

# Renal Function in Cirrhosis of Liver: Hospital-based Study in Tripura

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## Abstract

**Introduction:** Liver disease is a common disorder affecting multiple system. It accounts for approximately 2 million deaths every year worldwide and 1 million due to complications of cirrhosis. Current epidemiological trends show that common liver diseases in Asia-Pacific countries are alcohol-related liver diseases, non-alcoholic fatty liver disease (NAFLD), hepatitis B and C, etc. Most of them lead to cirrhosis of liver. Renal dysfunction is one of the most common complications of cirrhosis with high morbidity and mortality.

**Objectives:** The objectives of the study were to evaluate the state of renal function in patients with cirrhosis of liver among hospitalized patients.

**Methodology:** This study was cross-sectional hospital-based study in a period of 1½ year.

**Results:** The study was done on 200 consecutive patients of diagnosed cirrhosis of liver. Male preponderance of 72% observed in the study. The mean age of cirrhosis of liver was  $52.28 \pm 8.983$  years. The most common etiology of cirrhosis was alcohol-related liver cirrhosis (67%). Diabetes was found among 58% of cirrhotic. Chronic kidney disease (CKD) was found among 24% cirrhosis of liver patients. Among CKD patients, 16% were in Stage 3a of CKD, 8% in Stage 3b, 22% were in Stage 4, and 54% were in Stage 5. Prevalence of CKD among non-alcoholic liver cirrhosis was more compare to alcohol-related cirrhosis. CKD was more common among cirrhosis with diabetes. Hypokalemia and hyponatremia were closely related to hepatic encephalopathy.

**Conclusion:** End stage CKD is an important complication of cirrhosis. NAFLD-related cirrhosis is more prone to develop CKD. Regular evaluation of renal function among cirrhotic is of prime importance.

**Key words:** Alcohol-related liver disorders, Chronic kidney disease, Cirrhosis of liver, Hepatitis B, Hepatitis C, Non-alcoholic fatty liver disease, Renal function

## INTRODUCTION

Cirrhosis is a condition that is defined histopathologically and has a variety of clinical manifestations and complications, some of which can be life threatening. In the past, it has been thought that cirrhosis was never reversible; however, it has become apparent that when the underlying insult that has caused the cirrhosis has been removed, there can be reversal of fibrosis. The pathologic features of cirrhosis consist of architectural distortion with the formation

of regenerative nodules. This results in a decrease in hepatocellular mass and alteration of blood flow. This leads to induction of fibrosis with activation of hepatic stellate cells.<sup>[1]</sup> Liver disease accounts for approximately 2 million deaths per year worldwide. Cirrhosis is currently the 11<sup>th</sup> most common cause of death globally and liver cancer is the 16<sup>th</sup> leading cause of death; combined, they account for 3.5% of all deaths worldwide. Cirrhosis is within the top 20 causes of disability-adjusted life years and years of life lost. According to the WHO, alcohol consumption accounts for 3.8% of the global mortality.<sup>[2,3]</sup> Regarding hepatitis B as of 2016, 27 million people (10.5% of all people estimated to be living with hepatitis B) were aware of their infection, while 4.5 million (16.7%) of the people diagnosed were on treatment.<sup>[4]</sup> Globally, an estimated 71 million people have chronic hepatitis C virus infection. A significant number of those who are chronically infected will develop cirrhosis or liver cancer. The WHO estimated that in 2016,

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approximately 399,000 people died from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma.<sup>[5]</sup>

Current epidemiological trends of the most common liver diseases in Asia–Pacific countries reveal that alcohol consumption, non-alcoholic fatty liver disease (NAFLD), and hepatitis B virus (HBV) remain the primary cause of cirrhosis. The expanding implementation of HBV vaccination has been effective in reducing the incidence of liver cancer, especially in countries like India, China, and other countries.<sup>[3]</sup>

NAFLD prevalence is increasing owing to increasingly urbanized lifestyles and dietary changes; as a result, the rising trend of NAFLD is becoming comparable to that of Western countries. NAFLD is associated with the development of cardiovascular and kidney diseases, patients with this disease should receive tailor-made advice and continuous support for lifestyle modification.<sup>[3,6,7]</sup>

Cirrhosis is described as either compensated or decompensated. Decompensation means one or more of the following: Ascites, bleeding varices, hepatic encephalopathy, and jaundice. Acute kidney injury, chronic kidney injury, hyponatremia, and spontaneous bacterial peritonitis are also features of decompensation. Child Turcotte-Pugh (CTP) staging and model of end stage liver disease score used for prognosticating cirrhotic patients. However, CTP is clinically convenient and easy to use.<sup>[8]</sup>

Renal dysfunction is one of the most common complications of cirrhosis with high morbidity and mortality.<sup>[9-13]</sup> Renal dysfunction in this population may present acutely, or may be a result of underlying chronic kidney disease (CKD). An accurate assessment of renal function is recommended in all patients with cirrhosis. Indeed, the renal function assessment guides the management of patients, helps to define prognosis and to plan transplant strategies. Despite its limitations, serum creatinine is still the most used biomarker for the estimation of glomerular filtration rate (GFR) in patients with cirrhosis.<sup>[12-15]</sup> The most important chronic liver diseases (CLDs) associated with chronic renal disease are alcohol-related liver disease, NAFLD, and hepatitis B and C.<sup>[16]</sup> The prevalence of CKD among patients with cirrhosis has increased due to the increased prevalence of CKD-associated comorbidities such as diabetes.<sup>[3,17]</sup> There were CKD patients who had significantly higher serum creatinine and higher prevalence in non-alcoholic steatohepatitis (NASH) -related cirrhosis.<sup>[18]</sup>

Hence, evaluation of renal function is of immense value in the management of cirrhosis of liver and outcome of intervention and planning for liver transplantation have definite role with variations in renal function.

## Objectives

The objectives of the study were as follows:

1. To assess renal function by estimating serum urea, serum creatinine, serum uric acid, urine analysis, and estimated GFR among the patients of cirrhosis of liver
2. To evaluate the association of etiological factors causing liver cirrhosis with CKD.

## METHODOLOGY

This is a cross-sectional hospital-based study (IPD) of consecutive 200 patients of cirrhosis liver of different etiology admitted for management which was evaluated for renal function as per pre-defined protocol approved by Institutional Ethics Committee.

### Operational Definitions

#### *Cirrhosis of liver*

Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation. It is the end result of the fibrogenesis that occurs with chronic liver injury. The most common causes include alcohol excess, viral hepatitis, NASH, and autoimmune diseases.<sup>[6]</sup>

#### *CKD*

CKD encompasses a spectrum of pathophysiologic process associated with abnormal kidney function and a progressive decline in GFR. The risk of CKD progression is closely linked to both the GFR and the amount of albuminuria.<sup>[1]</sup> The kidney disease improving global outcome definition and classification were accepted, with clarifications. CKD is defined as kidney damage or GFR <60 mL/min/1.73 m<sup>2</sup> for 3 months or more, irrespective of cause.<sup>[19]</sup>

## RESULTS AND ANALYSIS

A total of consecutive 200 patients of cirrhosis of liver were evaluated for renal function during period of 1 year and data analyzed systematically.

### Etiology

The present study reveals that most common cause of cirrhosis of liver in Tripura at present is alcohol-related liver disorder (67%), followed by NAFLD (20%), hepatitis B (8%), and hepatitis C (3%). This is big shift [Figure 1].

### Demography

The present study shows that 72% total patient of cirrhosis of liver are male and 28% are female. On the contrary, 70% on NAFLD-related cirrhotic are female. The study reveals high prevalence of diabetes among patients of cirrhosis of liver (58%). The mean age of cirrhosis of liver was 52.28 ± 8.983 years in the present study.

### Stages of CLD

In the study group, 42% of patients were from CTP C, 57% were from CTP B, and rest 1% was from CTP A. Most of the patients in this study belong to advanced Liver disease group [Figure 2].

### CKD and Cirrhosis of Liver

In the present study, 24% of total cirrhosis patients was in CKD [Figure 3]. Among patients with CKD, 16% were in Stage 3a of CKD, 8% in Stage 3b, 22% were in Stage 4, and 54% were in Stage 5. It shows that most of the cirrhotic are having advance stage of CKD. It has also observed that cirrhotic without history of significant alcoholism is having higher prevalence (45%) of CKD.

### Metabolic Changes

In this study, hypokalemia (55.6%) and hyponatremia (35.6%) were noted only in patients of cirrhosis with higher grade of encephalopathy and were not noted among patients without encephalopathy. Hyperuricemia was noted in 23.5% of patient with cirrhosis of liver.

## DISCUSSION

CLD has got a wide spectrum. Cirrhosis of liver and hepatocellular carcinoma is two end stage conditions. Cirrhosis is associated with various multiorgan dysfunction and CKD is one of them. This cross-sectional study on 200 consecutive hospitalized cirrhosis of liver patient was done at a tertiary care hospital of Tripura, a state of Northeast region of India.

The study reveals the changing etiology of CLD. At present, alcohol-related chronic liver disorder is the most

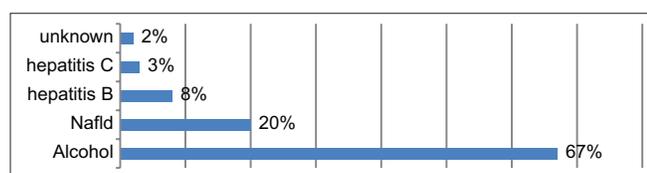


Figure 1: Etiology of cirrhosis of liver in Tripura

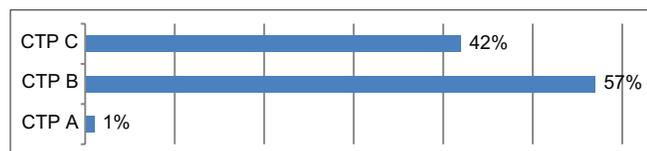


Figure 2: Stages of chronic liver disease

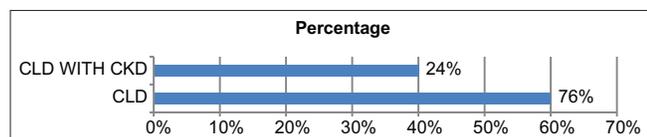


Figure 3: Chronic kidney disease among patients with cirrhosis of liver

common cause in this region (67%), which is a matter of concern from public health point of view (Mukherjee *et al.*, 2017; Ram *et al.*, 2019).<sup>[20,21]</sup>

In this evaluation, there is male preponderance in overall cirrhosis but NAFLD-related cirrhosis is more in female (70%). Florence also showed female preponderance (72.7%). As it has also been observed in some other recent studies from Tripura (Subarna and Pradip, 2018).<sup>[22]</sup>

Florence<sup>[23]</sup> conducted a cross-sectional study with 2346 patients, which showed male preponderance (63.2%) of total cirrhotic patient. The mean age of all liver cirrhosis patients in the present study was 52.28 years and it was 50.4 years in the study of Florence.

The present study shows that 58% patients of cirrhosis are having diabetes mellitus.

In this study, it was observed that 24% patients of cirrhosis of liver are having significant CKD and 54% of CKD patients are in Stage 5 disease. Florence<sup>[23]</sup> showed higher prevalence of CKD (46.8%) in cirrhosis.

It was noted in the present study that CKD is more among patients with NAFLD. It can be attributed that probably metabolic syndrome/NAFLD-related CLD patients are having more kidney disease. In the present study group, there is preponderance of alcohol-related liver disease; hence, CKD is less. Pearson Chi-square test is applied to find out the association between non-alcoholic liver cirrhosis and CKD, shows that there is a strong association ( $P = 0.003 < 0.05$ ) that is patients with non-alcoholic liver cirrhosis are more prone to develop CKD than alcohol-related liver cirrhosis. Diabetes (a component of metabolic syndrome) was more common among non-alcoholic liver cirrhosis than alcohol-related liver cirrhosis and CKD, has got a strong association with a  $P = 0.039 (< 0.05)$ . Rajender *et al.*, 2019<sup>[24]</sup> got similar result.

Hypokalemia and hyponatremia are associated with encephalopathy in Cirrhosis of liver. Hyperuricemia is associated with cirrhosis with advance CKD (Afzali *et al.*, 2010).<sup>[25]</sup>

More parameters and imaging to be performed to evaluate renal dysfunction in cirrhosis of liver with CKD.

## CONCLUSION

This study has clinical and public health implications, this study reveals that prevalence of CKD is more common in those who are suffering from non-alcoholic liver cirrhosis and females are more prone to develop non-

alcoholic liver disease compared to males. Researcher should look for NAFLD in diabetics, especially in the presence of metabolic syndrome. Once found, aggressive management of cardiovascular and renal morbidity should be the primary goal. It has only recently been appreciated that CKD represents an important burden of disease for patients with non-alcoholic liver cirrhosis.<sup>[26]</sup>

The study reveals that early evaluation of renal abnormalities at the time of diagnosis of CLDs and at a frequent interval thereafter is of paramount importance to reduce multiter trouble of CLDs, CKD, and metabolic syndrome.

Patients with CKD should be treated as a high-risk group among hospitalized patients with cirrhosis due to their poor survival, impact on liver transplantation and they should be monitored carefully for the development of superimposed AKI (Wong *et al.*, 2019).<sup>[16]</sup>

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