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ORIGINAL ARTICLE

The 30-Days readmission among hepatic encephalopathy patients and the associated factors: An experience of a tertiary care hospital in Karachi Pakistan.

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ABSTRACT… Objective: To determine the 30-days readmission rate among hepatic encephalopathy patients and its associated factors among patients admitted in a tertiary care hospital. **Study Design:** Prospective Cohort study. **Setting:** Department of Gastroenterology, Liaquat National Hospital, Karachi, Pakistan. **Period:** July 2023 to June 2024. **Methods:** Patients of cirrhosis with hepatic encephalopathy discharged from hospital were followed up in out-patient and inpatient department as per the hospital protocol. Data were entered into SPSS version 26 to perform statistical analysis. **Results:** Total 215 patients were included into the study. Mean age of patients was 55.40 ± 11.05 years and most of the patients were males (59.3%). Incidence of 30 day readmission was 15.3%. Causes of readmission were constipation (51.5%), infection (30.3%), electrolyte imbalance (12.1%) and renal failure (6.1%). Presence of hypertension and diabetes was associated with increased risk of readmission. Increasing potassium levels at the time of discharge were also found to be associated with increased readmission rate. **Conclusion:** The present study analyzed that main cause of 30 days readmissions were incidence of constipation and infection after discharge. Moreover, the study also showed that patients with comorbidity of hypertension and diabetes were likely to readmit.

Key words: Electrolyte Imbalance, Hepatic Encephalopathy, Hypertension, Infection, Renal Failure.

INTRODUCTION

Liver cirrhosis stands as leading contributor to global mortality and morbidity. It ranks as 11th leading death cause and 15th leading factor for morbidity and contributing to 2.2% of total deaths.[1] The most challenging complication of liver cirrhosis is hepatic encephalopathy (HE), alternatively termed as portosystemic encephalopathy (PSE). Typically HE is characterized as a reversible neuropsychiatric dysfunction, varying from mild cognitive deficiencies to coma, particularly in patients having underlying cirrhosis.[2]

The HE prevalence varies from 30% to 45% cirrhotic patients and is related with recurrent episodes.[3] It is reported that during initial cirrhosis diagnosis, overt HE presents 10%-14% of total patients, 16%-21% in decompensated cirrhosis cases and 10%-50% in cases of transjugular intrahepatic portosystemic shunt.[4]

HE risk factors encompass hypertension and cirrhosis presence, alcohol intake and drug-induced infections.[5] There are two manifestation forms of HE; minimal and overt. Patients present with subtle symptoms in minimal HE and show normal for certain diagnostic evaluation for HE. On the other hand, overt HE is symptomatic and needs hospital care.[6] There may be rapid HE progression, and due to symptoms severity hospitalization is required for therapeutic intervention.[7] The prognosis following overt HE incidence is poor, with one-year survival rate of 40-50% and 3-year survival rate of around 20%.[3]

Earlier research investigations have analyzed higher re-hospitalization rate among cirrhotic patients. A larger study of 130,455 cirrhosis patients reported 12.9% 30-days readmission rate and 21.2% 90-days readmission rate.[8] While there were multi complications of cirrhosis and

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associated comorbidities accounting for re-hospitalization, it was seen that HE was the most potent factor of repeated hospital admissions. Similar results were also analyzed in large cohorts of decompensated cirrhosis patients, collectively highlighting that not only high readmission rate but also underscoring the predictive role of cirrhosis associated complications in repeated hospital admissions.[9-11]

Rehospitalization reflects quality indicator of healthcare provider. Additionally, readmissions are linked to financial burden for family and psychological distress for patients.[12] Thus, HE management imposes a substantial economic burden. The effects of HE and the symptoms it causes include higher indirect expenses for carers and lower patient quality of life. Reducing the frequency of HE episodes and the ensuing readmissions to hospitals is an essential step in reducing the overall impact of HE. Therefore, it is critical to determine the readmission rate, particularly in light of the lack of available data in Pakistan to date. This study was performed to determine the 30-days readmission rate among hepatic encephalopathy patients and its associated factors among patients admitted in a tertiary care hospital.

METHODS

This prospective cohort study was performed in Gastroenterology Department, Liaquat National Hospital, Pakistan, from July 2023 to June 2024. The study was commenced after acquiring approval from Ethical Review Committee (Number: 0818-2022-LNH-ERC, dated: September 12, 2022). Patients were enlisted into the study with their written informed consent. Cirrhotic patients having HE of age 18 years and above of any gender were included into the study. Patient left against medical advice on their first admission, underwent liver transplantation and expires were excluded. Sample size of 215 patients was computed at 95% confidence interval and 5% margin of error taking 16.8% readmission rate from previous similar study.[5] Online calculator Open-Epi was used to perform sample size calculation. Non-probability consecutive sampling technique was employed to enlist patients.

Patients of cirrhosis with hepatic encephalopathy discharged from hospital were followed up in out-patient department as per the hospital protocol. Patients not visiting out-patient department as per advice will be given a phone call to record their status and ask them to re-visit. In case of readmission, the assigned data collector will fill out the study proforma and record all of the required variables. Patients' demographics including age, gender, clinical features such as disease etiology, presenting complaints, Childs–Pugh class and laboratory markers including Hemoglobin, white blood cells, bilirubin, AST, ALT, albumin, INR, BUN, creatinine, sodium and potassium at the time of discharge on first visit and at the time of readmission were recorded. The study outcome variable is 30-day all-cause readmission, defined as readmission to the hospital within 30 days after an index HE discharge.

Data were entered into SPSS version 26 to perform statistical analysis. Frequencies and percentages were computed for categorical variables. Numerical variables were expressed as mean ± standard deviation if they exhibited normal distribution, and otherwise, they were expressed as median with interquartile range (IQR). Shapiro-Wilk test was used to assess normality assumption. Chi-square or Fisher-exact test was applied to compare categorical features among those who were readmitted and who did not whereas non-normally numerical variables were compared using Mann-Whitney U test. Binary logistic regression was applied to compute odds ratio for determining association of patients' features with re-admission. P-value less than or equal to 0.05 was taken as statistically significant.

RESULTS

Mean age of patients was 55.40 ± 11.05 years and most of the patients were males (59.3%). Patients presented with altered level of consciousness (86.6%), abdominal distention (16.7%), fever (12%), vomiting (3.7%) and shortness of breath (2.8%). Table 1 displays summary of patients' socio-demographic and clinical features.

Variables	Frequency	Percentage
Age groups		
24-49 years	60	27.8
50-59 years	59	27.3
60 years and above	97	44.9
Gender		
Male	128	59.3
Female	88	40.7
Residence		
Rural	129	59.7
Urban	87	40.3
Disease etiology		
HCV CLD	126	58.3
HBV CLD	24	11.1
Alcoholic CCD	13	6.0
NASH CLD	48	22.2
Autoimmune	6	2.8
Drug	2	0.9
Comorbidity		
Diabetes	72	33.3
Hypertension	34	15.7
Childs–Pugh class		
Childs A	48	22.2
Childs B	113	52.3
Childs C	55	25.5
Laboratory markers on discharge	**Median**	**Inter-quartile Range**
Hemoglobin (g/dl)	9.6	8.7-11
White blood cell count (million cells/ mcL)	6.8	4.3-10
Platelet count (10^9/L)	100	69.3-150
Bilirubin (mg/dl)	1.4	0.6-2.5
Aspartate Transaminase (U/L)	38	26-70
Alanine Transaminase (U/L)	37	29.3-55.3
Albumin (g/dl)	2.7	2.4-3.2
International Normalized Ratio	1.3	1.2-1.5
Blood Urea Nintrogen (mg/dl)	30	20-40
Creatinine (mg/dl)	1	0.7-1.3
Sodium (mEq/L)	136	132-140
Potassium (mEq/L)	3.7	3.5-4.2

Table-I. Summary of patients socio-demographic and clinical features

Table-II shows incidence and causes of readmission. Incidence of 30 day readmission was 15.3%. Causes of readmission were constipation (51.5%), infection (30.3%), electrolyte imbalance (12.1%) and renal failure (6.1%). Out of 33 re-admitted patients, 60.6% patients were non-compliant of lactulose dose following discharge.

Variables	Frequency (%)
30-day readmission	
Yes	33(15.3)
No	183(84.7)
Causes of readmission	
Constipation	17(51.5)
Infection	10(30.3)
Electrolyte imbalance	4(12.1)
Renal failure	2(6.1)

Table-II. Incidence and causes of readmission

Table-III compares patients' features among those who were readmitted and were not readmitted. None of patients' features was significantly different among those who were readmitted within 30 days and did not readmit except for altered level of consciousness (p=0.014), NASH (p=0.049), hypertension (p=0.013) and diabetes (p=0.001).

Table-IV displays univariate association of patients' features with 30 days readmission. Presence of hypertension and diabetes was associated with increased risk of readmission. Increasing potassium levels at the time of discharge were also found to be associated with increased readmission rate.

DISCUSSION

Hospitalized patients with cirrhosis, particularly those with hepatic encephalopathy frequently encounter a 30-day readmission. These readmissions after hospitalization leads to additional financial burden for the patient and family and can be prevented.[13,14] In our study, the 30 day readmission rate for cirrhotic patients was reported to be 15.3%. These findings are aligned with present literature which reports 30 day readmission of patients with cirrhosis to be 17% and 20%, respectively.[15,16] In contrast, there have been studies done in the United States that have a higher hospital readmission rate i.e. 31.4% and 32%[13,17], however these studies have taken into account a much larger sample size compared to the current study. The former study was a nationwide study that investigated readmissions from 27 geographically diverse states in the US whereas our study is limited to a single tertiary-care center.[13]

Variables	Groups	30 Days Readmission		P-Value
		Yes N (%)	No N (%)	
Age	24-49 years	11(18.3)	49(81.7)	0.733
	50-59 years	8(13.6)	51(86.4)	
	60 years and above	14(14.4)	83(85.6)	
Gender	Male	21(16.4)	107(83.6)	0.578
	Female	12(13.6)	76(86.4)	
Residence	Urban	16(18.4)	71(81.6)	0.296
	Rural	17(13.2)	112(86.8)	
	No	12(13.2)	79(86.8)	
Fever	Yes	4(15.4)	22(84.6)	1.000
	No	29(15.3)	161(84.7)	
SOB	Yes	0(0)	6(100)	f0.594
	No	33(15.7)	177(84.3)	
Altered level of consciousness	Yes	33(17.6)	154(82.4)	*0.014
	No	0(0)	29(100)	
Constipation	Yes	0(0)	17(100)	f0.082
	No	33(16.6)	166(83.4)	
Vomiting	Yes	3(37.5)	5(62.5)	f0.106
	No	30(14.4)	178(85.6)	
Disease etiology	HCV CLD	21(16.7)	105(83.3)	0.502
	HBV CLD	3(12.5)	21(87.5)	0.688
	Alcoholic CCD	4(30.8)	9(69.2)	0.118
	NASH	3(6.3)	45(93.8)	0.049
	Autoimmune	2(33.3)	4(66.7)	0.229
Comorbidity	Hypertension	10(29.4)	24(70.6)	0.013
	Diabetes	19(26.4)	53(73.6)	0.001
Parameters at the time of discharge				
MELD score	-	15 (10.5-22.5)	15 (11-20)	0.956
Child Pugh class	Childs A	9(18.8)	39(81.3)	0.523
	Childs B	18(15.9)	95(84.1)	
	Childs C	6(10.9)	49(89.1)	
Hemoglobin (g/dl)	-	10(8.7-11)	9.6(8.8-11)	0.123
White blood cell count (million cells/mcL)	-	8.1(5.2-9.5)	6.8(4.2-10)	0.954
Platelet count (10^9/L)	-	91(69.5-143)	103(68-153)	0.926
Bilirubin (mg/dl)	-	0.9(0.8-1.95)	1.4(0.6-2.5)	0.130
Aspartate Transaminase (U/L)	-	34(24.5-66)	40(26-72)	0.485
Alanine Transaminase (U/L)	-	33(24-42)	39(30-57)	0.076
Albumin (g/dl)	-	2.5(2.3-3.1)	2.8(2.5-3.3)	0.146
International Normalized Ratio	-	1.3(1.2-1.5)	1.3(1.2-1.5)	0.689
Blood Urea Nintrogen (mg/dl)	-	34(22-80)	30(20-40)	0.468
Creatinine (mg/dl)	-	1.1(0.5-1.7)	1(0.7-1.3)	0.862
Sodium (mEq/L)	-	136(129-140)	136(133-139)	0.888
Potassium (mEq/L)	-	4(3.6-4.55)	3.7(3.4-4.2)	0.245

Table-III. Comparison of patients' features among those with and without 30 day readmission

Variables	OR (95% CI)	P-Value
Age groups		
24-49 years	1.33 (0.56-3.16)	0.517
50-59 years	0.93 (0.36-2.37)	0.879
60 years and above	Reference category	
Gender		
Male	1.24 (0.58-2.68)	0.579
Female	Reference category	
Residence		
Urban	1.48 (0.71-3.12)	0.298
Rural	Reference category	
Disease etiology		
HCV CLD	1.62 (0.76-3.46)	0.208
HBV CLD	0.77 (0.22-2.74)	0.689
Alcoholic CCD	2.67 (0.77-9.23)	0.122
Autoimmune	2.88 (0.51-16.44)	0.232
NASH	0.31 (0.08-1.05)	0.060
Comorbidity		
Hypertension	2.88 (1.22-6.79)	*0.016
Diabetes	3.32 (1.55-7.12)	**0.002
MELD score	1 (0.95-1.06)	0.942
Child Pugh class		
Childs A	1.88 (0.62-5.74)	0.265
Childs B	1.54 (0.57-4.14)	0.386
Childs C	Reference category	
Laboratory markers on discharge		
Hemoglobin (g/dl)	0.94 (0.75-1.17)	0.603
White blood cell count (million cells/ mcL)	0.97 (0.92-1.04)	0.450
Platelet count (10^9/L)	1.00 (0.99-1.01)	0.941
Bilirubin (mg/dl)	1.03 (0.88-1.14)	0.962
Aspartate Transaminase (U/L)	0.99 (0.99-1.00)	0.302
Alanine Transaminase (U/L)	0.99 (0.99-1.00)	0.397
Albumin (g/dl)	0.57 (0.29-1.12)	0.105
International Normalized Ratio	1.13 (0.32-3.97)	0.838
Blood Urea Nintrogen (mg/dl)	1.00 (0.99-1.01)	0.354
Creatinine (mg/dl)	1.10 (0.73-1.66)	0.640
Sodium (mEq/L)	0.97 (0.91-1.04)	0.414
Potassium (mEq/L)	2.14 (1.23-3.71)	*0.006

Table-IV Univariate association of patients features with 30 days readmission

The study analyzed that causes of readmission were constipation (51.5%), infection (30.3%), electrolyte imbalance (12.1%) and renal failure (6.1%). A similar study reported that a total of 402 patients with cirrhosis had 165 readmissions within the first month following discharge, with a median timing of 67 days; of these, 22% may have been avoided. The most common reasons for preventing hospital readmissions was fluid imbalance. The HE readmissions were determined to be avoidable because poor titration of lactulose resulted in insufficient stool production.[13] According to Tapper BE et al., acute complications (in 41.0% of cases) and cancer complications (16.2% of cases) were the most frequent causes of readmission for patients with a history of cirrhosis problems.[8]

Our study demographics revealed a higher proportion of male cirrhotic patients (59.35%) were readmitted and the mean age of readmitted patients was 55.40 ± 11.05 years. In 2019, a large Asian cohort prospective study conducted in India showed similar trends, highlighting that men were statistically more likely to be readmitted in first 30 days than women (32.3% vs. 17.4%, respectively).[18] Chirapongsathorn and colleagues investigated that the risk of readmission is seen to increase with age particularly in the age parameters of 65 and above.[17] Nevertheless, considering the higher liver cirrhosis prevalence at an earlier age, average age in this study was comparatively lower. This observation corroborate with results of other similar studies.[18,19]

Studies conducted across various regions have reported an elevated risk of readmission among cirrhotic patients with various etiologies, encompassing HCV CLD, HBV CLD, alcohol-related, contrarily, our results did not indicate any such correlation with these etiologies. This observation aligns with an Indian cohort study, which similarly concluded that the etiology of cirrhosis (HBV, HCV and NASH) does not contribute to risk for readmission.[13,18-20] This discrepancy of our study in comparison to Western literate might arise as distinct medical conditions and risk factors are prevalent among different ethnicities and regions worldwide.

Our study demonstrated that preexisting conditions such as hypertension and diabetes was associated with increased risk of readmission. This relationship has been well documented in

previous literature. These studies have shown that comorbid conditions such as diabetes and hypertension could result in poor outcome for the cirrhotic patient as they are at a substantial risk for developing hepatic encephalopathy, resulting in greater occurrence of readmission and prolonged hospital stay.[21-24] Garg et al, in addition to these also stated other coexisting comorbid conditions which could contributed towards rehospitalization but none of these associations were seen in our study.[13]

Currently, several scoring systems, such as model for end-stage liver disease (MELD) score, Child–Turcotte–Pugh (CTP) score, among others, have been proposed to predict prognosis and survival in liver cirrhosis patients.[25] Earlier studies have shown that a higher CPT class has a significant impact on readmission rates.[18-20] In contrast, our study revealed no association between Child-Pugh classification and 30-day hospital readmissions in cirrhosis patients. The same findings have also been by seen in additional literature.[26] Our findings are aligned with Patel H et al[19] and Sood Kt et al.[26] On the other hand, Chirapongsathorn S et al, and Patel R et al reported that MELD score were significantly higher at the time of discharge in patients who later on needed re-hospitalization.[15,18]

In regard to patient-related predictors of readmission, lab values play a vital role. Prior research have identified various laboratory parameters such as low serum sodium (< 133 mEq/L), serum bilirubin, alanine aminotransferase, aspartate aminotransferase, and INR as indicators for 1-month readmission.[19,27] However, our study suggested increasing potassium levels at the time of discharge to be an independent predictor of readmission. The reason for this discrepancy is because other studies assessed these values during the hospital stay while we measured them at the time of discharge. Studies that considered laboratory indicators upon discharge reported low hemoglobin as a predictor for readmission but did not measure electrolytes including potassium at time of discharge.[28]
Unfortunately in this study, we did not record variables like Portal hypertension, ascites, and presence of infections and variceal hemorrhage. These comorbidities may linked to preventable hospitalizations and can respond to effective outpatient management. Additionally, this study is an experience of single center. Hence, further research is imperative to validate findings of current study and for identification and characterization of combinations of comorbidities that elevate risk of adverse outcomes.

CONCLUSION

The present study analyzed that 30 days readmission was significantly common among patients having comorbidity of hypertension and diabetes. The findings of current suggest to well monitor and manage hypertension and diabetes after discharge to avoid readmission.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Narjis Raza	Conceptualized the study, Involved in data collection, Initial manuscript writing.	
2	Mansoor ul Haq	Designed the study protocol, Critically revised the initial manuscript draft.	
3	Adeel Rahat	Data collection, Literature review, Data analysis.