ORIGINAL RESEARCH

Factors Predicting Early Re-Admission and Mortality in Cirrhotic Patients - Experience of a Tertiary Care Centre

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ABSTRACT
Background& Objectives: Over the years, liver cirrhosis has become an increasingly common cause of death worldwide. Early hospital readmission rate after discharge is now considered as a surrogate marker of quality of any healthcare delivery system. Each such readmission puts financial burden on patients and their families as well as employs significant amount of healthcare resources. Identification of factors influencing these readmissions and thereby their prevention is of utmost importance for a sustainable healthcare system. In the present study, we intended to study hospital readmission, mortality rates and predictive factors for hospital readmission and mortality in adults with cirrhosis in Indian scenario.**Methods:**This prospective observational study was conducted in medicine department of NSMCH, Bihta, Bihar, India over 2 years from December 2021 to November 2023 including adults admitted with liver cirrhosis at our institute for the first time. Data was collected regarding demography, aetiology, complications, laboratory parameters, MELD score and CPT score. All participants were followed up for 3 months. Occurrence of readmission and/or death was recorded and studied.**Result:**Over the study period, we included 143 hospitalized cirrhotic patients in our study. Mean age was 48.4 ± 11.9 years. 119 (83.2%) were males and only 24 (16.8%) were females. The commonest aetiology of cirrhosis was alcoholism (56.6%), followed by hepatitis B (16.1%), non-alcoholic steatohepatitis (10.5%) and cryptogenic cirrhosis (9.1%). Decompensation events responsible for index hospitalization were ascites (48.3%), GI bleed due to portal hypertension (19.6%), renal failure (10.5%), spontaneous bacterial peritonitis (9.1%) and hepatic encephalopathy (7.7%). Mean duration of hospitalization was 8.42 ± 4.36 days and average MELD score was 13.71 ± 4.7. Overall, 56 (39.2%) patients needed to be re-admitted before 3 months for 1 or more times. Patients who needed readmission had a worse cirrhosis as indicated by a significantly higher MELD score and CTP score. Also, ALT level and INR were significantly higher in patients requiring re-admission. There were 20 (14%) deaths in the study population within 3 months of discharge. Age more than 60 years and higher MELD scores were associated with an increased risk of 90-day mortality.**Conclusion:**Our study underscores a high rate of readmission as well as short term mortality in patients with advanced liver disease. We suggest that patient–physician discussions should be detailed out so as to direct either very aggressive treatment or palliative care.
Key words:cirrhosis, decompensated liver disease, hospital, MELD score, mortality, readmission.

INTRODUCTION

Cirrhosis of liver is defined as late stage of progressive liver fibrosis characterized by distortion of the liver architecture and the formation of regenerative nodules in response to chronic liver injury, that leads to portal hypertension and end stage liver disease.[1] Over the years, liver cirrhosis has become an increasingly common cause of death worldwide. The two main contributors for its occurrence are alcohol abuse in developed countries and viral hepatitis in developing countries.[2] In the Indian scenario, liver cirrhosis has become a major cause of mortality largely due to high burden of both viral hepatitis and heavy alcohol consumption.[3] Mortality aside, this condition also contributes to significant morbidity requiring frequent hospitalizations and readmissions. It is estimated that the prevalence of liver cirrhosis ranges from 4.5 to 9.5% in the general population. However, this estimation is under-rated owing to the fact that up to one third of the cases remain asymptomatic till the disease progresses to an advanced stage.[4]

Recent advances in the understanding of the natural history and pathophysiology of cirrhosis, and in

treatment of its complications has resulted in improved management, quality of life and life expectancy of cirrhotic patients. At present, liver transplantation remains the only curative option for a selected group of patients, but pharmacological therapies that can halt progression to decompensated cirrhosis or even reverse cirrhosis are currently being developed.[5,6]

Early hospital readmission rate after discharge is now considered as a surrogate marker of quality of any healthcare delivery system.[7] Each such readmission obviously puts financial burden on patients and their families as well as employs significant amount of healthcare resources, doctors' consultations and economic plus social burden on the society.[8] Common factors responsible for readmissions include: relapsing nature of the underlying disease itself, complications arising from previous hospitalization/procedure, poor communication & coordination between discharging hospital and physicians giving outpatient care and poor compliance on the part of patients. Therefore, identification of such causes and thereby their prevention are of utmost importance for a sustainable healthcare system. Over the last few years, much light has been shed on predictors of readmissions in congestive heart failure and chronic obstructive pulmonary disease. This has enabled a significant reduction in number of readmissions through implementation of modifiers in inpatient care.[9,10]

Recently, some researchers have come up with studies evaluating predictors of early readmissions in cirrhosis. However, most of such studies have been conducted in western world. Moreover, most of their work have been conducted in single centres that have not yielded very consistent results.[11,12] There is also non-uniformity in defining what duration after discharge is to be considered as early readmission. Whereas, some studies have considered 30 days as the cut-off time for readmission, others have taken 90 days for the same which might have inherently resulted in divergent conclusions.

Based on the above rationale that complications of cirrhosis are one of the major causes of hospital admission that bears both social and economic burden, we intended to prospectively study hospital readmission, mortality rates and predictive factors for hospital readmission and mortality in adults with cirrhosis.

AIM AND OBJECTIVES
Aim: To study the factors predicting short-term outcome of admitted cirrhotic patients.

Objectives
1. To characterize the patient population admitted with liver cirrhosis at our institute.
2. To study factors associated with re-admission within 3 months of their discharge.
3. To study factors affecting mortality rates in such patients.

MATERIALS AND METHODS
Study Setting: IPD of department of Medicine NSMCH, Bihta, Bihar, India.

Study duration: 2 years, from December 2021 to November 2023.

Study design: prospective observational study.

Inclusion criteria: In the present study we included all adult patients (>18-year age) admitted with liver cirrhosis at our tertiary care level institute for the first time and who survived till discharge, after obtaining their consent for the same.

Exclusion criteria: non-sick liver cirrhosis patients who were admitted for an elective indication or procedure (such as cirrhotic patient with hepatocellular carcinoma admitted for TACE), cirrhosis patients admitted for conditions unrelated to liver cirrhosis, patients with a doubtful diagnosis of liver cirrhosis, patients who went for liver transplantation or died during their first hospitalization and patients unwilling to participate in the study were excluded.

Study technique: After obtaining written informed consent from the patient or relative, we enrolled participants in the present study. Information regarding baseline characteristics such as age, sex, duration of disease, etiology of cirrhosis was collected and entered in a structured proforma. Special focus was given on recording values of laboratory parameters such as complete blood count, liver function test, renal function tests, prothrombin time (PT), international normalized ratio (INR), etc. We also collected data about occurrence of complications due to cirrhosis and/or portal hypertension such as gastrointestinal (GI) bleed, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy (HE), HRS (hepatorenal syndrome) and hepatic hydrothorax. Presence of infections (pneumonia, urinary tract infections, SBP, cellulitis, soft tissue infections, etc.) and associated comorbidities were also taken into account. Child Turcotte Pugh (CTP) score at discharge, Model for End-Stage Liver Disease (MELD) score at discharge and length of stay during hospitalization was also recorded. We followed up our study participants for 3 months through phone calls and review of medical records. Occurrence of readmission and/or death was recorded and studied. Patients with incomplete follow up were excluded from the final analysis.

Statistical analysis: Data so collected was recorded, tabulated and entered in Microsoft excel sheet, and then analyzed by using statistical software "SPSS ver.20®. Data were expressed as mean, standard deviation, proportions and percentiles as appropriate. We used Pearson's chi-square test for categorical parameters and independent samples' t test for continuous parameters. P-value <0.05 was taken as significant.

RESULT

Over the two year study period, we included 143 hospitalized cirrhotic patients in our study. Mean age was 48.4 ± 11.9 years. Among them, 119 (83.2%) were males and only 24 (16.8%) were females. Table 1 depicts the demographic, biochemical and etiological characteristics of the study population. The commonest aetiology of cirrhotic liver disease in these patients was alcoholism (56.6%), followed by hepatitis B (16.1%) non-alcoholic steatohepatitis or NASH (10.5%) and cryptogenic cirrhosis (9.1%). Similarly, the commonest decompensation event responsible for index hospitalization was ascites (48.3%) followed by GI bleed due to portal hypertension (19.6%), renal failure (10.5%), spontaneous bacterial peritonitis (9.1%) and hepatic encephalopathy (7.7%). Mean duration of hospitalization during the index admission was 8.42 ± 4.36 days and average MELD score at discharge was 13.71 ± 4.7. Interestingly, we observed that 23.5% (19 out of 81) of the alcoholics with liver cirrhosis continued their alcohol consumption after discharge from the hospital.

Table 1: Demographic, biochemical and etiological characteristics of the study population

Patient parameter	Value
Age in years (Mean ± SD)	50.4 ± 11.9
Gender	
Male (n, %)	109 (76.2%)
Female (n, %)	34 (23.8%)
Etiology of cirrhosis	
Alcohol (n, %)	81 (56.6%)
Hepatitis B (n, %)	23 (16.1%)
Hepatitis C (n, %)	7 (4.9%)
Non alcoholic steatohepatitis (n, %)	15 (10.5%)
Cryptogenic (n, %)	13 (9.1%)
Others (n, %)	4 (2.8%)
Cause of index hospitalization	
Ascites (n, %)	69 (48.3%)
Portal hypertensive bleed (n, %)	28 (19.6%)
Renal failure (n, %)	15 (10.5%)
Hepatic encephalopathy (n, %)	11 (7.7%)
Spontaneous bacterial peritonitis (n, %)	13 (9.1%)
Others (n, %)	7 (4.9%)
Length of hospital stay in days (Mean ± SD)	8.42 ± 4.36
MELD score at discharge (Mean ± SD)	13.71 ± 4.77
CPT score at discharge (Mean ± SD)	8.94 ± 3.23
3 months readmission (n, %)	56 (39.2%)
Presence of diabetes mellitus (n, %)	27 (18.9%)
Continued alcohol intake at 3 months among the alcoholics (n, %)	19 (23.5%)

Readmission by 3 months: In the present study 56 (39.2%) patients needed to be re-admitted before 3 months for 1 or more times. Alcohol consumption was the commonest etiology of cirrhosis in both the groups while ascites was the commonest primary cause of hospitalization during the index admission in both the groups as shown in table 2. The two groups didn't differ significantly in terms of age, gender and aetiology of the cirrhosis (p>0.05 for each). Also, the primary reason for index hospitalization was comparable between the two groups (p>0.05 for each). However, among the different etiologies of cirrhosis, readmission rate was the highest in patients with hepatitis B virus infection (10/23 or 43.5%) followed by chronic alcoholics (34/81 or 42%). Similarly, among the different causes of index hospitalization, readmission rate was the highest in patients with hepatic encephalopathy (6/11 or 54.5%) followed by portal hypertensive bleed (12/28 or 42.9%) and ascites (28/69 or 40.6%). Males had a significantly higher rate of readmission than females (45% vs 20.6%, p=0.01). Continued alcohol intake post discharge was reported in 19 (23.5%) patients; out of them, readmissions were seen in 11/19 or 58% of such patients. 27 (18.9%) of cirrhotic patients were also suffering from diabetes mellitus; out of them, readmissions were seen in 13/27 or 48% of such patients. In univariate analysis of comparison of index hospitalization variables, patients who needed readmission had a significantly worse cirrhosis as indicated by a statistically significant difference in MELD score (p < 0.001) and CTP score (p < 0.001). Not surprisingly, these patients also had a statistically significant longer duration of hospital stay during their index hospitalization (p<0.001).

Table 2. Comparison of various parameters in re-admitted versus non-readmitted group

Parameter	Re-admitted group (n= 56)	Non-readmitted group (n= 87)
Age in years (mean ± SD)	50.73± 10.53	51.66 ± 10. 89
Gender:		
Male	49 (87.5%)	60 (69%)
Female	7 (12.5%)	27 (31%)
Etiology of cirrhosis		
Alcohol (n, %)	34 (60.7%)	47 (54.0%)
Hepatitis B (n, %)	10 (17.9%)	13 (14.9%)
Hepatitis C (n, %)	2 (3.6%)	5 (5.7%)
Non-alcoholic steatohepatitis (n, %)	5 (8.9%)	10 (11.5%)
Cryptogenic (n, %)	4 (7.1%)	9 (10.3%)
Others (n, %)	1 (1.8%)	3 (3.4%)
Cause of index hospitalization		
Ascites (n, %)	28 (50.0%)	41 (47.1%)
Portal hypertensive bleed (n, %)	12 (21.4%)	16 (18.4%)
Renal failure (n, %)	5 (8.9%)	10 (11.5%)
Hepatic encephalopathy (n, %)	6 (10.7%)	5 (5.7%)
Spontaneous bacterial peritonitis (n, %)	4 (7.1%)	9 (10.3%)
Others (n, %)	1 (1.8%)	6 (6.9%)
Length of index hospital stay in days (Mean ± SD)	9.12 ± 4.97	7.91 ± 4.07
MELD score at discharge (Mean ± SD)	14.26 ± 5.11	12.98 ± 4.27
CPT score at discharge (Mean ± SD)	9.35 ± 3.53	8.33 ± 2.96
Presence of diabetes mellitus	13 (23.2%)	14 (16.1%)
Continued alcohol intake (n, %)	11 (19.6%)	8 (9.2%)

Laboratory parameters: We also compared important laboratory parameters between the two groups during their index hospitalization as shown below in table 3. The important hematological parameters viz Hb level, TLC as well as platelets count was comparable between the two groups (p>0.05). Among the important hepatic parameters, ALT level and INR were significantly higher in patients requiring re-admission. Similarly, the subset of patients requiring subsequent re-admission had a lower serum Sodium level during their index hospitalization.

Table 3: comparison of various laboratory parameters in re-admitted versus non re-admitted group

Lab parameters	Re-admitted group (n= 56)	Non-readmitted group (n= 87)	p value
Hemoglobin (g/dl) (Mean ± SD)	9.21 ± 1.53	9.28 ± 1.59	0.89
TLC (number/cu mm) (Mean ± SD)	6641 ± 3870	6596 ± 3408	0.91
Platelets (number/cu mm) (Mean ± SD)	1,24,919 ± 81,117	1,36,628 ± 81,129	0.29
Bilirubin (mg/dl) (Mean ± SD)	3.75 ± 4.28	2.78 ± 4.63	0.61
ALT (IU/L) (Mean ± SD)	105.49 ± 57.46	76.32 ± 39.12	**<0.001**
AST (IU/L) (Mean ± SD)	87.91 ± 56.23	73.24 ± 45.45	0.08
Total protein (gram/dl) (Mean ± SD)	6.53 ± 0.74	6.63 ± 0.78	0.31
Albumin (gram/dl) (Mean ± SD)	2.48 ± 0.58	2.69 ± 0.66	0.57
INR (number) (Mean ± SD)	1.52 ± 0.45	1.36 ± 0.42	**0.03**
BUN (mg/dl) (Mean ± SD)	16.21 ± 7.59	15.98 ± 8.03	0.57
Creatinine (mg/dl) (Mean ± SD)	1.17 ± 0.61	1.06 ± 0.59	0.28
Sodium (mEq/L) (Mean ± SD)	132.77 ± 5.23	135.65 ± 6.49	**0.006**
Potassium (mEq/L) (Mean ± SD)	4.18 ± 0.75	3.97 ± 0.68	0.09

Mortality by 90 days of discharge from hospitalization: After excluding 9 patients who had died during their index hospitalization, there were 20 (14%) deaths in the study population within 3 months of discharge. Mortality rate for patients who required readmission was 25 % (n=14) compared with 6.9% (n=6) in those without readmission. Age more than 60 years and higher MELD scores were associated with an increased risk of 90-day mortality (OR, 1.07; 95% CI, 1.02–1.08; P < 0.001; and OR, 1.09; 95% CI, 1.03–1.16; P = 0.013, respectively). Male gender was not associated with increased risk of mortality at 90-days (P = 0.58).

DISCUSSION
Adults suffering from decompensated hepatic cirrhosis are vulnerable to hospital readmissions after discharge because of several reasons such as recurrent

nature of complications, adverse effects of medications, noncompliance to drugs and diet, continued exposure to alcohol etc. In the present study, we found that 39.2% of such patients required readmission atleast once by 3 months. Such high incidence of readmission speaks of the morbidity of liver disease and suggests that there should be potential room for improvement. However, this readmission rate is lower than those found in the North American cohorts, which showed readmission rates of 53% at 3 months.[13] In the present study, females had nearly 24% lower readmission rates as compared to their male counterparts. Although the same has been reported previously in some noncirrhotic patient groups, the reason of this protective effect is not clear.[14,15] This difference can be probably explained by psychosocial differences in the manner women or their family members seek hospital care in chronic diseases.

Our study shows that severity of liver disease during index hospitalization, as indicated by MELD and CPT score has a role in prediction of readmission in these patients which correlates well to the findings of other researchers.[16,17] MELD score was originally developed to predict 3-months survival of patients who had undergone transjugular intrahepatic portosystemic shunt (TIPS). But as this scoring system incorporates function of 2 organs (renal and hepatic), estimation of the severity of disease state becomes less cumbersome. Such scoring does not only help in improving the selection process for both transplant and non-transplant surgery, but it is also useful in predicting survival in cirrhotic patients with sepsis, variceal bleeding, fulminate hepatic failure and alcoholic hepatitis.[18,19] In our study, readmission rate for MELD score upto 15 was only 21%, compared to 34% when the discharge MELD score was 15 to 20 and 48% for a discharge MELD of 20 to 30.

It is imperative to note that the risk factors for 90-day readmission are either difficult to modify or not modifiable at all, yet they do allow for identification of patients who may benefit from early medical intervention. This can be achieved by paying additional attention towards these patients in the form of careful discharge planning and closer follow-up evaluation. Recent studies have also revealed that changes in post discharge care has a positive influence on readmission rates in other conditions.[20] Therefore, it is suggested to direct interventions in discharge planning for patients with liver disease toward those patients with coexisting comorbidities like diabetes and/or a higher MELD score.

In the present study we found that short-term mortality among hospitalized patients with liver disease is quite high with an overall 90-day mortality rate of 14%. This again is reflective of the severity of illness in these patients and partly also explains the high rate of readmissions in our study. Not surprisingly, mortality rate for patients who required readmission was 25 % (n=14) compared with 6.9%

(n=6) in those without readmission. Similar to other researchers, we also found that age more than 60 years and higher MELD scores were associated with an increased risk of 90-day mortality.[21].

CONCLUSION

The present study underscores a high rate of readmission by 90 days in patients with advanced liver disease. CPT as well as MELD score and male gender are associated with an increased risk of readmission as well as hospital stay in these patients. This finding may be potentially useful to guide future interventions aimed at reducing readmission in these unfortunate adults. In addition, we have also reported that patients readmitted within 90 days have a high risk of short-term mortality which is associated with age more than 60 years and advanced MELD. This reiterates worse prognosis in these patients and postulates that patient–physician discussions should be detailed out so as to direct either very aggressive treatment or palliative care.

7. Limitations: First limitation is that ours is a single center study.Second limitation is the relatively smaller number of study participants. Third limitation is that we did not separately study predictors of early (at 1 month), intermediate (at 3 months) and late (at >6 months) readmission in our study. But this was done for the sake of simplicity.

8.Financial disclosure: We declare that our study has not received financial assistance of any sort.

9: Conflict of interest: None to declare.

REFERENCES

1. Tsochatzis EA, Bosch J, Burroughs AK. Liver cirrhosis. Lancet. 2014; 383(9930):1749-61.
2. Schuppan D, Afdhal NH. Liver cirrhosis. Lancet. 2008; 371: 838–51.
3. Gupta M, Rao C, Lakshmi PV, Prinja S, Kumar R. Estimating mortality using data from civil registration: a cross-sectional study in India. Bull World Health Organ. 2016; 94(1): 10–21
4. Mukherjee PS, Vishnubhatla S, Amarapurkar DN, Das K, Sood A, Chawla YK, et al. Etiology and mode of presentation of chronic liver diseases in India: A multi centric study. PLoS One. 2017;12(10):e0187033.
5. Kockerling D, Nathwani R, Forlano R, Manousou P, Mullish BH, Dhar A. Current and future pharmacological therapies for managing cirrhosis and its complications. World J Gastroenterol. 2019; 25(8): 888-908.
6. Yoshiji H, Nagoshi S, Akahane T, Asaoka Y, Ueno Y, Ogawa K, et al. Evidence-based clinical practice guidelines for Liver Cirrhosis 2020. Journal of Gastroenterology. 2021; 56:593–19.
7. Balla U, Malnick S, Schattner A. Early readmissions to the department of medicine as a screening tool for monitoring quality of care problems. Medicine. 2008; 87: 294-300.
8. Wong EL, Cheung AW, Leung MC, Yam CH, Chan FW, Wong FY, et al. Unplanned readmission rates, length of hospital stay, mortality, and medical costs of ten common medical conditions: a retrospective analysis

of Hong Kong hospital data. BMC Health Serv Res. 2011; 11: 149-59.

9. Hernandez AF, Greiner MA, Fonarow GC, Hammill BG, Heidenreich PA, Yancy CW, et al. Relationship between early physician follow-up and 30-day readmission among Medicare beneficiaries hospitalized for heart failure. JAMA. 2010; 303: 1716-22.

10. Gudmundsson G, Gislason T, Janson C, Lindberg E, Hallin R, Ulrik CS, et al. Risk factors for rehospitalization in COPD: role of health status, anxiety and depression. Eur Respir J. 2005; 26: 414-19.

11. Volk ML, Tocco RS, Bazick J, Rakoski MO, Lok AS. Hospital readmissions among patients with decompensated cirrhosis. Am J Gastroenterol. 2012; 107(2): 247-52.

12. Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL, et al. A model to predict survival in patients with end-stage liver disease. Hepatology. 2001; 33: 464–70.

13. Bajaj JS, Reddy KR, Tandon P, Wong F, Kamath PS, Garcia-Tsao G, et al. North American Consortium for the study of End-Stage Liver Disease. The 3-month readmission rate remains unacceptably high in a large North American cohort of patients with cirrhosis. Hepatology. 2016; 64(1):200-8.

14. Fernández Gracia J, Martínez González MA, García Rodríguez J, Bueno Cavanillas A, Lardelli Claret P, García Martín M. Factoresasociados a la incidencia de reingresoshospitalarios [Factors associated with the incidence of hospital readmission]. Med Clin (Barc). 1997 Jan;108(1):4-8. (Original article in Spanish)

15. González JR, Fernandez E, Moreno V, Ribes J, Peris M, Navarro M, et al. Sex differences in hospital readmission among colorectal cancer patients. J Epidemiol Community Health. 2005 June;59(6):506-11.

16. Kamath PS, Kim WR. The model for end-stage liver disease (MELD). Hepatology. 2007; 45:797–805.

17. Katoonizadeh A, Decaestecker J, Wilmer A, Aerts R, Verslype C, Vansteenbergen W, et al. MELD score to predict outcome in adult patients with non-acetaminophen-induced acute liver failure. Liver Int 2007; 27(3): 329-34.

18. Terra C, Guevara M, Torre A, Gilabert R, Fernández J, Martín-Llahí M, Baccaro Me et al. Renal failure in patients with cirrhosis and sepsis unrelated to spontaneous bacterial peritonitis: value of MELD score. Gastroenterology. 2005 Dec;129(6):1944-53.

19. Kim HY, Kim CW, Kim TY, Song DS, Sinn DH, Yoon EL, et al. Korean Acute-on-Chronic Liver Failure Study Group. Assessment of scoring systems for acute-on-chronic liver failure at predicting short-term mortality in patients with alcoholic hepatitis. World J Gastroenterol. 2016; 22(41): 9205-13

20. Jack BW, Chetty VK, Anthony D, Greenwald JL, Sanchez GM, Johnson AE, et al. A reengineered hospital discharge program to decrease rehospitalization: a randomized trial. Ann Intern Med. 2009 Feb;150(3):178-87.

21. Berman K, Tandra S, Forssell K, Vuppalanchi R, Burton JR Jr, Nguyen J, et al. Incidence and predictors of 30-day readmission among patients hospitalized for advanced liver disease. Clin Gastroenterol Hepatol. 2011 Mar;9(3):254-9.