Original Research Article

A study on renal function in chronic liver disease

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Abstract

Aim & Objectives: To determine the usefulness of serum creatinine and creatinine clearance as parameters in assessing renal function abnormalities in patients with chronic liver disease.**Methodology:** Inpatients in the medical ward/IMCU admitted with chronic liver disease with seemingly normal renal function were included in this analytical study which was conducted from June 2018 to October 2019. 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. **Results:** In the present study, 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 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. There was no significant variation in blood urea levels in all the three groups. Eighteen percent ie, five out of the twenty-eight patients with creatinine clearance more than 60 ml / minute by Cockcroft gault formula were found to have creatinine clearance values less than 40 ml/minute when done by timed urine collection. Serum bilirubin levels were found to have no significant correlation with renal function.**Conclusion:** Finally we conclude that, In chronic liver disease, serum creatinine alone is not a reliable marker to assess renal dysfunction. Calculating creatinine clearance by using Cockcroft Gault formula over estimates renal function in cirrhotics

Keywords: Liver diseases, Renal Function, Creatinine, Cockcroft Gault Formula.

Introduction

The interrelationship between liver disease and renal dysfunction was recognized as early as the era of Hippocrates and this has been the object of a considerable amount of research since then.Kidney dysfunction in liver disease can be due to different etiologies and can have diverse manifestations. Most of the abnormalities of kidney function in cirrhosis are of functional origin- namely, sodium retention, impaired free water excretion and renal vasoconstriction with decrease in renal perfusion and glomerular filtration rate. Renal dysfunction in chronic liver disease usually follows a progressive course – the final phase being Hepatorenal syndrome (HRS)[1-3].There is no explanation that fully defines the complex relationship between the diseased liver and disturbances in kidney function, though substantial progress is being made in recent years regarding research in this aspect.One of the most difficult issues in the clinical evaluation of patients with cirrhosis is the accurate assessment of renal function.Standard measures of renal function like blood urea nitrogen and serum creatinine are likely to give erroneous impressions and hence alternative methods to determine renal reserve must be used.Detection of renal insufficiency is clinically important because it contributes significantly to high morbidity and mortality in cirrhosis. Moreover, renal dysfunction is one of the most important risk factors when liver transplantation is being considered. Patients with cirrhosis and renal failure are at high risk for death while awaiting transplantation and have an increased frequency of complications and reduced survival after transplantation, as compared with those without renal failure[4-6].To determine the usefulness of serum creatinine and creatinine clearance as parameters in assessing renal function abnormalities in patients with chronic liver disease.To find if etiology of chronic liver disease has a bearing on renal dysfunction.

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Materials and Methods

Inpatients in the medical ward/IMCU admitted with chronic liver disease with seemingly normal renal function were included in this analytical study which was conducted from June 2018 to October 2019.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 using a proforma.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).

$(U_{Cr} / P_{Cr}) \times V$

This was divided by 1440 to get the value in ml/minute. Creatinine clearance was also calculated using the Cockcroft and Gault formula(CGF).

(140- AGE) x WEIGHT /(SERUM CREATININE x 72)

This value is to be multiplied by 0.85 if the patient is female. Comparison between serum creatinine and creatinine clearance calculated by these two methods were done.

Observations and analysis

50 patients with chronic liver disease were enrolled in the study. 7 patients did not satisfy inclusion criteria and were excluded. So, a total of 43 patients were included.The following observations were made:

Table 1: Age and sex

Age of the patients ranged from a minimum of 22 years to a maximum of 58 years. The mean age was 42.14 years. The age distribution is as follows:

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

Patients above 60 years were excluded as GFR decreases with age. False low GFR thus calculated would interfere with the findings of this study. Of the patients included in the study 35 were male, while remaining 8 were female.

Table 2:Etiology

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.

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:Assessment of Renal Function By Different Methods

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.

	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

Blood urea levels

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.

Serum creatinine

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.

24 hour urine volume

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 4:Measured creatinine clearance by timed urine collection

The patients were grouped into three based on their creatinine clearance

Group	Creatinine clearance	No. of patients
Group I	>60 ml/minute	14
Group II	30-60 ml/minute	19
Group III	<30 ml/minute	10

Table 5:Measurement of creatinine clearance using the Cockcroft Gault formula (CGF) showed significantly higher values, suggesting overestimation of GFR by this method

CREATININE CLEARANCE	BY (U x V) / P	BY COCKCROFT GAULT FORMULA
<20 ml/mt	6(13.95 %)	0 (0 %)
20-40 ml/mt	12 (27.90 %)	4(9.30 %)
40-60 ml/mt	11 (25.58 %)	11 (25.58 %)
60-80 ml/mt	5(11.63 %)	17 (39.54 %)
>80 ml/mt	9(20.93 %)	11 (25.58 %)

Eighteen percent ie, five out of the twenty-eight patients with creatinine clearance more than 60 ml / minute by Cockcroft gault formula were found to have creatinine clearance values less than 40 ml/minute when done by timed urine collection.P value calculated was found to be less than 0.0001 which is statistically significant.

Table 6:Renal function according to etiology

ETIOLOGY	Number of Patients		
	GROUP I	GROUP II	GROUP III
Alcoholism	5	10	6
Hepatitis B	3	2	1
Wilson's	0	0	1
Auto Immune	0	1	0
Unknown	6	6	2

Out of the 21 alcoholic liver disease patients, only 5 (20 %) had creatinine clearance more than 60 ml/minute, whereas 3 (50%) out of the 6 HBsAg positive patients had creatinine clearance more than 60 ml/minute.

Serum albumin and renal function: Mean serum albumin was 3.37 mg/dL. The distribution of serum albumin in the three groups was as follows:

Table 7:Serum albumin and renal function

Serum Albumin(mg/dL)	GROUP I	GROUP II	GROUP III
>3.5	8	2	0
3.2-3.5	4	14	3
<3.2	2	3	7

Average serum albumin (mg/dL) in the three groups was:

GROUP I - 3.59

GROUP II - 3.34

GROUP III - 3.11

Serum albumin was found to have direct correlation with renal function, ie, patients with higher rates of creatinine clearance were seen to have higher albumin levels.

Serum bilirubin and renal function: The distribution of serum bilirubin levels in the three groups were as follows:

Table 8: Serum bilirubin and renal function

SERUM BILIRUBIN(mg/dL)	GROUP I	GROUP II	GROUP III
< 1.2	2	2	3
1.2 – 2	8	12	4
> 2	4	5	3

The mean bilirubin was 1.64 mg/dL. Average bilirubin levels in the 3 groups:

Group I - 1.67

Group II - 1.61

Group III - 1.64

Serum bilirubin levels were found to have no significant correlation with renal function.

Discussion

Many patients with cirrhosis and ascites will have a glomerular filtration rate of less than 60 ml/minute but a normal serum creatinine level. Our study showed that serum creatinine alone in patients with advanced liver disease is of limited value for identification of renal dysfunction. This is in agreement with the findings in a study by McAulay et al[6].Another prospective study of a large number of cirrhotic patients by Papadakis and Arieff also indicated that the glomerular filtration rate can be very low even when the serum creatinine is less than 1.0 mg/dl[7]The level of serum creatinine required for the diagnosis of HRS is 1.5 mg/dL, in the absence of diuretic therapy. Although this value may seem rather low, patients with cirrhosis and a serum creatinine above mg/dL have a GFR below 30 ml/min[8]. Hence, patients with creatinine levels more than 1.5 mg/dL were excluded from our study.Our study also shows that calculating creatinine clearance by Cockcroft Gault formula overestimates renal function. This is probably due to discrepancies in weight due to fluid retention which is one of the consequences of renal impairment in cirrhotics. As weight is one of the variables in the numerator of the formula, an increase in weight due to edema or ascites will give a spuriously high creatinine clearance[9,10]. The study by McAulay also supports this finding[6]. This overestimation of renal function was highest in patients with lower GFR, which was observed in our study also.But a study by Hampel et al[11] showed no significant difference in serum levels of albumin and did not consider it as a risk factor for renal dysfunction[11] The same study showed no significant differences in age, etiology of cirrhosis, serum levels of bilirubin, prothrombin time, encephalopathy, bacteremia, urinary tract infection, or occurrence of esophageal variceal bleeding in cirrhotic patients with or without renal dysfunction. Patients who developed renal dysfunction were more likely to have ascites. This was seen in our study also[12].Our study showed that patients with alcoholic liver disease were predisposed to develop renal impairment when compared with liver disease of other etiologies. Only 20 % of alcoholic patients had a creatinine clearance of more than 60 ml/mt as compared to 50 % of cirrhotic patients due to hepatitis B.Our study showed that standard measures of renal function, namely blood urea and serum creatinine should not be the only criteria to assess renal reserve in chronic liver disease, as they may seem normal even in gross renal dysfunction.Hence, to check for renal dysfunction in advanced liver disease, routine tests like blood urea and serum creatinine will be insufficient. Other methods like measured creatinine clearance should be employed to get an accurate picture of the renal status.

Conclusion

In chronic liver disease, serum creatinine alone is not a reliable marker to assess renal dysfunction. Calculating creatinine clearance by using Cockcroft Gault formula over estimates renal function in cirrhotics. Creatinine clearance measured by timed urine collections should be done routinely to assess renal reserve in advanced liver disease. Alcoholism appears to have adverse effect on renal function when compared with other etiologies of cirrhosis.

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