ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

Renal Function in Chronic Liver Disease

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Abstract
Background: It has been observed that the changes in the systemic arterial circulation, portal hypertension, commencement of vasoconstrictors and inhibition of vasodilatory factors acting on the renal circulation were the factors which led to development of renal impairment in CLD and cirrhosis. **Material and Methods:** This study was done in Department of Biochemistry in Prasad Institute of Medical sciences, Banthra, Lucknow, U.P. Total 43 cases were included in this study. The duration of study was over a period of two year. **Results:** Out of the 43 patients of cirrhosis, the cause of liver disease was attributed to alcoholism in 21 patients. 6 patients were found to be positive for Hepatitis B surface antigen. Out of the 43 patients, renal function was assessed by serum creatinine, creatinine clearance from timed urine collection [(UxV)/P] and creatinine clearance by Cockcroft Gault formula (CGF). **Conclusion:** It can be concluded that estimation of Serum creatinine alone has not been found to be a reliable marker to assess renal dysfunction in CLD.
Keywords: Renal Function, Liver Diseases, Oliguria, Creatinine.

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Introduction

Chronic liver disease is common clinical problem in our country. Chronic liver disease involves a process of progressive destruction and regeneration of liver parenchyma leading to fibrosis and cirrhosis.[1] Acute kidney injury, chronic kidney disease and the evaluation of numerous exogenous and endogenous measures of kidney function continue to be the focus of much research different patient population.[2] The presence of renal impairment in both groups is a poor prognostic indicator. Hepato-renal syndrome is a unique form of renal failure associated with advanced liver disease or cirrhosis and is characterized by functional renal impairment without significant changes in renal histology.[3] Chronic liver disease and cirrhosis are frequently complicated with renal dysfunction and this combination leads to significant morbidity and mortality.[4] There is considerable evidence that renal failure in patient with cirrhosis primarily related to disturbances in circulatory function-mainly, a reduction in system vascular resistance due to primary arterial vasodilatation in the splanchnic circulation, triggered by portal hypertension.[5] Intrinsic renal diseases may occur in patient with hepatitis B or hepatitis C and alcoholic cirrhosis. Moreover, patients with cirrhosis may develop a specific acute renal failure called type-I hepatorenal syndrome. Independent of event that leads to acute renal failure, patient with cirrhosis may have diseases, such as diabetes mellitus or hypertension and atherosclerosis, which may cause chronic renal injury.[6,7]

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Frerichs and Flint were first to describe in their respective studies that the disturbed renal functions had been found in the chronic liver diseases (CLD) in late nineteenth century.[8] In patients of chronic liver disease, the development of oliguria was observed in their reports without proteinuria and with a normal renal histology. They were first to describe the pathophysiology of hepatorenal syndrome by correlating the disturbances in the systemic circulation with abnormalities of renal functions.

Hippocrates also stated the concurrence of renal impairment with CLD.[9] In 1932 while describing renal failure in a patient of biliary tract disease, Helwig and Schutz introduced the term Hepato - Renal Syndrome.[10] HRS was described at a later stage in 1950s by Serlock, Papper, and Vessin.

It has been observed that the changes in the systemic arterial circulation, portal hypertension, commencement of vasoconstrictors and inhibition of vasodilatory factors acting on the renal circulation were the factors which led to development of renal impairment in CLD and cirrhosis.

It has been found that the patients suffering from hepatic problems have more chances of developing pre-renal failure mainly because of disorders in circulatory functions, a decrease in systemic vascular resistance because of primary arterial vasodilatation in the splanchnic circulation which is elicited by the portal hypertension.[11] Increased production or activation of vasodilator factors such as nitric oxide, carbon monoxide, and endogenous cannabinoids can be attributed as a causative agent for the arterial vasodilation.

Hypovolemia can also be labeled as important factor responsible for renal impairment in CLD. And this hypovolemia can be caused by gastrointestinal tract hemorrhage due to varices or peptic ulcers or gastropathy, excessive dieresis; vomiting, and diarrhea. Large volume paracentesis without intravascular volume replacement may be held responsible for hypovolemia. The use of NSAIDs, bacterial infections such as spontaneous bacterial peritonitis and septic shock can also lead to pre-renal failure in these patients.

Methodology

Study Area: This study was done in Department of Biochemistry in Prasad Institute of Medical sciences, Banthra, Lucknow, U.P.

Study Population: Total 43 cases were included in this study.

Study Duration: The duration of study was over a period of two year.

Inclusion and exclusion criteria:

This study included patients with chronic liver disease being treated as in-patients. Elderly patients (>60 years), Overt renal failure (S. creatinine >1.5), Known primary renal disease, Diabetes mellitus / Hypertension, Grade 4 hepatic encephalopathy were excluded from this study.

Data Collection:

Data regarding demographic variables (age, weight), clinical features (presenting complaints, ascites, jaundice, encephalopathy, history of alcoholism, etc) and clinical examination findings of liver cell failure were collected. Diuretics were withheld for 3 days before carrying out lab investigations. Lab investigations including complete Liver function test, Renal function tests, Viral marker for hepatitis B, Urine analysis, 24 hour urine volume and Urine creatinine was done and results noted. Patients were subjected to an ultrasound scan of abdomen with regard to liver echotexture and size, evidence of splenomegaly or portal hypertension, presence of ascites and kidney pathology. Creatinine clearance for the patient was calculated by the formula (Urine creatinine / Serum creatinine multiplied by 24 hour urine volume). (UCr / PCr) x V

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RESULTS

Age of the patients ranged from a minimum of 22 years to a maximum of 58 years. The mean age was 42.14 years. Out of total patients included in the study 35 were male, while remaining 8 were female. Out of the 43 patients of cirrhosis, the cause of liver disease was attributed to alcoholism in 21 patients. 6 patients were found to be positive for Hepatitis B surface antigen. One patient was a case of Wilson's disease and another patient was found to have autoimmune hepatitis. In the other 14 patients, causative etiology could not be ascertained. Out of the 43 patients, renal function was assessed by serum creatinine, creatinine clearance from timed urine collection [(UxV)/P] and creatinine clearance by Cockcroft Gault formula(CGF).

The patients were grouped into three based on their creatinine clearance [(UxV)/P]. Group I having values more than 60 ml/mt, Group II 30-60 ml/mt and Group III less than 30 ml/mt. There was no significant variation in blood urea levels in all the three groups, suggesting that estimation of blood urea will not be of much use in determining renal impairment. Mean blood urea level was 22.42 mg/dL. Only patients with creatinine levels less than 1.5 mg/dL were included in this study. It was seen that in 7 patients with creatinine clearance less than 30 ml/mt, serum creatinine levels failed to rise above 1.2 mg/dL, suggesting that moderate to severe renal dysfunction may be masked by seemingly normal creatinine levels. The mean serum creatinine level was 1.01 mg/dL. Patients with greater amount of renal impairment were found to have lesser urine output, thus suggesting that eliciting history of oliguria in a patient with normal serum creatinine levels should call for a high index of suspicion of renal dysfunction. The mean 24 hour urine volume was 1317.44 ml.

Table 1: Age Distribution

Age group	Number of patients
Less than 30 years	2
30 to 39 years	9
40 to 49 years	24
Above 50 years	8

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

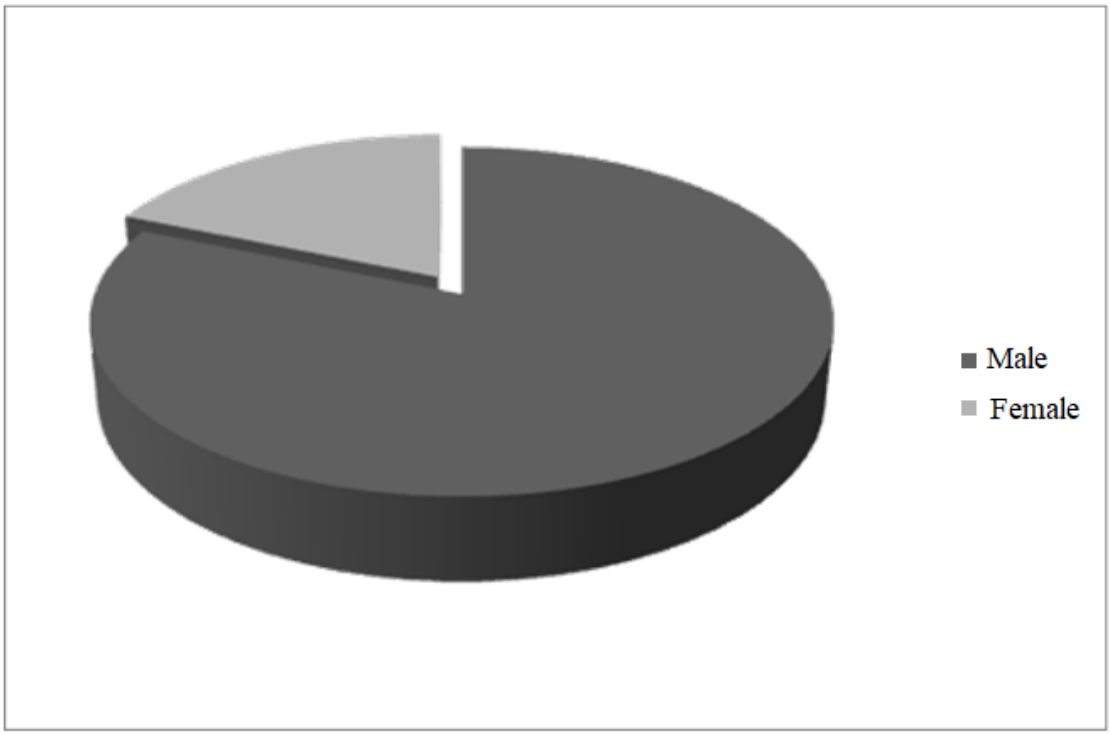

Figure 1: Gender distribution

Table 2: Distribution of cases according to Etiology

Etiology	No. of patients	Percentage
Alcoholism	21	48.83 %
Hepatitis B	6	13.95 %
Wilson's	1	2.33 %
Auto Immune Hepatitis	1	2.33 %
Unknown	14	32.56 %

Table 3: Group distribution based on their creatinine clearance

	Group I	Group II	Group III
Blood urea mg/dL	22.43	22.42	22.4
Serum creatinine mg/dL	0.90	1	1.2
24-hour urine volume ml	2010.71	1136.84	690
Creatinine clearance (UxV / P) ml/mt	85.33	43.41	18.55
Creatinine clearance (CG formula) ml/mt	85.02	63.87	44.90

DISCUSSION

The present study was conducted on 43 patients of chronic liver disease (CLD) with disturbed renal function.

It has been observed that various patients of cirrhosis and ascites have glomerular filtration rate (GFR) less than 60 ml/minute but a normal serum creatinine. It was observed in the present study that the serum creatinine in patients with CLD cannot identify renal impairment alone. This claim was supported by the findings of McAulay et al.[12]

A prospective study of Papadakis and Arieff involving numbers of cirrhotic patients showed very low GFR even with serum creatinine less than 1.0 mg/dL.[13] It has been found that for the diagnosis of HRS, the serum creatinine level should only be 1.5 mg/dL or less, in the

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

absence of diuretic therapy. Therefore, the patients having creatinine levels more than 1.5 mg/dL were excluded from the present study. It has also been observed in the present study that calculating creatinine clearance by the Cockcroft Gault formula overestimates renal functions. Variation in weight due to fluid retention can be held responsible for this overestimate as weight is one of the variables in the numerator of the formula. Enhancement in weight because of edema or ascites leads to a false high creatinine clearance. These findings are supported by the study of McAulay.[12] In the present study, overestimation of renal functions in patients with low GFR was also observed.

Study group of Modification of Diet in Renal Disease (MDRD) developed a Cr-based GFR formula based on the patient's Creatinine levels, age, sex, race and serum urea nitrogen and serum albumin levels. This formula was labeled as MDRD formula. This formula was found equivalent to the radionuclide GFR in advanced liver disease patinets. The supremacy and accuracy of MDRD formula among the Cr-based GFR formulas were established by MacAulay et al. In their study, this formula was proven to be the best for detection of moderate renal impairment among cirrhotics.[12] One limitation observed with MDRD formula was that it required web based calculations. So, it cannot be used in less developed setups.

In routine clinical practices, estimation of creatinine clearance from timed urine collections has been found to be a relatively inexpensive and accessible method. In the present study, this method has been found to assess renal reserve better than serum creatinine or predicted creatinine clearance by Cockcroft-Gault formula (CGF). A systematic review and meta-analysis of cirrhotics by Proulx et al found creatinine clearance estimated by timed urine collections overestimating the GFR but showed this method to be a more reliable one than serum creatinine or predicted creatinine clearance by CGF.[14]

CONCLUSION

Estimation of Serum creatinine alone has not been found to be a reliable marker to assess renal dysfunction in CLD. In cirrhosis patients, estimation of creatinine clearance using CGF has been found to overestimate the renal functions. With the results of the present study, it can be very clearly stated and suggested that the creatinine clearance estimated by timed urine collections can be done routinely to assess renal reserve in advanced liver disease.

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