosis patients with established hepatorenal syndrome . The resistance index in interlobar arteries of both kidney were more than 0.70 in patients associated with established "hepatorenal syndrome" .while In liver cirrhotic patients ,renal dysfunction in which hepatorenal syndrome were not developed , the arterial resistance index in interlobar arteries were less than 0.70 in seven and arterial resistance index in interlobar arteries were more than 0.70 in the remaining two patients, respectively. Renal dysfunction in these cases displayed a gradual form and hepatorenal syndrome developed. In conclusion, intra lobar artery ultrasound with Duplex-Doppler is a rapid, accurate and non-invasive approach that allow for early diagnosis of renal hemodynamic abnormalities even earlier than renal dysfunction will become clinically apparent in patients with liver cirrhosis. A subgroup of liver cirrhosis patients who may be at greater risk of developing hepatorenal syndrome can also additionally be identified. In 2011, Y Wang et al[12]. carried out a study in which colour doppler flow imaging was used to examine renal haemodynamic in '50 cirrhotic patients and 15 healthy controls' in prospective, cross-sectional study. In liver cirrhosis patients, the 'mean renal arterial resistive index' (RI) was greater than in healthy controls. In liver cirrhosis patients with non-refractory ascites, mean RI was also higher than the patients in which ascites were not developed, suggesting that with the severity of ascites, the degree of renal vasoconstriction varies. In cirrhotic patients, also in the decompensatory stage with non-refractory ascites, the RI values across the renal arteries were not change and RI values changed in reactory ascites patients

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who were on decompensatory stage. Disappearance of this gradient in the evaluation of 'hepatorenal syndrome' may be an important prognostic factor (HRS). For all cirrhotic patients, an inverse association was shown between creatinine clearance and interlobular arterial RI, indicating that such patients of liver cirrhosis with refractory ascites are in 'HRS prophase'.

In 2012, a broad range of 'liver and renal Doppler US parameters' had been evaluated in 67 liver cirrhosis patients by D. Popov, et al[13]. Significant differences were found between child's score and MELD score , in all examined 'intrarenal blood flow doppler US parameters' with the exception of 'renal artery peak systolic velocity' but only in certain hepatic parameters . Complication in liver cirrhosis are widely associated with changes in the US 'renal dopplerparameters' , and surrogate markers of kidney function. A relation was found between hepatic and renal artery variables in Doppler US. There was no relationship found between Doppler US variables and age. Their findings point out that renal Doppler US parameters associate with liver cirrhosis severity and complications. In advance stages of liver cirrhosis patients renal doppler US variables showed variations , therefore follow up of these patients is necessary with Doppler US of the renal arteries .

According to a report by MudumalaIssacAbhilash et al [14]., in 2017, study included thirty patients different stages of severity of cirrhosis were studied. In cases where MELD>20, the key resistivity index was found to be higher. The resistivity index improved further as the severity of the cirrhosis increased. Similarly, as the severity of cirrhosis increased, the MDRD EGFR decreased. They suggested that through further understanding the hepatorenal syndrome pathophysiology, the measurement of the kidney resistivity index seems to be a responsive and easy way to examine early renal hemodynamic changes in cirrhotic patients..
In the study conducted by Anil Kumar et al[15]., in 2019 serum creatinine levels were compared with renal Doppler indices in different groups of increasing severity. Around 65 percent of cases display an irregular liver surface, and in Groups II, III, and IV, the irregular liver surface is substantially higher than in Group 1. 78%, 11%, and 11%, respectively, of heterogeneous, homogeneous and fatty echo texture were seen. In their analysis, the mean systolic peak velocity and end-diastolic velocity were 33.99 cm/s and 11.55 cm/s, respectively. The mean case pulsatility index was 1.17. RI levels in cirrhotic patients were significantly higher and there was a strong correlation between RI and the study groups. The RI value is also elevated as the severity of the group's liver disease increases. In conclusion for a subgroup of CLD patients with a higher risk of developing kidney failure or HRS, intrarenal RI seems to be helpfull predictor, which may translate into the early start of care for upcoming HRS.Hence this study is designed in such a manner that the outcome of this study will be compared with above mentioned research.

Morato et al., in 1994 [16]evaluated total 28 clinical and laboratory variables for prognostic benefit. In patients with kidney disease, the resistive index was slightly improved relative to those of the other three categories and was significantly linked with 'glomerular filtration rate, arterial pressure, plasma renin activity and the clearance of free water' in patients with cirrhosis. The sensitivity and precision of the resistive index were 71 percent and 80 percent respectively in the detection of kidney failure in patients with ascites. In the univariate study, 'nine factors, including resistive index, age, hepatomegaly, blood urea nitrogen, serum creatinine, plasma sodium concentration, glomerular filtration intensity, plasma renin activity and antidiuretic hormone plasma concentration', were associated with survival. Just three independent survival predictors were discovered by multivariate analysis: 'plasma renin activity, antidiuretic hormone plasma concentration, and serum sodium concentration'. In

summary, in patients with cirrhosis and ascites, resistive index is a sensitive approach to test intrarenalhemodynamics. In these patients, it has predictive importance for survival as well.
Annalisa Berzigotti et al.[17], in 2006, Thirty-one patients of cirrhosis with esophagealvarices were enrolled in the study. There was portal hypertension in all patients. Neither portal pressure nor renal impedance was associated with the cirrhosis Child-Pugh score. Indexes of renal artery impedance are associated with HVPG. For the diagnosis of extreme portal hypertension, higher-than-normal renal impedance displayed a strong positive predictive value. Renovascular impedance was associated directly with HVPG in conclusion.
Few more studies on fatty liver[18,19] and cirrhosis of liver [20,21,22] were reported. Related studies with renal diseases were reported by Balwaniet. al.[23-25].

CONCLUSION:

The data obtained through this study can be used to understand the 'relationship between renal Doppler US parameters and liver cirrhosis' severity and complications.

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