Original Research Article

Study of infections in decompensated liver cirrhosis in North India

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Abstract

Introduction: Cirrhosis of liver is an acquired immunocompromised state. The development of infection in cirrhosis is associated with significantly higher mortality that has been shown to be independent of the severity of liver disease. The in-hospital mortality of cirrhotic patients with infection is approximately 4-5 folds higher than that of patients without infection cirrhosis and is directly responsible for 30–50% of deaths. This study was planned to study clinical profile of common infections in decompensated cirrhosis of liver patients **Aims and objectives:** This study aims to determine the clinical profile of infections in decompensated cirrhosis of the liver with main objectives: a) Finding various causative organisms of common infections in decompensated cirrhosis of liver b) To study the possible risk factors associated with infections in decompensated cirrhosis liver c) To study the impact of infections in the outcome of patients with decompensated cirrhosis of the liver. **Methods:** All patients attending Medical or Gastroenterology OPD were screened for decompensated cirrhosis of liver. They were clinically examined for evidence of any focus or site of infection. These patients were admitted and underwent estimation of hemogram, liver function tests, renal function tests, serum electrolytes, serum CRP and procalcitonin, urine routine and microscopic examination, urine culture, stool routine or microscopic examination, blood culture, ascitic fluid analysis chest X-ray and ultrasonography abdomen. These patients were followed up for 30 days. **Results:** There was a higher prevalence of culture positive in alcoholic cirrhotic patients in comparison with nonalcoholic cirrhotic with p value of 0.01. The mortality after 30 days of follow up was 1.2%. There was no statistically significant difference found in the mortality of the patients seen. In this study, cirrhotic patients with smoking history, associated with other co morbidities, presence of fever at the time of presentation, jaundice, presence of spontaneous bacterial peritonitis and body fluids showing positive cultures are predictors of bad outcome. Among 117 (69.2%) alcohol related decompensated liver cirrhosis patients 66.7% had worst outcome. **Conclusion:** The most common infection in decompensated cirrhosis of liver found was spontaneous bacterial peritonitis. The 30 days outcome of infection in DLF was 98.8% in this study. The common risk factor for infection in DLF was alcohol as etiology and development of SBP. The study concludes that infections are more common in alcohol related cirrhosis than others.

Keywords: Decompensated liver failure (DLF), spontaneous bacterial peritonitis (SBP), CRP, procalcitonin, antibiotics, alcoholic cirrhosis.

Introduction

Cirrhosis is an immunocompromised state that predisposes patients to a variety of infections from uncommon pathogens. Once an infection develops, the excessive uptake response on pre-existing cirrhosis further facilitates severe complications wide septic shock, acute-on-chronic liver failure (ACLF), multiple organ failure, and death. Bacterial infection with cirrhosis is prevalent in clinical practice, and is the main reason for intensive care unit admission and death [1, 2]. The incidence of resistant bacteria has been increasing, especially in healthcare-associated settings. Preventive measures, early recognition, and proper management are necessary to minimize morbidity and mortality of infections in cirrhosis [1].

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Decompensated cirrhosis has more frequent episodes of infections than compensated cirrhosis. Once an infection develops, renal failure, shock, and encephalopathy may follow, which adversely affect survival. 32– 34% of cirrhotic patients develop a bacterial infection either at the time of admission or later during hospitalization, as against 5–7% overall infection rates for the general population [3, 4, 5, 6]. This emphasizes the concept of cirrhosis as an acquired immuno compromised state. The development of infection in cirrhosis is associated with significantly higher mortality that has been shown to be independent of the severity of liver disease. The in-hospital mortality of cirrhotic patients with infection is approximately 4-5 folds higher that of patients without infection cirrhosis [1]., and is directly responsible for 30–50% of deaths [3,4]. This study was planned to study clinical profile of common infections in decompensated cirrhosis of liver patients.

Aim& Objectives

This study aims to determine the clinical profile of infections in decompensated cirrhosis of the liver with main objectives: a) Finding various causative organisms common infections in decompensated cirrhosis of liver b) To study the possible risk factors associated with infections in decompensated cirrhosis liver c) To study the impact of infections in the outcome of patients with decompensated cirrhosis of the liver.

Methods

This prospective observational study was conducted in a tertiary care Government center in Northern India from 01 Jun 2019 to 31 Mar 2021.The sample size was calculated based on the prevalence of infections [2] in decompensated liver disease in India (37%), using formula $n = 4PQ/L^2$ where n- sample size, P- prevalence Q=100-P, and Allowable relative error (L) – 20%. The calculated sample size was 164. All patients more than 18 years of age with decompensated cirrhosis of the liver and were consented to be a part of this study were included in this study. The exclusion criterion was patients who die within 12hrs after admission, post-liver transplant status, and on steroids and immunosuppressive drugs were excluded.

The Institutional Ethical Committee approved this study wide letter no. IEC regn no. 82/2019. All patients attending Medical or Gastroenterology OPD were screened for decompensated cirrhosis of liver. The criteria of decompensated liver cirrhosis used were development of overt clinical signs like ascites, bleeding, encephalopathy, and jaundice. Any history of fever, breathlessness, cough, and symptoms of lower urinary tract symptoms or suggestive of infection was noted. They were clinically examined for evidence of any focus or site of infection. These patients were admitted and underwent estimation of hemogram, liver function tests, renal function tests, serum electrolytes, serum CRP and procalcitonin, urine routine and microscopic examination, urine culture, stool routine or microscopic examination, blood culture, ascetic fluid analysis chest X-ray and ultrasonography abdomen. These patients were followed up for 30 days.

In this study we defined the presence on infections in DLF cases as below:

1. Spontaneous bacteremia: positive blood cultures without a source of infection.
2. Spontaneous Bacterial Peritonitis: Ascitic fluid polymorphonuclear cells > 250/µL with or without a positive fluid culture.
3. Lower Respiratory Tract Infection: New pulmonary infiltrate in the presence of at least one respiratory symptom with at least one finding on auscultation or one sign of systemic inflammatory syndrome in the form of core body temperature 38 C or less than 36 C or Total Leukocyte Count above 10,000/ cumm or less than 4000/mm.
4. Bacterial Enterocolitis: Diarrhea or dysentery with a positive stool culture for Salmonella, Shigella, Campylobacter, Yersinia or pathogenic Escherichia coli.
5. Skin infection: Fever with cellulites.
6. Urinary Tract Infection: Symptoms consistent with cystitis or pyelonephritis along with more than 10 pus cells/HPF on urine microscopy with significant bacteriuria.
7. Diagnosis of other infections was made by raised serum CRP or procalcitonin levels.

All continuous variables were described as mean and standard deviation. The categorical variables were defined as numbers and percentages. Contingencies tables were made. 't' test and chi-square test were used for association. The data was analyzed using Stata Corp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC.

Results

In this study of 169 patients, 145(85.8%) were males, 24(14.2%) were females with a mean of 53.8 years of age, and alcohol was a common etiology in 117 (69.2%). It was found that fever was the most common presenting symptom seen in 75 (44.4%) patients, followed by breathlessness 67(39.6%) patients. The details of various symptoms suggestive of infections in DLF patients are placed in Fig 1.

In this study, past history of jaundice seen in 111 (65.7%) patients, 55/169 patients had history of spontaneous bacterial peritonitis followed by history of soft tissue infection. Patients with prior antibiotics usage before admission was 76 (45%) the details of the past history suggestive of infection in DLF are shown in Fig 2.

The most evident clinical sign of infection in DLF noted in this study was abdominal distention in 153 (90.5%). It was followed by pedal edema in 145 (86.3%) cases and which was further followed by jaundice in 106 (62.7%) cases. The details of the various clinical signs suggestive of infection in DLF are shown in Fig.3.

The infection in DLF was confirmed on hematological parameter in 65 (38.5%) patients, by raised serum CRP & Procalcitonin levels in 71 (42%) patients, by ascitic fluid analysis in 56 (33.1%) patients and by body fluids Cultures in 37 (21.9%) patients. There was a higher prevalence of culture positive in alcoholic cirrhotic patients in comparison with nonalcoholic cirrhotic with p value of 0.01.

In this study, upgradation of antibiotics during hospitalization with 30 days follow up was considered as bad outcome which was done in 60 (35.5%) patients. The details of various predictors where antibiotics were considered to be upgraded are shown in table 1. Upgradation of the antibiotics was done more in patients with fever, history of smoking, past history of jaundice, Known hypertensive, and other co-morbidities. The other predictors where antibiotics upgradation was considered in this study are patients with leukocytosis, higher bilirubin, serum alkaline phosphate, raised CRP and procalcitonin levels, and culture positivity.

In this study, the mortality after 30 days of follow up was 2(1.2%) patients. There was no statistically significant difference found in the mortality of the patients seen. In this study, cirrhotic patients with smoking history, associated with other comorbidities, presence of fever at the time of presentation, jaundice, presence of spontaneous bacterial peritonitis and body fluids showing positive cultures are predictors of bad outcome. Among 117 (69.2%) alcohol related decompensated liver cirrhosis patients 40 (66.7%) had worst outcome.

Table 1: Predictors of bad outcome in this study group

Sno	Characteristic	Description	Upgradation of treatment		P value
			No 109	Yes 60	
1	Smoking No Yes	 160 (94.7) 9 (5.3)	 106 (97.3) 3 (2.7)	 54 (90) 6 (10)	0.05
2	Fever No Yes	 94 (55.6) 75 (44.4)	 67 (61.5) 42 (38.5)	 27 (45) 33 (55)	0.04
3	Past history of Jaundice No Yes	 58 (34.3) 111 (65.7)	 45 (41.3) 64 (58.7)	 13 (21.7) 47 (78.3)	0.01
4	Past history of SBP No Yes	 114 (67.5) 55(32.5)	 85 (78) 24 (22)	 29 (48.3) 31 (51.7)	<0.001
5	Co-morbidities No Yes	 146 (86.4) 23 (13.6)	 100 (91.7) 9 (8.3)	 46 (76.7) 14 (23.3)	0.006

6	Serum Total bilirubin	6.6 (7.3)	5.7 (5.7)	8.4 (9.4)	0.02
7	Serum Alkaline Phosphate	119.4 (71.4)	107.5 (61.5)	140.9 (82.7)	0.003
8	CRP	10.7 (2.02)	10.5 (2)	11.1 (2.1)	0.06
9	Ascitic Fluid analysis	113 (66.9) 56 (33.1)	82 (75.2) 27 (24.8)	31 (51.7) 29 (48.3)	0.002
10	Culture No Yes	 132 (78.1) 37 (21.9)	 103(94.5) 6 (5.5)	 29 (48.3) 31 (51.7)	 <0.001

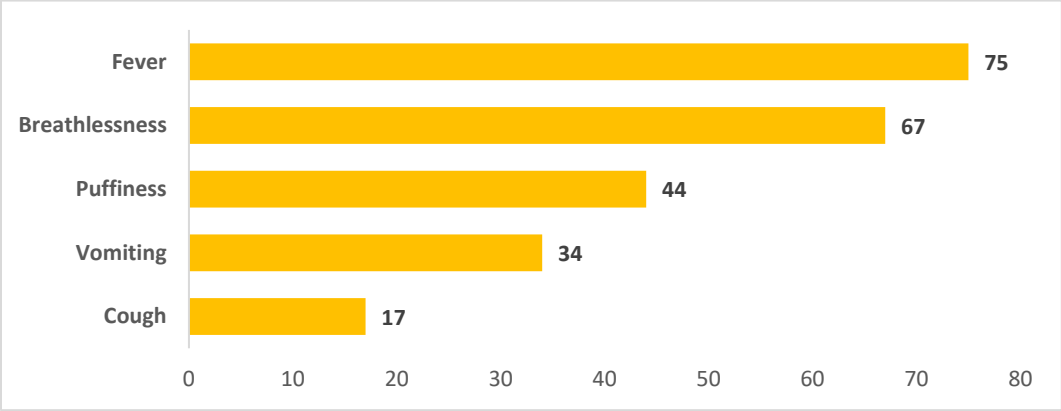

Fig. 1: The details of various Symptoms recorded in study group

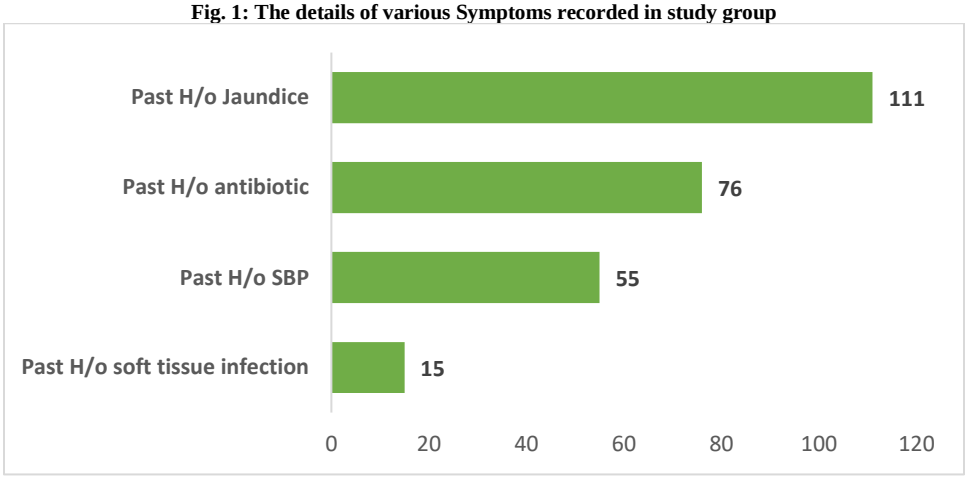

Fig.2: details of cases where significant past history was noted

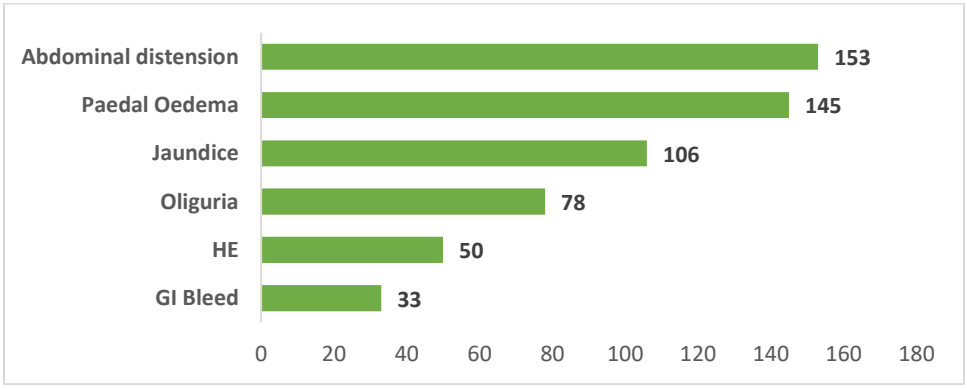

Fig. 3: The details of various Signs noted in the study group

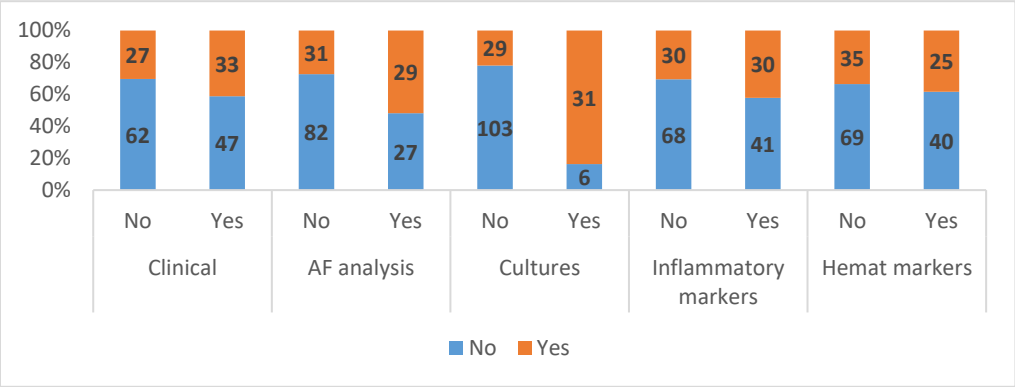

Figure 4 : Record of study group where up gradation of antibiotics were considered

Discussion

Bacterial infections are found to be one of the common causes of decompensation at presentation and are a leading cause of mortality in liver cirrhosis. Effective strategies for the diagnosis and management of infections in cirrhosis form a basic method in the treatment. The main problem with the diagnosis of infections in cirrhosis is that in cirrhotic SIRS is not fully active and negative cultures are seen in 30-50% of cirrhosis [1]. Serum biomarkers that are sensitive, reliable and inexpensive are being pursued in order to improve the diagnosis of bacterial infection in the setting of cirrhosis. General inflammatory markers, such as C-reactive protein (CRP, synthesized by the liver), ferritin (synthesized by the liver) or white blood cells (WBC), lack specificity for bacterial infections. Procalcitonin (PCT) is potentially a more specific marker for bacterial infection [1]. More information regarding the modulation of infections by the underlying immune state, gut barrier function and super-imposed medications such as β-blockers, proton pump inhibitors and antibiotics is still required. In the present study, out of 169 cases of cirrhosis is more common age group was 50-60 years with mean age 53.8 years. In this study males were found to be having cirrhosis predominantly with a ratio of 6: 1 (males to females). It is in keeping with reports by Rollenston et al 3:1 [3]. The Probable cause of preponderance of cirrhosis in males may be due to fact that alcoholism in very common in men than women. A higher prevalence of bacterial infection in alcoholic cirrhotic in comparison with nonalcoholic cirrhotic was also found in this study ($p < 0.05$) as per reports by Rosa et al [4]. However, the clinical evolution did not seem to have been influenced by the use of alcohol, given that there was no statistically significant difference in outcome between the two groups of patients. In this study, among the symptoms ascites153 (90.5), jaundice106 (62.7) and fever 75 (44.4) were the most common symptoms This value is consistent with that stated by Rimola et al.No patient of SBP was Asymptomatic in this study. This is also similar to 3.5% which is the percentage of patients of SBP who are asymptomatic quoted by Boixeda et al .The extent of infections in cirrhosis is not easily quantifiable because of many confounding factors. From the study by Runyon BA et al in 1988, it was found that almost 30–50% of infections, such as spontaneous bacterial peritonitis (SBP), can remain culture negative. Also a partial SIRS-like state is present in most patients with decompensated cirrhosis and so cannot be used to identify infections. Measuring C-reactive protein and procalcitonin may be helpful in selected patients, but a specific marker is still needed. A heightened suspicion of potentially resistant organisms is also required in order to change therapy as needed .In this study shows upgradation of antibiotics in considerations with clinical condition of patients, lab parameters and cultures will help in better outcome in patients. It is keeping with reports stated by Puneeta Tandan et al [5].

Conclusion

The most common infection in decompensated cirrhosis of liver was found was spontaneous bacterial peritonitis. The 30 days outcome of infection in DLF was 98.8% in this study. The common risk factor for infection in DLF was alcohol as etiology and development of SBP. The study concludes that infections are more common in alcohol related cirrhosis than others[5,6].

Recommendations of this study

This study reinforces the clinical decision of upgradation of antibiotics based on hematological and inflammatory parameters. The patients suffering from DLF during hospitalization show negative culture in body fluids and upgradation of antibiotics will help in better outcome of such patients.

Limitation

The limitation of this study is the less follow-up period of 30 days . A longer follow-up with 12 months' duration of study could have given more accurate results.

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