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Original research article

Study on assessment of renal function in chronic liver disease

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Abstract

Introduction: Renal dysfunction in chronic liver disease is characterized by impaired natriuresis, decreased free water clearance, and decreased glomerular filtration rate (GFR). Hyponatremia, ascites, and hepatorenal syndrome (HRS) represent the clinical consequences of disturbances in renal function. Optimal management of renal dysfunction in cirrhosis is extremely important in that renal dysfunction frequently complicates the clinical course of advanced liver disease and is invariably associated with poor clinical outcomes.

Materials and Methods: This study included patients with chronic liver disease being treated as in-patients in the Department of General Medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru from March 2017 to August 2017. Inpatients in the medical ward/ AMCU admitted with chronic liver disease with seemingly normal renal function were included in this analytical study. 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.

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. 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. In this study mean blood urea level was 22.42 mg/dL. Creatinine clearance calculated at 20-40 ml/min, there are 12 patients (27.90%) calculated by timed creatinine clearance, whereas 4 patients (9.3%) by CGF formula. Creatinine clearance calculated at 60-80 ml/min, there are 5 patients (11.63%) calculated by timed creatinine clearance, where as 17 patients (39.54%) by CGF formula. Creatinine clearance calculated at >80 ml/min, there are 9 patients (20.93%) calculated by timed creatinine clearance, where as 11 patients (25.58%) by CGF formula.

Conclusions: In chronic liver disease, serum creatinine alone is not a reliable marker to assess renal dysfunction. Calculating creatinine clearance by using Cockcroft Gault formula overestimates 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.

Keywords: Renal function, chronic liver disease, glomerular filtration rate

Introduction

Renal dysfunction in chronic liver disease is characterized by impaired natriuresis, decreased free water clearance, and decreased glomerular filtration rate (GFR). Hyponatremia, ascites and hepatorenal syndrome (HRS) represent the clinical consequences of disturbances in renal function [1]. Optimal management of renal dysfunction in cirrhosis is extremely important in that renal dysfunction frequently complicates the clinical course of advanced liver disease and is invariably associated with poor clinical outcomes [2]. Hyponatremia is present in about 50% of patients with cirrhosis and is associated with increased rate of other complications such as gastrointestinal bleeding, spontaneous bacterial peritonitis, and hepatic encephalopathy [3].

The presence of ascites predicts poor clinical outcome in cirrhotic patients, as shown by the 3-year survival rate for patients with ascites at 50% [4]. Progressive liver failure and superimposition of precipitating events culminate in the development of HRS, a state of severe intrarenal vasoconstriction and reduced GFR without intrinsic renal damage. Survival of patients with liver disease continues to be affected by the presence of renal dysfunction, even after they underwent liver transplantation [5].

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Renal dysfunction in cirrhosis is a clinical consequence of peripheral arterial vasodilatation and hyperdynamic circulation caused by portal hypertension. Clinical observations and recent experimental studies have shed light on the pathogenesis of hyperdynamic circulation in chronic liver disease [6]. Better understanding of the pathophysiology enabled clinicians to introduce effective therapies for renal dysfunction once considered irreversible or medically intractable, and led to the proposal of new concepts and diagnostic criteria for HRS [7].

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 [8]. Renal dysfunction in chronic liver disease usually follows a progressive course-the final phase being Hepatorenal syndrome (HRS) [9].

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.

Materials and Methods

This study included patients with chronic liver disease being treated as in-patients in the Department of General Medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru from March 2017 to August 2017.

Inclusion criteria

- A compatible Clinical profile (signs of liver cell failure or reduced liver span).
- Biochemical (altered liver function tests, reversal of albumin-globulin ratio).
- Sonographic evidence (altered echotexture of liver).

Exclusion criteria

- Elderly patients (>60 years).
- Overt renal failure (S. creatinine >1.5).
- Known primary renal disease.
- History of known Diabetes mellitus/Hypertension.
- Grade 4 hepatic encephalopathy.

Inpatients in the medical ward/AMCU admitted with chronic liver disease with seemingly normal renal function were included in this analytical study.

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

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.

Results

In table 1, Age of the patients ranged from a minimum of 22 years to a maximum of 58 years. The mean age was 42.14 years.

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

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Table 2: Distribution of sex among the study population

Male	35
Female	8

In table 2, of the patients included in the study 35 were male, while remaining 8 were female.

Table 3: Comparisons of variables in 3 different groups

	Group I	Group II	Group III
Blood Urea mg/dL	22.43	22.42	22.4
Serum Creatinine mg/dL	0.9	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

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. In this study mean blood urea level was 22.42 mg/dL.

Table 4: Distribution of study population in 3 groups based on measured creatinine clearance by timed urine collection

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: Distribution of study population based on creatinine clearance value by (U x V)/P and CGF formula

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 %)

Creatinine clearance calculated at 20-40 ml/min, there are 12 patients (27.90%) calculated by timed creatinine clearance, whereas 4 patients (9.3%) by CGF formula. Creatinine clearance calculated at 60-80 ml/min, there are 5 patients (11.63%) calculated by timed creatinine clearance, where as 17 patients (39.54%) by CGF formula. Creatinine clearance calculated at >80 ml/min, there are 9 patients (20.93%) calculated by timed creatinine clearance, where as 11 patients (25.58%) by CGF formula.

Table 6: Distribution of serum albumin in the three groups

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

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

Table 7: Distributions of serum bilirubin levels in the three groups

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

Table 8: Ultrasound finding of patients with ascites and without ascites

Ascites	38
No Ascites	5

Ascites was present in 38 out of the 43 patients. It was noted that the patients without ascites had relatively better renal function; i.e., all the 5 patients belonged to group I (Creatinine clearance > 60 ml/mt). Thus suggesting that ascites may be one of the first changes in worsening renal function.

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Discussion

Age of the patients ranged from a minimum of 22 years to a maximum of 58 years. The mean age was 42.14 years in the present study. Hill NR das *et al*. [10]. Study on Study on Assessment of Renal Function in Chronic Liver Disease the mean age of study population was 43.58. This finding Fleming KM *et al*., [11] who also found an increased incidence of chronic liver disease with increase in age.

The present study showed that the majority of patients were male which is similar to Fleming KM *et al*., [11] The study also found that the incidence was higher in men compared with women. Hill NR *et al*. [10] study also found that the incidence was over 50% higher in men compared with women.

Many patients with cirrhosis and ascites will have a glomerular filtration rate of less than 60 ml/minute but a normal serum creatinine level. The present 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*. [12].

Another prospective study of a large number of cirrhotic patients by Papadakis and Arieff [13] also indicated that the glomerular filtration rate can be very low even when the serum creatinine is less than 1.0 mg/dL. 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 1.5 mg/dL have a glomerular filtration rate below 30 ml/min [14]. Hence, patients with creatinine levels more than 1.5 mg/dL were excluded from the present study.

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. The study by McAulay also supports this finding [12].

Kidney function is evaluated by assessing the glomerular filtration rate (GFR), which can be determined by measuring the volume of plasma that can be completely cleared of a given substance over a defined unit of time. The ideal marker for glomerular filtration rate determination is often quoted as having the following characteristics: Appears constantly in the plasma, can be freely filtered at the glomerulus, and does not undergo tubular reabsorption, secretion or extra renal elimination [13].

Serum creatinine concentration displays an exponential relationship with glomerular filtration rate, rendering it specific, but not a sensitive measure of glomerular filtration rate. The creatinine pool is affected by gender, age, ethnicity, nutritional state, protein intake and importantly liver disease [14].

In chronic liver disease, the reduction in the serum creatinine pool is due to a 50% decrease in hepatic production of creatine; increases in the volume of distribution due to the accumulation of extracellular fluid, edema and ascites; malnutrition and loss of muscle mass, which is related to repeated episodes of sepsis and large volume ascites affecting satiety [15-18].

The serum creatinine level was below 1.5 mg/dl in all three groups. Serial measurement of renal function was performed in 18 patients over a mean of 310 days (range four to 1,176 days). Eighty-six percent of patients studied from Groups I and II maintained a normal or supranormal glomerular filtration rate over one year.

However, most patients in Group III showed a progressive decline in filtration rate, despite no change in serum creatinine value. Sixty-seven percent of Group III patients died over a mean of one year. The mean 24hour solute excretion among Group III patients was only 263 mOsm per day, significantly less than the control value of 874 mOsm per day in other hospitalized non-cirrhotic patients.

Conclusions

In chronic liver disease, serum creatinine alone is not a reliable marker to assess renal dysfunction. Calculating creatinine clearance by using Cockcroft Gault formula overestimates 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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