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A Study of Clinical Profile of Chronic Liver Disease with Special Reference to Renal Function Test

Dr. S.V. Birajdar[1], Dr. S.S. Chavan[2] & Dr. Sayali Baban Shinde[*3]

[1]Professor and Head, Department of Medicine, SRTR GMC, Ambajogai, Maharashtra.

[2]Associate Professor, Department of Medicine, SRTR GMC, Ambajogai, Maharashtra.

[3]Junior Resident, Department of Medicine, SRTR GMC, Ambajogai, Maharashtra.

HIGHLIGHTS

1. Chronic liver disease impacts renal function significantly.
2. Renal tests reveal liver disease severity correlations.
3. Early detection improves patient management outcomes.
4. Study highlights importance of multidisciplinary care.
5. Findings guide treatment strategies for affected patients.

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ABSTRACT

Background: Chronic liver disease accounts for major morbidity and mortality worldwide. It can affect renal function and lead to complications such as hepatorenal syndrome. **Aim:** To study clinical profile of chronic liver disease with special reference to renal function tests. **Objectives:** 1. To study clinical profile of chronic liver disease. 2. To assess renal function in chronic liver disease. 3. To evaluate the association of alteration of renal function with gradation of liver disease (assessed by Child Pugh score). **Materials and Methods:** This hospital based longitudinal study was conducted at a tertiary care centre under Department of Medicine from 1st Oct. 2022 to 31st June 2024. A total of 150 patients with chronic liver disease were enrolled and their demographic, clinical and laboratory data was collected. RFT was performed using blood urea and serum creatinine. Severity of CLD was assessed using Child Pugh score. Data was analysed by R Software version 4.3.2. **Results:** The result shows that-1. Mean age of the study population was 49.89 years and 80.67% were male. 2. Most common cause of CLD was alcoholic liver disease (72.67%) followed by Hepatitis B (19.33%) and Hepatitis C (3.33%). 3. The distribution of serum urea and serum creatinine according to severity of liver disease as per Child Pugh classification were statistically significant. **Conclusion:** CLD significantly impacts renal function. Prognostic markers like Child Pugh score along with biochemical parameters help identify patients at risk. Present study has found significant association between severity of liver dysfunction and certain parameters of renal dysfunction.

* Corresponding author.
Dr. Sayali Baban Shinde, Junior Resident, Department of Medicine, SRTR GMC, Ambajogai, Maharashtra.
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INTRODUCTION

The liver, being a highly vascular organ, receives a significant proportion of the total cardiac output when at rest, surpassing the vascular supply to any other organ. Its distinctive dual blood supply involves the hepatic artery, contributing 25% to 30%, and the portal vein, responsible for the remaining 70% to 75%. The convergence of arterial and portal blood occurs within the hepatic sinusoids before it is directed into the systemic circulation through the hepatic venous system [1]. Chronic liver disease poses a prevalent clinical challenge in our nation. It encompasses a continuum of events involving the ongoing cycle of liver parenchymal damage and regeneration, ultimately culminating in the development of fibrosis and cirrhosis [1].

It represents a clinical expression of changes in both the structure and function of the liver. Its clinical presentation may include manifestations associated with portal hypertension [2].

Cirrhosis is characterized by the histological formation of regenerative nodules encircled by fibrous bands, a response to prolonged liver injury. This progression results in the development of portal hypertension and ultimately leads to end-stage liver disease [3].

Chronic liver disease and cirrhosis often present with concurrent renal dysfunction, contributing significantly to morbidity and mortality [4]. Substantial evidence indicates that renal failure in cirrhotic patients is primarily associated with disruptions in circulatory function, particularly a decrease in systemic vascular resistance resulting from primary arterial vasodilation in the splanchnic circulation, triggered by portal hypertension [5]. Intrinsic renal diseases can manifest in patients with hepatitis B, hepatitis C, or alcoholic cirrhosis. Additionally, individuals with cirrhosis may experience a specific form of acute renal failure known as type-I hepatorenal syndrome. Regardless of the triggering event for acute renal failure, patients with cirrhosis may also have pre-existing conditions such as diabetes mellitus, hypertension, and atherosclerosis, which can contribute to chronic renal injury [6].

The association between liver disease and renal dysfunction has been acknowledged since the time of Hippocrates, and substantial research has been dedicated to this relationship. Kidney dysfunction in the context of liver disease can arise from various causes and manifest in diverse ways. Functional origins, particularly sodium retention, impaired free water excretion, and renal vasoconstriction leading to decreased renal perfusion and glomerular filtration rate, account for most kidney function abn-ormalities in cirrhosis. In chronic liver disease, renal dysfunction typically follows a progressive course, culminating in the final phase known as Hepatorenal syndrome (HRS) [7].

The correlation between liver disease and renal dysfunction has been acknowledged since the time of Hippocrates, sparking considerable research. Renal insufficiency frequently emerges in patients with chronic liver disease, with an estimated prevalence of 20% to 25% [8]. A South Indian study found that 22% of cirrhosis patients exhibited renal dysfunction [9].

The etiological spectrum of chronic liver disease (CLD) is extensive, encompassing factors such as toxins, prolonged alcohol abuse, infections, and autoimmune diseases, genetic and metabolic disorders [10].

Clinical manifestations of CLD can be nonspecific, including symptoms like fatigue, anorexia, and weight loss, or may depend on the complications developed by the patient [11]. Substantial evidence suggests that renal failure in cirrhotic patients is primarily associated with circulatory disturbances, particularly a reduction in systemic vascular resistance caused by arterial vasodilation in the splanchnic circulation due to portal hypertension [12]. This arterial vasodilation is attributed to increased production or activity of vasodilator factors, notably nitric oxide, carbon monoxide, and endogenous cannabinoids, mainly in the splanchnic circulation [13].

Three distinct clinical scenarios can be identified: simultaneous involvement of both the liver and kidneys, primary liver disease with secondary renal dysfunction, or liver disease secondary to nephropathy [14].

The latter is uncommon, and in the former scenario, both liver and kidney damage may share the same causative agent, such as infection or metabolic disease. Notably, there has been a notable increase in the diagnosis of chronic kidney disease (CKD) among cirrhotic patients [15].

The assessment of renal function in liver disease serves various clinical purposes, including diagnostic assessment, evaluation of possible drug therapy, prognosis assessment, and defining potential transplant strategies for one or both organs [16]

Accurate evaluation of renal function, particularly through the (GFR), is crucial for establishing the onset, severity, and progression of renal disease. This is vital for precise drug dosing, staging CKD, and determining candidates for combined liver-kidney transplantation.

Renal dysfunction in liver cirrhosis is diagnosed by observing a reduction in the rate of glomerular filtration. While tubular and interstitial damage are es-

-sential predictors of renal failure, assessing their function lacks practical value. Inulin clearance is considered the gold standard for measuring GFR, being the only accurate method for assessing renal function in liver cirrhosis. However, methods involving the clearance of endogenous and exogenous markers pose technical challenges, are expensive, impractical for repeated investigations, and are imprecise at determining GFR [17]. Therefore, the present study aims to explore the clinical profile of chronic liver disease with a specific focus on renal function tests.

OBJECTIVES

The study was undertaken to study the clinical profile of chronic liver disease and to use renal function in chronic liver disease to find out the association of alteration of renal function with gradation of liver disease (assessed by Child Pugh score).

MATERIALS AND METHODS

Present study was a hospital based longitudinal study conducted at a tertiary care centre under Department of Medicine from 1st October 2022 to 31st June 2024. It included 150 patients of chronic liver disease with different etiologies.

Inclusion Criteria :

1. Patients with age>20 years and <60 years of either gender.
2. Patients with a definite etiology for CLD such as Hepatitis B, Hepatitis C, alcoholic liver disease, autoimmune hepatitis, non alcoholic steatohepatitis, Wilson's disease.
3. Valid consent from patient or guardian.

Exclusion Criteria :

1. Unconscious patients.
2. Known patient of kidney disease.
3. Patients taking any nephrotoxic drugs.
4. Patients of chronic diseases such as diabetes, tuberculosis, malignancy, etc.

Total 150 cases were studied. A detailed history including demographic details, family history, risk factors like hypertension, diabetes, history of renal or liver disease was recorded. General examination was done to assess presence of anemia, jaundice, clubbing , pedal edema. The patients were also examined for ascites, hepatosplenomegaly, dilated veins, spider nevi, gynecomastia, bleeding manifestations to assess the severity of liver dysfunction. Lab investigations like complete blood count, fasting/post prandial sugar levels, lipid profile, AST, ALT, serum bilirubin, ALP, serum proteins, prothrombin time, HIV, HbsAg, HCV, ANA were done.

For assessment of renal function, serum urea and serum creatinine, serum sodium and potassium were tested. Radiographic investigations like USG KUB were performed. Routine and microscopic examination of urine and measurement of 24 hr urine output were also done.

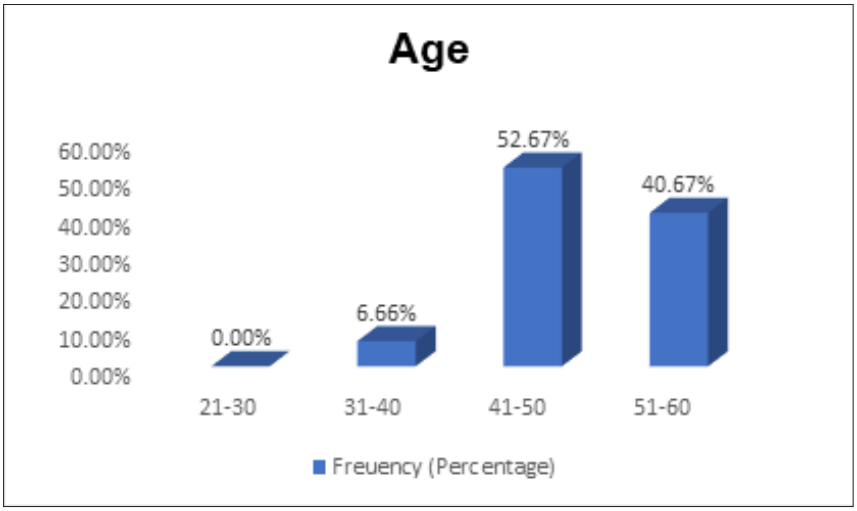
Statistical Analysis :

The data was collected using study proforma and collected data variables obtained were complied using Excel spreadsheets. The data was analysed using R software version 4.3.2 and statistical tests like Mann-Whitney.

RESULTS

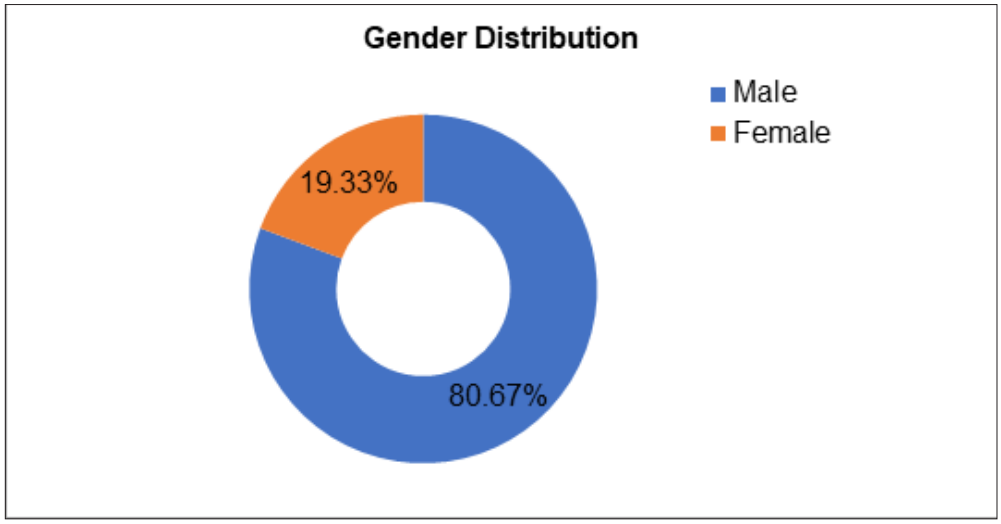
In this study, mean age of the population was 49.89 years, majority were male (80.67%). Study revealed the most common cause of chronic liver disease was alcohol followed by Hepatitis B and Hepatitis C.

Age-Mean age of patients was around 50 years.



Graph 1: Age of Patients Suffering from CLD

Gender-Majority were male (80.67%). Female patients were 19.33%.

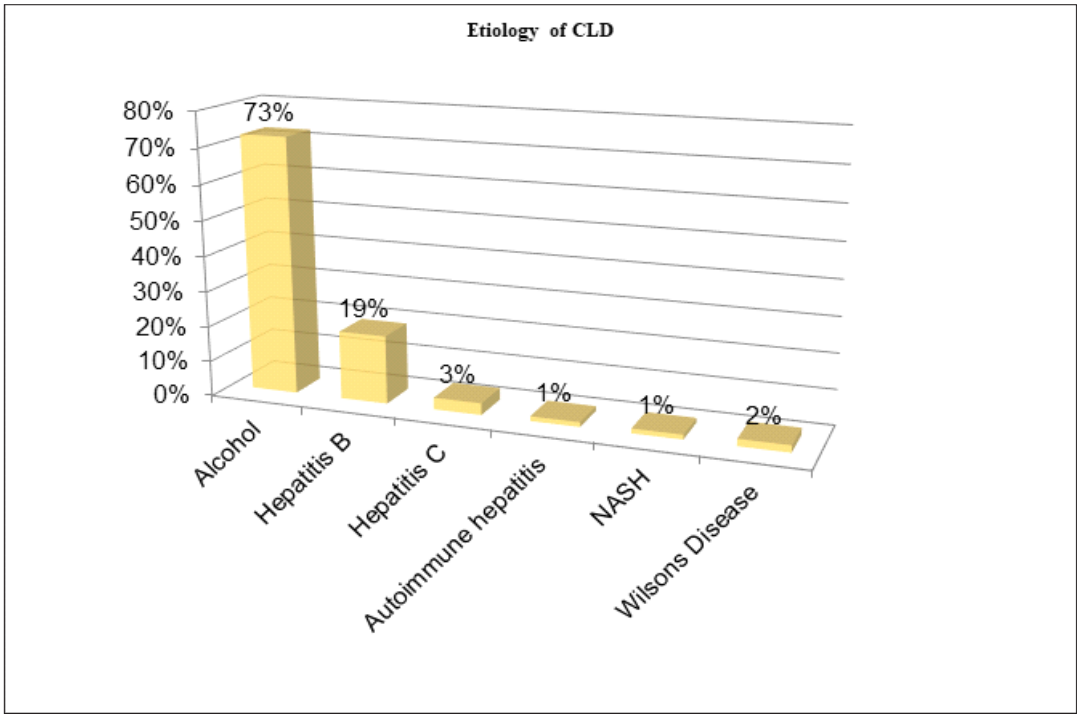


Graph 2: Gender Distribution of Patients Suffering from CLD

Causes of Chronic Liver Disease-Maximum 72.67% followed by Hepatitis B 19.33% and Hepatitis C 3.33%. patients are showing alcohol as etiology of CLD

Table 1: Etiology of CLD

Causes	No of Patients	Percentage
Alcohol	109	72.67 %
Hepatitis B	29	19.33 %
Hepatitis C	5	3.33 %
Wilsons disease	3	2 %
Autoimmune Hepatitis	2	1.33 %
NASH	2	1.33 %
Total	150	100 %



Graph 3: Etiology of Patients Suffering from CLD

Liver Function Tests-

Table 2: Serum Bilirubin Levels in CLD Patients

Serum Bilirubin (Mg/Dl)	Number of Patients	Percentage
<2	43	28.67 %
2-3	78	52.0 %
>3	29	19.33 %
Total	150	100 %

A maximum (52%) of patients fall under the range of 2-3 mg/dl serum bilirubin followed by 28.67% <2 mg/dl range.

Table 3, 4: Liver Enzymes in CLD Patients

Serum AST (IU/L)	Number of patients	Percentage
40-100	73	48.67 %
101-200	52	34.67 %
>200	25	16.67 %
Total	150	100 %

Maximum (48.67%) patients fall under the range of 40-100 (U/L) AST followed by 34.67% in 101-200 (U/L) range.

Serum ALT (IU/L)	Number of patients	Percentage
40-100	83	55.33 %
101-200	57	38.0 %
>200	10	6.67 %
Total	150	100 %

Maximum (55.33%) patients fall under the range of 40-100 (U/L) ALT followed by 38% in 101-200 (U/L) range.

Serum Proteins-

Table 5: Serum Proteins in CLD Patients

Serum Albumin (Gm/Dl)	Number of Patients	Percentage
<3	99	66.0 %
3-3.5	31	20.67 %
>3.5	20	13.33 %
Total	150	100 %
Serum Globulins (Gm/Dl)	**Number of Patients**	**Percentage**
<2	7	4.67 %
2-3.5	141	94.0 %
>3.5	2	1.33 %
Total	150	100 %

Maximum (66%) patients are from range < 3 mg/dl serum albumin followed by 20.67% from range 3-3.5 mg/dl.

Maximum 94% patients are from range 2-3.5 mg/dl serum globulin followed by 4.67% from range <2 mg/dl

Renal Function Tests–

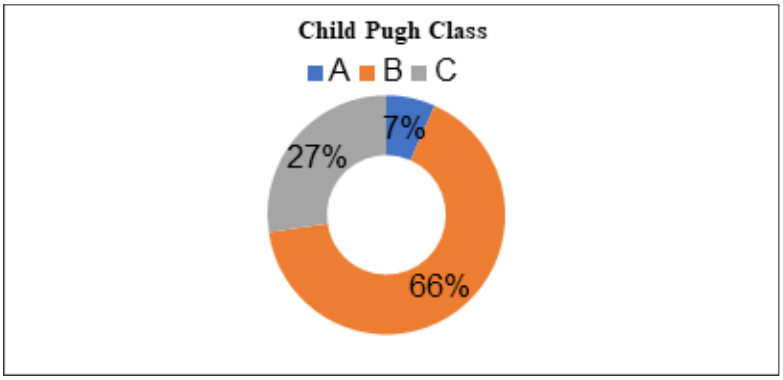
Table 6: Renal Function Tests in CLD Patients

Serum Urea (Mg/Dl)	Number of Patients	Percentage
15-40	119	79.33 %
>40	31	20.67 %
Total	150	100 %
Serum Creatinine (Mg/Dl)	**Number of Patients**	**Percentage**
<1.2	119	79.33 %
>1.2	31	20.67 %
Total	150	100 %

Maximum 79.33% patients are from range 15-40 mg/dl serum urea followed by 20.67% from range >40 mg/dl.

Maximum 79.33% patients are from range <1.2 mg/dl serum creatinine followed by 20.67% from range >1.2 mg/dl.

Table 7: Alterationin Renal Function According to Gradation of Liver Disease



Graph 4: Child Pugh Classification of Patients Suffering from CLD

It was found in the study that distribution of serum urea and creatinine according to severity of liver disease as per Child Pugh classification was statistically significant.

Renal Function Tests	Child Pugh Score		
Serum urea	**B**	**C**	
<40	99	10	**P-value < 0.05 (Statistically Significant)**
>40	0	31	
Serum Creatinine			
<1.2	99	10	**P-value < 0.05 (Statistically Significant)**
>1.2	0	31	

Here P value for both the tests is coming greater than 0.05 level of significance. So serum urea and serum creatinine was not found to be significan-tly distributed among different etiologies of chronic liver disease as tested by Kruskal Wallis Test.

Table 8: Association in Relation to Alteration of Renal Function with Etiologies of Liver Disease

Renal Function Test in Chronic Liver Disease	Statistical Test on Distribution of Etiologies (Independent Sample) Kruskal Wallis Test
Serum urea	0.8492
Serum creatinine	0.7116

DISCUSSION

Renal dysfunction, particularly acute kidney injury (AKI) in patients admitted to the intensive care unit and adult acute renal unit, has been extensively investigated in numerous small and large-scale studies [18]. The incidence of renal dysfunction in the emergency department (ED) is poorly defined, primarily due to variations in case definitions and case-mix [19].

The demographic characteristics of patients with renal dysfunction in this study revealed a predominance of males, with 80.67% of the cases being male. In contrast, an emergency department (ED)-based study conducted by Sylvanus et al. found that males accounted for 75.3% of patients with renal failure.[20] Additionally, Dlamini et al. and Kaze et al. in Yaoundé, Cameroon, reported similar male proportions of 58.5% and 60%, respectively [19,21].

The investigation's participants' average age of 49.89 years was similar to that of Sylvanus et al.'s research (49 years; interquartile range [IQR] 32-66 years) [20]. The current study revealed that the majority of patients were in their forties, with a mean age of 49.89 years. This observation aligns with findings from Fleming KM et al. who also noted an increased incidence of chronic liver disease with advancing age. Additionally, the study highlighted a male predominance, which is reliable with the outcomes of Fleming KM et al. [22] Moreover, the study indicated that the incidence was 50% higher in men compared to women.

Various causes of cirrhosis were identified, including alcohol consumption, Hepatitis B, Hepatitis C etc. The present study found that alcohol was the most common cause, followed by Hepatitis B and Hepatitis C.

In the study conducted by Nupur Das et al.,[23] 94% of the study subjects had serum albumin levels less than 3 g/dL, 4% of patients had levels between 3-3.5 g/dL, and 2% had levels exceeding 3.5 g/dL. A noteworthy association between serum albumin levels and the degree of renal dysfunction was also discovered by Nupur Das et al. in their study [23].

Liver enzymes such as AST and ALT typically show modest increases in cirrhosis, usually in the ra-nge of 300 U/L [24]. In the current study, there was a modest elevation observed in both enzymes. ALP levels generally remain within normal limits in cirrhosis. In our study, the majority of patients were found in the range between 40-100 U/L for AST and ALT enzyme levels. Albumin levels were reduced, and there was an altered albumin-to-globulin ratio, which is a common laboratory finding in chronic liver disease [25].

The current study demonstrated a direct correlation between deranged serum urea and serum creatinine levels with increasing severity of chronic liver disease. This correlation may suggest that renal dysfunction increases with advancing classes of the Child-Pugh classification. In a study by Amarapurkar et al.,[28] a correlation with albumin levels and higher mortality in patients with lower creatinine clearance was observed. However, a study by Hampel et al. [29] showed no significant difference in serum albumin levels and did not consider it a risk factor for renal dysfunction. In the same study, no significant differences were found in age, etiology of cirrhosis, serum bilirubin levels, encephalopathy, prothrombin time, urinary tract infection, bacteremia, or the occurrence of esophageal variceal bleeding between cirrhotic patients with or without renal dysfunction. Patients who developed renal dysfunction were more likely to have ascites.

In current study on the clinical profile of chronic liver disease (CLD) in adults, with a focus on renal function, it is evident that CLD presents a multifaceted challenge in patient management, particularly due to the high prevalence of renal dysfunction. Our findings align with existing literature, indicating that renal impairment is a common complication in CLD, often contributing to increased morbidity and mortality. The study revealed that a significant proportion of patients with CLD exhibited renal dysfunction, elevated serum creatinine, and increased blood urea levels.

The interplay between liver and kidney function, often referred to as hepatorenal syndrome, underscores the need for vigilant monitoring of renal parameters in patients with chronic liver disease. This is crucial not only for early detection of renal impairment but also for guiding therapeutic interventions that could potentially mitigate the prog-

-ression of both hepatic and renal dysfunctions. The study's findings suggest that routine renal function tests should be an integral part of the clinical evaluation for all patients with CLD, given the high likelihood of concurrent renal issues.

Moreover, the study highlights the importance of addressing the broader spectrum of complications associated with chronic liver disease, including anemia, coagulopathy, and portal hypertension, which were prevalent among the study cohort. These findings reinforce the need for a comprehensive, multidisciplinary approach in managing CLD, where renal function assessment plays a pivotal role in optimizing patient outcomes. Further research is warranted to explore the mechanisms underlying renal dysfunction in CLD and to develop targeted strategies for its prevention and management in this vulnerable patient population.

CONCLUSION

This study provides a comprehensive overview of chronic liver disease (CLD) in 150 patients at a tertiary care center. The findings indicate a notable male predominance with an average age of 50 years among CLD patients. Alcohol emerged as the leading etiology of CLD, accounting for 72.67% of cases.

One of the key observations was the statistically significant association between serum urea and creatinine levels and the severity of liver disease based on Child-Pugh classification. However, there were no significant differences in renal function observed among different etiologies of CLD.

Overall, these findings underscore the importance of considering various demographic and clinical factors in the management and understanding of chronic liver disease, particularly in relation to renal function and disease severity.

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