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## **Frequency of in hospital mortality of cirrhotic patients due to sepsis**

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**Abstract--Introduction:** Infection is a common complication of liver cirrhosis, as 30–50% of patients with cirrhosis either present with infection during admission, or develop infection during hospitalization. The severity of the underlying liver disease makes patients with cirrhosis more susceptible to the development of sepsis, compared to the general population. Patients with cirrhosis have a high risk of developing sepsis. According to the Global Burden of Disease study, liver cirrhosis caused 1.2% of global disability adjusted life years and 2% of all deaths worldwide in 2010. **Objective:** To determine the frequency of in hospital mortality of cirrhotic patients

due to sepsis. **Materials and Methods:** It is Descriptive Study conducted at Department of Gastroenterology, Asian Institute of Medical Science (AIMS), Hyderabad, Pakistan from January 31, 2020 to July 30, 2020. All patients who fulfilled the inclusion criteria and visited to AIMS; Hyderabad were included in the study. Child-Turcotte-Pugh (CTP) score was calculated by clinical parameters, i.e. encephalopathy and ascites, and laboratory results, i.e. bilirubin and albumin concentrations, and prothrombin time and MELD score were calculated by it using laboratory parameters bilirubin, serum creatinine and international normalization ratio (INR). Patient was followed during in hospital stay in order to note stable discharge or in hospital mortality. **Results:** Out of 162 patients, 108 (66.7%) were male while 54 (33.3%) were female, mean of age was  $53.5 \pm 11.2$  years. Sixty (37.0%) patients were classified as CTP B while 102 (63%) were classified as CTP C, MELD score was  $21.27 \pm 8.69$ . In hospital mortality was noted in 29 (17.9%) patients. **Conclusion:** It is to be concluded that in-hospital mortality was documented in considerable number of patients presenting with cirrhotic due to sepsis, in-hospital mortality was more in patient with CTP C, MELD score more than 20 and hospital stay more than 5 days.

**Keywords**---Mortality, Cirrhotic, Sepsis, MELD, Survival, Infection, Child-Pugh Score.

## Introduction

Liver cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules. It is generally considered to be irreversible in its advanced stages, at which point the only option may be liver transplantation [1]. Many causes can result in cirrhosis: the most common causes of cirrhosis worldwide are chronic hepatitis B and C, alcoholic liver disease, and non-alcoholic fatty liver disease [2]. The clinical course of cirrhosis is traditionally divided into two phases, Compensated cirrhosis defines the period between the onset of cirrhosis and the first major complication. During this period (10–15 years), patients have no or minor symptoms, but histological liver lesions and portal pressure steadily progresses if the etiological factor of cirrhosis persists. The term "decompensated cirrhosis" is used following the development of ascites, variceal haemorrhage, and/or hepatic encephalopathy. Decompensated cirrhosis is associated with a short survival (3–5 years) [3].

Patients with cirrhosis have an elevated risk of developing bacterial infections and sepsis. Simplified definitions of sepsis include systemic inflammatory response syndrome (SIRS) plus infection, severe sepsis is sepsis associated with organ dysfunction, hypo-perfusion or 5 hypotension, and septic shock is sepsis with arterial hypotension, despite adequate fluid resuscitation [4]. When sepsis occurs, it is associated with a fourfold increase in mortality rate in patients with cirrhosis. Thus, early diagnosis, treatment and prognostic stratification of patients with cirrhosis and sepsis are crucial [5]. Reported in hospital mortality in cirrhotic

patients due to sepsis varies in different studies done in different centres. Study conducted by Majumdar A et al [6] showed mortality of 32.4% in cirrhotic patients. In hospital mortality reported in study was 29% done by Piano S et al [5]. Another study showed in hospital mortality of 25% in cirrhotic due to infection leading sepsis M. Bartoletti et al [7]. Spontaneous bacterial peritonitis is one of leading cause of sepsis in cirrhotic patients in hospital mortality reported in one of study was 17.6% done by Niu B et al [8].

**Rationale** After robust literature search no local published data was found on in hospital mortality in cirrhotic patients due sepsis, this provided me a strong rationale to conduct this study in our local population, to see the magnitude of this problem in our population so that the policy makers could use the information and make the strategy to recognize sepsis in cirrhotic patient as early as possible and can prevent cirrhotic patients from sepsis and sepsis related complication i.e. septic shock, liver failure and death. If sepsis related in hospital mortality in cirrhotic patient found high then robust action can be done to screen all cirrhotic patients for sepsis efficiently treat the source of sepsis, and quality preventive measure could be taken in future to prevent cirrhotic patient from detrimental effects of sepsis.

### **Material & Methods**

It is Descriptive Study with Non-Probability, Consecutive Sampling conducted at Department of Gastroenterology, Asian Institute of Medical Science (AIMS), Hyderabad, Pakistan from January 31, 2020 to July 30, 2020. All Cirrhotic patients compensated or decompensated irrespective of the cause and duration cirrhosis of either gender between age 18 to 65 years were enrolled after fulfilling the inclusion criteria and visited to AIMS; Hyderabad were included in the study. Patients were excluded on the basis of medical record and history, not cirrhotic and Patients with hepatocellular carcinoma were excluded.

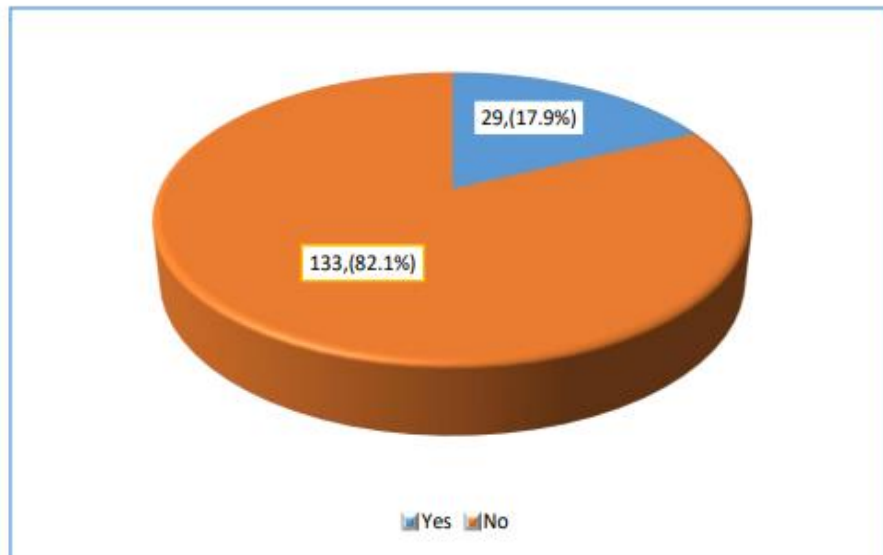
### **Data Collection and Analysis**

Study was conducted after approval by ethical review committee of the hospital. Written informed consent was obtained from all fulfilling inclusion criteria. History was taken, vital sign was noted and examination was done. Sepsis was labelled when patient had systematic inflammatory response syndrome i.e. 2 of the following i) Axillary temperature  $38^{\circ}\text{C}$  ( $100.4^{\circ}\text{F}$ ) or less than  $36^{\circ}\text{C}$  ( $96.8^{\circ}\text{F}$ ), ii) Heart rate of more than 90 beats per minute, iii) Respiratory rate of more than 20 breaths per minute, iv) Complete blood picture showed white blood cell count ( $12,000/\mu\text{L}$  or less than 4000) and source of infection. Investigation was done to rule out source of infection. Child-Turcotte-Pugh (CTP) score was calculated by clinical parameters, i.e. encephalopathy and ascites, and laboratory results, i.e. bilirubin and albumin concentrations, and prothrombin time and MELD score were calculated by it using laboratory parameters bilirubin, serum creatinine and international normalization ratio (INR) Patient was followed during in hospital stay stable discharge or in hospital mortality was noted. All the data was entered in the structural proforma and was used for statistical analysis. SPSS 20.0 used for analysis; chi-square test was applied by taking p values  $\leq 0.05$  was considered as significant.

## Results

In this study 162 patients were included to assess the frequency of in hospital mortality of cirrhotic patient due to sepsis at Asian Institute of Medical Science Hospital Hyderabad, out of 162 patients, 108 (66.7%) were male while 54 (33.3%) were female, mean age of the patients with standard deviation was  $53.5 \pm 11.2$ , Child Pugh classification showed that 60 (37.0%) were classified as B having child score (7-9) while 102 (63%) were classified as C with a score of (10-15), Mean  $\pm$  SD of child score was  $10.78 \pm 2.60$ , MELD score was  $21.27 \pm 8.69$ , hospital stay was  $5.03 \pm 2.37$ . In hospital mortality was noted in 29 (17.9%) patients as shown in FIGURE 1

Stratification of age group, gender, child Pugh class, MELD score and in hospital stay were done with respect to in hospital mortality in order to found significant difference from TABLE [1-5]



Frequency of in hospital Mortality

**Table 1**

**STRATIFICATION OF AGE GROUP WITH IN HOSPITAL MORTALITY**  
n=162

AGE GROUP (In Years)	IN HOSPITAL MORTALITY		P- VALUE
	YES	NO	
18 – 40	6 (3.7%)	15 (9.3%)	0.172
> 40	23 (14.2%)	118 (71.8%)	

Applied Chi-square test

**Table 2**

**STRATIFICATION OF GENDER WITH IN HOSPITAL MORTALITY**  
n=162

GENDER	IN HOSPITAL MORTALITY		P- VALUE
	YES	NO	
Male	20 (12.3%)	88 (54.3%)	0.772
Female	9 (5.6%)	45 (27.8%)	

Applied Chi-Square test

**Table 3**

**STRATIFICATION OF CHILD PUGH CLASS WITH IN HOSPITAL MORTALITY**  
n=162

CHILD PUGH CLASS	IN HOSPITAL MORTALITY		P- VALUE
	YES	NO	
Class B	4 (2.5%)	56 (34.6%)	0.003
Class C	25 (15.4%)	77 (47.5%)	

Applied Fisher's Exact test

**Table 4**

**STRATIFICATION OF MELD SCORE WITH IN HOSPITAL MORTALITY**  
n=162

MELD SCORE	IN HOSPITAL MORTALITY		P-VALUE
	YES	NO	
9 – 20	7 (4.3%)	78 (48.1%)	0.001
> 20	22 (13.6%)	55 (34.0%)	

Applied Chi-Square test

**Table 5**

**STRATIFICATION OF HOSPITAL STAY WITH IN HOSPITAL MORTALITY**  
n=162

HOSPITAL STAY [In Days]	IN HOSPITAL MORTALITY		P-VALUE
	YES	NO	
2 – 5	11 (6.8%)	94 (58.0%)	0.001
> 5	18 (11.1%)	39 (24.1%)	

Applied Chi-Square test

**Discussion**

It has been recognized that in-hospital mortality in cirrhotic patients with acute decompensation is high, and it is higher than that of patients with other diseases [9]. Acute-on-chronic liver failure is a recently identified entity characterized by acute decompensation of cirrhosis associated with organ failure and a very high in-hospital mortality rate [10,11]. Its identification is crucial for establishing outcome, and in turn, offering patients the appropriate medical management. Two studies in Peru, one in Ecuador, and one in Brazil described in hospital mortality rates similar to the results of our study (23.8, 19.8, 23.7, and 24.2%, respectively) [12-15], whereas another Peruvian study reported a much lower mortality rate (5.1%) [16]. The fact that there are numerous factors that determine hospital mortality must be taken into account, and they include disease stage, complications, associated comorbidities, infections, organ dysfunction, acute-on chronic liver failure, and clinical status upon admission [17-19]. The natural

history of cirrhosis is characterized by an asymptomatic phase termed compensated cirrhosis, followed by a rapidly progressive phase marked by the development of complications of portal hypertension and/or liver dysfunction (ascites, variceal bleeding, portosystemic encephalopathy, jaundice), termed decompensated cirrhosis. These complications further worsen mortality. Our evaluation of infection suggests that the occurrence of bacterial infection could be considered a further prognostic stage, defining the critically ill cirrhotic. The high incidence of infection, particularly SBP, in patients with variceal bleeding has long been recognized [20]. A subsequent prospective study confirmed the high frequency of infection in patients with variceal bleeds, and found that infection predicted variceal rebleeding [21]. In a retrospective study, antibiotic therapy and proven bacterial infection were the only factors independently predicting failure to control bleeding [22]. Conversely, in patients with controlled bleeding, the incidence of sepsis was significantly lower versus those with uncontrolled bleeding [21], a finding confirmed in further studies [23,24]. Infection may favour variceal bleeding by increasing sinusoidal pressure and altering haemostasis. In fact, endotoxaemia stimulates endothelin production, which activates sinusoidal stellate cell contraction. Sinusoidal pressure increases, significantly enhancing the risk of variceal bleeding [24]. Endotoxins also stimulate endothelial NO production, leading to abnormal platelet aggregation and primary haemostasis failure [23]. Mortality from liver cirrhosis has sharply declined in most countries around the world in the last few decades [25-28]. Conversely, the persisting upward trends up to the recent calendar period were observed in Thailand. Our analysis demonstrated the absolute rate of dying in the hospital increased steadily by 12% from 9.6% in 2009 to 10.8% in 2013. This observation coincides with the report on the increasing in cirrhosis mortality in developing countries, particularly in Central Asia and Africa [25]. The consistent increase in mortality rate for Thai cirrhosis patients requiring hospitalization, year to year, has been not related to the aging of the patient cohort. The average age at hospitalization for advanced liver disease has remained stable at 53 years. Indeed, the pattern in death from cirrhosis is attributable to changes in several cirrhosis-related conditions, sex, geographic region, and hospital level. In particular, the variations in mortality trends over time are primarily driven by changes in clinical manifestations of portal hypertension. In this study, the mean age was  $53.5 \pm 11.2$  years. Piano S, et al [5] noted mean age as  $61 \pm 12$  years. The study of Zubieta-Rodríguez R, et al [29] reported a higher mean age of 61.5 years whereas Arvaniti V, et al [30] reported 56 years mean age. Charatcharoenwitthaya P, et al [31] also noted age as 53.8.12.8 years. Another study of Safi W, et al [32] noted mean age as  $61.1 \pm 10.5$  years. In current study, the mean child score was  $10.78 \pm 2.60$ . Piano S, et al [5] noted  $9 \pm 2$  as mean child-pugh score whereas Safi W, et al [32] noted as is  $9 \pm 2$ . In recent study, the mean MELD score was  $21.27 \pm 8.69$ . Piano S, et al [5] noted mean MELD score as  $20 \pm 7$ . Safi W, et al [32] noted MELD score as  $16.2 \pm 6.5$ . In our study, the mean in hospital stay was  $5.03 \pm 2.37$  days. In present study, out of 162 patients, 108 (66.7%) were male while 54 (33.3%) were female. Zubieta-Rodríguez R, et al [29] noted to have 36 (58%) males and 26 (42%) females. 68.3% patients were found male in Arvaniti V, et al [30] and 66.6% in Charatcharoenwitthaya P, et al [31]. Piano S, et al [5] reported 162 (62%) male patients in study and Safi W, et al [32] reported 156 (71.2%) males. In this study, child pugh classification showed that 60 (37.0%) were classified as B having child score (7-9) while 102 (63%) were classified as C with a score of (10-15). Zubieta-

Rodríguez R, et al [29] also reported that there were 10 (17.2%) patients in A, 34 (58.6%) in B and 14 (24.2%) in C. Arvaniti V, et al [30] reported to have 109 (33.6%) patients in A, 104 (32.15) in B and 111 (34.25) patients in C. In our study, in hospital mortality was noted in 29 (17.9%) patients. Zubieta-Rodríguez R, et al [29] documented in hospital mortality in 09 (14.5%) patients. 10.8% mortality was noted in Charatcharoenwiththaya P, et al [31]. Mortality was noted in 21 (9.6%) patients in Safi W, et al [32]. In present study, stratification of confounders / effect modifiers with respect to in hospital mortality, significant difference was noted in age group ( $P=0.012$ ), gender ( $P=0.772$ ), child pugh class ( $P=0.003$ ), MELD score ( $P=0.001$ ) and hospital stay ( $P=0.001$ ).

## Conclusion

It is to be concluded that in-hospital mortality was documented in considerable number of patients presenting with cirrhotic due to sepsis. Furthermore, our findings outline the need for future research to investigate those factors that could be considered as higher risk of mortality. Future prospective more epidemiological studies are necessary to evaluate the mortality among large sample size with multiple study centers in Pakistan are needed to confirm the findings of the present study.

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