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Original Research Article

Assessment of INR to Albumin Ratio in Predicting Outcome during Hospital Stay in Patients with Cirrhosis of Liver with Sepsis

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Conflict of interest: Nil

Abstract

Background: Cirrhosis of liver with sepsis are at an increased risk of mortality. Our study aimed to estimate the international normalized ratio and albumin levels in patients of cirrhosis of liver with sepsis and to find out the association between PT-INR to Albumin Ratio (PTAR Score) on the day of admission with patients outcome during hospital stay.

Patients and methods: A total of 93 patients were entered into the study, and all the participants were followed up during hospital stay. Clinical parameters on the day of admission were included to compare survivors with nonsurvivors.

Results: The association between the risk of mortality during hospital stay and PTAR score remained statistically significant. The PTAR score showed good discrimination ability for predicting mortality during hospital stay. To improve its feasibility, we regrouped the PTAR scores into three levels of risk (low risk: <0.55, intermediate risk:0.55–1.00, and high risk: ≥1.00); the in-hospital mortality rates were 14.29% (4/28), 23.08% (9/39), and 76.93% (20/26), respectively.

Conclusion: The PTAR score system is a convenient and practical tool for predicting the prognosis of patients with cirrhosis of liver with sepsis.

Keywords: Cirrhosis of liver, Sepsis, International normalized ratio, Prothrombin time-international normalized ratio (PTAR) Score.

Introduction

Cirrhosis of Liver is a frequent consequence of the long clinical course of all chronic liver diseases, and it is characterized by tissue fibrosis and the transformation of normal liver architecture into structurally abnormal nodules.[1] Natural history of cirrhosis of liver is characterized by an asymptomatic phase known as 'compensated' cirrhosis,

which is followed by a rapidly progressive phase known as 'decompensated' cirrhosis, which is marked by the development of complications of portal hypertension and/or liver dysfunction.[2] Patients with compensated cirrhosis are not jaundiced and have not yet developed ascites, variceal bleeding, or hepatic encephalopathy.[2] Decompensated cirrhosis is defined by the presence of ascites, variceal bleeding, hepatic encephalopathy and/or jaundice.[3] Transition from a compensated to a decompensated stage occurs at a rate of 5-7% per year.[2] Patients with cirrhosis of liver progress over a period of time to end-stage liver disease (ESLD), liver failure, multiorgan failure, and death.[4, 5, 6] Cirrhosis is one of the leading causes of mortality and morbidity all over the world.[7] Around 2 million deaths worldwide per year are due to liver disease, with 1 million deaths due to the complications of cirrhosis and 1 million deaths due to viral hepatitis and hepatocellular carcinoma.[8] Cirrhosis of the liver is the 11th most common cause of death worldwide, whereas hepatocellular carcinoma is the 16th leading cause of death; together, they account for 3.5% of all deaths worldwide.[8]

The international normalised ratio (INR) derived from prothrombin time (PT) is used to assess bleeding risk and prognosis in cirrhosis, and to guide management of associated coagulation disturbances.[9] It represents a clinical tool to assess the effectiveness of vitamin-K antagonist therapy. However, it is often used in the acute setting to assess the degree of coagulopathy in patients with cirrhosis of liver or acute liver failure.[10] Serum albumin is the principal regulator of colloid osmotic pressure and plays a crucial role in maintaining homeostasis.[11] In hospitalised patients hypoalbuminemia is frequently observed and it can be associated with several diseases including cirrhosis of liver, sepsis, nephrotic syndrome and malnutrition.[12] Prothrombin time-internatinal normalized ratio (PT-INR) and Serum albumin level reflect the synthetic property of the liver.[13] PT-INR is included in the model for end- stage liver disease (MELD), Liver injury and failure evaluation (LiFe), and Chronic liver failure-sequential organ failure assessment (CLIF-SOFA) scores and as an important factor to predict the mortality risk of patients.[14]

Sepsis is defined as "life-threatening organ dysfunction due to a dysregulated host response to infection" by the Third International Consensus Definition Task Force.[15] The annual incidence of sepsis is estimated to be 300/100000 or 1/100 hospital admissions for any cause.[16] The incidence of sepsis in cirrhosis of liver is estimated to be at least 30–50% of hospital admissions.[17] In addition to the factors which predispose the general population to the development of sepsis, the severity of the underlying liver disease also makes patients with cirrhosis more susceptible to the development of sepsis.[6] Infections in cirrhosis of liver are mainly caused by bacteria, and are a common cause of death. Ascites, lungs, urinary tract, skin and soft tissue and blood are the most common sites of infection.[18,19] Escherichia coli, followed by Staphylococcus aureus, Enterococcus faecalis, Streptococcus pneumoniae, Pseudomonas aureginosa, and Staphylococcus epidermidis, are the most common microorganisms responsible for infection in patients with cirrhosis of the liver.[19] Patients with suspected infection can be predicted to have poor outcomes typical of sepsis, a new bedside clinical score is termed as quick Sequential Organ Failure Assessment Score (q SOFA) and it has a predictive value for sepsis. [15] Haruki et al. [20] created a novel, objective score named the prothrombin time-international normalized ratio (PT-INR) to Albumin Ratio (PTAR SCORE), to determine the liver functional reserves in patients with hepatocellular carcinoma after hepatic resection. They demonstrated that the PTAR SCORE performed well in predicting the short-and long-term outcomes in a retrospective study comprising 199 patients. Like the patients after hepatocellular carcinoma resection, cirrhosis patients also have disorders of liver function and diminished reserves. The PTAR SCORE can

be quickly calculated at the patients bedside using a simple formula, INR divided by Serum albumin. As PT-INR to Albumin Ratio is a good tool to assess in patients of cirrhosis of liver with sepsis and no such studies have been conducted in Assam till now. we, therefore, have planned to undertake a study on patients of cirrhosis of liver with sepsis and to assess PT-INR to albumin ratio and its prognostic value.

Objectives

The study was conducted with the aim to study the prognostic value of INR to albumin ratio amongst the study subjects and to find out the association between PT-INR to Albumin Ratio (PTAR Score) on the day of admission with patients outcome during hospital stay.

Methods

This is a hospital based observational study conducted in the department of medicine at Assam Medical College and Hospital, Dibrugarh. Data was collected from patients attended in the Department of medicine, Assam medical college and Hospital. The study was approved by the ethical committee of Assam Medical College and Hospital, Dibrugarh. We obtained a written informed consent from all study participants before enrolling them in the study.

Inclusion Criteria:

All patients of cirrhosis of liver with sepsis with age>12 years

Exclusion Criteria:

- Pregnancy
- Patients having malignancy
- Liver transplanted patients
- Patients with AIDS
- Cirrhosis patient not presented with sepsis.
- Patients who do not give an informed written consent.

A detailed clinical history, thorough general and systemic examination and required investigations are done. The data for the purpose of study was collected in a predesigned proforma. Laboratory parameters such as Hb, Total Count, Urea, Serum Creatinine, LFT and PT with INR, Blood culture, Serological diagnosis such as HbSAg, Anti HCV and PCR if required and Radiological diagnosis- Ultrasound Abdomen.

Diagnostic Criteria for Chronic Liver Disease:[21]

Although biopsy is the gold standard for diagnosing liver cirrhosis, it is not always necessary because clinical, laboratory, and radiological results may be sufficient to establish the diagnosis. **q SOFA score** was calculated for all the patients at the time of admission. The score consists of three components with 1 point to each component.

Component	Point
Respiratory Rate (≥22 breaths per minute)	1
Change in Mental Status (GCS <15)	1
Systolic Blood Pressure<100mmhg	1

A score of two or more points in patients with presumed infection defines sepsis. [22]

Statistical Analysis:

The data recorded on predesigned and pretested proforma was tabulated and master chart was prepared. For statistical analysis data were entered into a Microsoft excel sheet and then analysis by SPSS-20 and Epi Info software. Data has been summarized as mean and standard deviation for numeric variables and numbers and percentage for categorical variable. Chi-square test used to see if there is any association between categorical variables.

A p-value of less than 0.05 was considered as statistically significant at 95% confidence interval.

Results

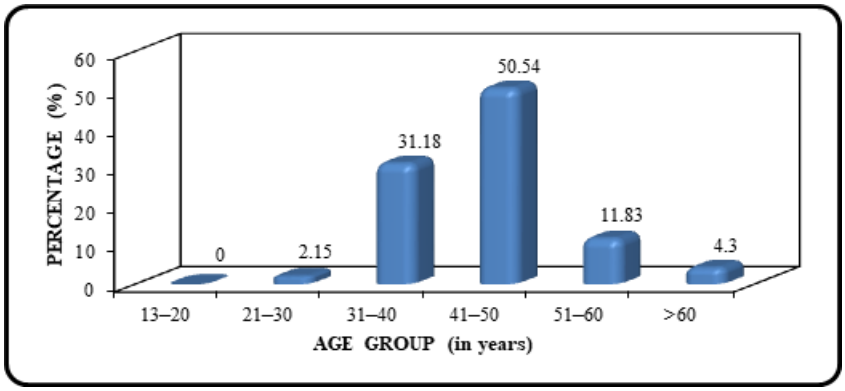

Figure1: Age wise distribution of patients with cirrhosis of liver with sepsis

The above graph shows distribution of the patients with Cirrhosis of liver with sepsis in various age group. Here, it can be seen that maximum patients (n=47) are in the age group of (41-50) which comprises of 50.54% of the patients studied followed by 29 patients are in the age group of (31-40) comprising 31.18%. There were no patients in age group (>12-20), whereas 4 patients are in age group (>60) which comprises of 4.30% and only 2 patient in age group (21-30) which comprises of 2.15%.

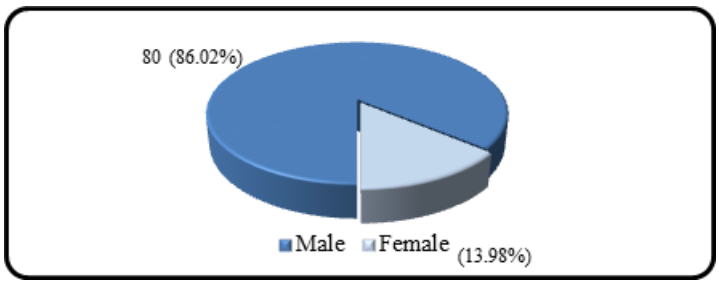

Figure 2: Gender wise distribution of patients with cirrhosis of liver with sepsis

From the above graph, it can be seen that there is male predominance in cirrhosis of liver with sepsis. Here male comprises 86.02 % (80 cases) whereas female 13.98% (13 cases).

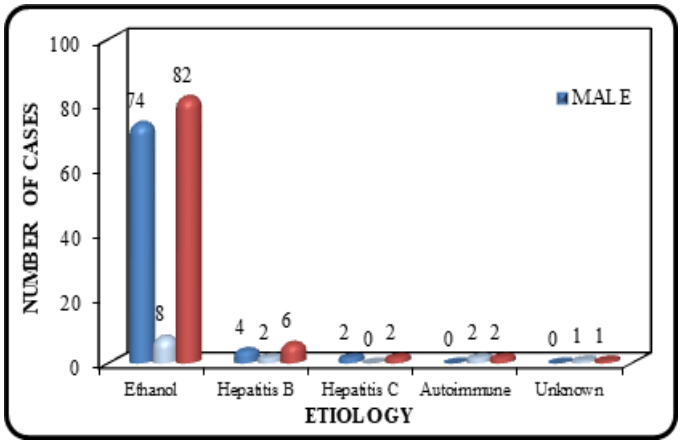

Figure 3: Etiology of cirrhosis of liver

Form the above graph, it can be seen that most common etiology of CLD in the study group was alcohol which comprised 82 (88.17%) patients of all cases, followed by Hepatitis B in 6 patients. Hepatitis C related CLD was present in 2 (2.15%) cases, auto immune related CLD was present in 2 (2.15%) cases, whereas no etiology could be elucidated in 1 patient (1.08%).

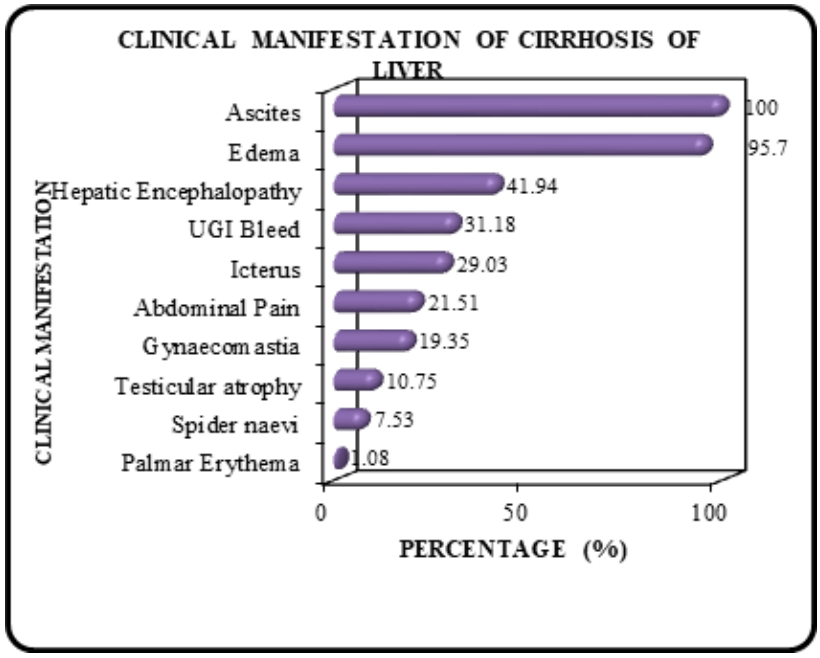

Figure 4: Clinical manifestations of cirrhosis of liver with sepsis

From the above graph, it can be seen that most common presentations of patients with cirrhosis of liver were Ascites 93 (100%) followed by edema 89 (95.70%), Hepatic encephalopathy 39 (41.94%), UGI Bleed 29 (31.18%), Icterus 27 (29.03%), Abdominal pain 20 (21.51%), Gynaecomastia 18 (19.35%), Testicular atrophy 10 (10.75%), Spider naevi 7 (7.53%), Palmar erythema 1 (1.08%).

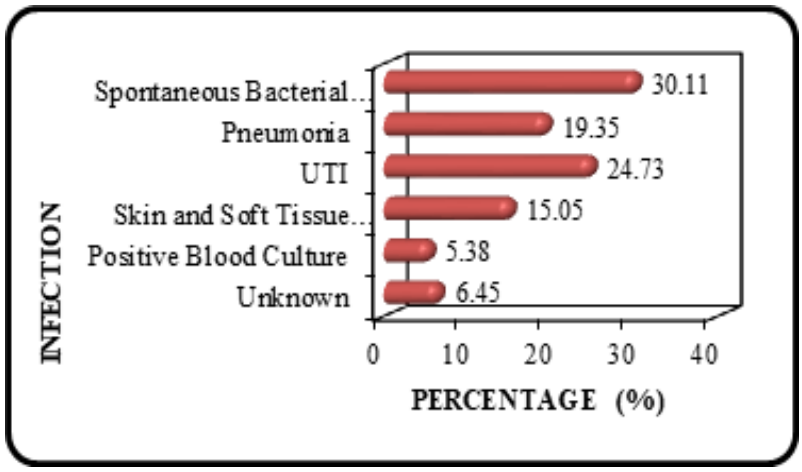

Figure5: Different bacterial infections in chirrhosis of liver

From the above graph, it can be seen that in patients with bacterial infections, 28 patients had SBP (30.11%), followed by UTI 23 (24.73%) and, 18 (19.35%) patients had pneumonia, 14 (15.05%) patients had skin and soft tissue infection, Septicemia with positive blood culture comprising of 5 (5.38%) cases. No cause could be found in 6 (6.45%) patients.

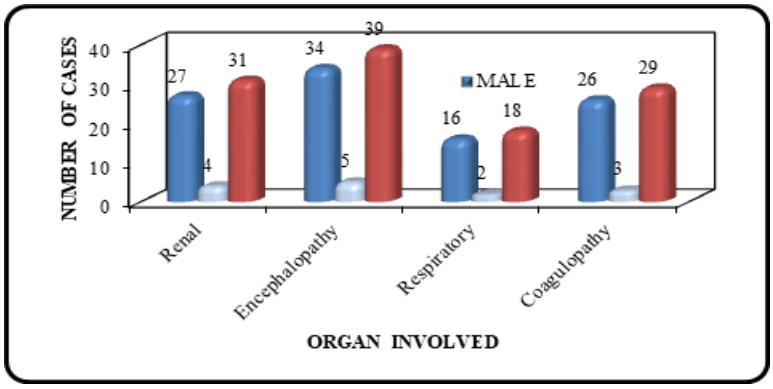

Figure 6: Organ involved in cirrhosis of liver with sepsis

From the above graph, it can be seen that 41.93% of cirrhosis of liver with sepsis patients developed encephalopathy, whereas 33.3% renal involvement as Hepatorenal syndrome and acute kidney injury. 18 (19.35%) patients had respiratory involvement in the form of Hepatopulmonary syndrome. 29 (31.18%) patients developed coagulopathy in the form of UGI Bleed.

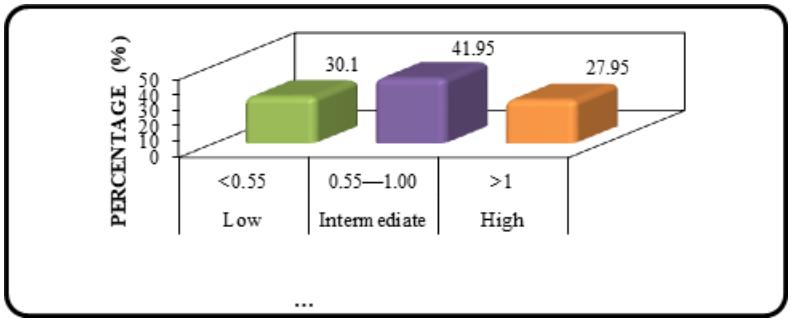

Figure 7: Percentage distribution of patients with cirrhosis of liver with sepsis in various PTAR score

The above graph shows no. of patients with cirrhosis of liver with sepsis with PTAR SCORE <0.55 (LOW RISK) were 28 (30.10%), and PTAR SCORE 0.55-1.00 (INTERMEDIATE RISK) were 39 (41.95%), PTAR SCORE >1 (HIGH RISK) was 26 (27.95%).

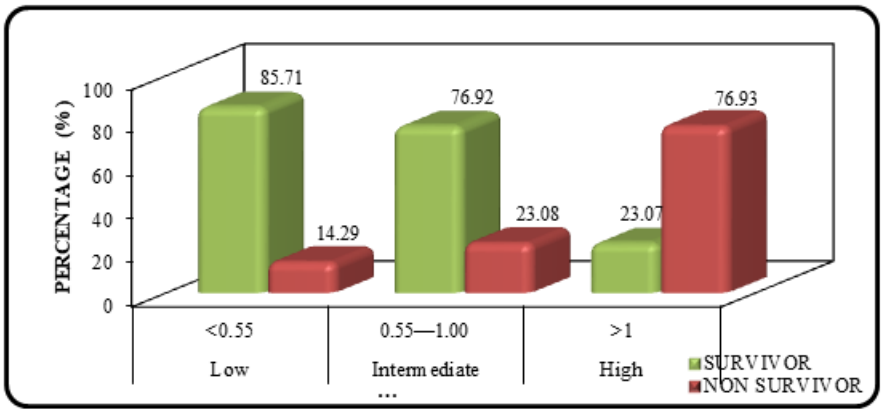

Table 8: Percentage distribution of survivor and non survivor in patients with cirrhosis of liver with sepsis in various PTAR score

The above graph shows number of patients discharged and number of patients succumbed to illness during an average hospital stay of 7-10 days. Discharged

patients were not followed up in the study. From the above graph, it can be seen that Out of 28 (30.10%) LOW RISK PATIENTS, 24 (85.71%) patients were survived and discharged from the hospital whereas 4 (14.29%) patients died during the hospital stay.

Out of 39 (41.95%) INTERMEDIATE RISK PATIENTS, 30 (76.92%) were survived and discharged from the hospital whereas 9 (23.08%) patients died during the hospital stay.

Out of 26 (27.95%) HIGH RISK PATIENTS, 6 (23.07%) were survived and discharged from the hospital whereas 20 (76.93%) patients died during the hospital stay.

Discussion

In our study, maximum patients were in the age group[41-50] comprising 47 patients (50.54%), followed by 29 patients (31.18%) in the age group of (31-40). Mean (±SD) age in this study group was 44.37±7.20. Similar findings were found in the studies conducted by Mishra et al.[23] and Kothari et al.[24] in India. In this study of total 93 patients, 80 cases were male accounting for 86.02%, whereas 13 cases were female comprising 13.98%. In our study shows that there is a male preponderance of Cirrhosis of liver cases, which is found similar to other studies conducted by Acharya et al.[25], Wang et al.[26]. In our study, most common etiology of Cirrhosis of liver was Alcohol which accounted for 82 cases (88.17%), followed by Hepatitis B in 6 cases (6.45%), Hepatitis C and autoimmune accounts for 2 cases each. Whereas cause couldn't be found in 1 patient (1.08%). Similar findings were found in the studies conducted by Mukherjee et al.[27], Sharma et al.[28]

In most parts of the world, hepatotropic viruses are the leading cause of end-stage liver disease.[29] In developed countries, as well as in some parts of India, alcohol is a major cause of end-stage liver disease.[30] There was significant interregional differences (hepatitis C in North, hepatitis B in East and South, alcohol in North-east, Non-alcoholic Fatty Liver Disease in West) in the predominant cause of chronic liver disease.[27] Alcohol related CLD is rare in the northern part of india[31], whereas Alcohol is the most common cause of cirrhosis of liver in north-eastern part of india.[32] Our study showed that alcohol was the major cause of cirrhosis of liver in this region. Alcohol-related cirrhosis is also a major concern among the tribal population in the north-eastern part of India. Alcohol use is increasing in Northeast India, which has a large tribal population with a long tradition of ritualistic drinking.[33] Alcohol dependence is also an independent risk factor for sepsis and associated mortality.[34]

In our study the most common presentations of patients with cirrhosis of liver were ascites 93 (100%) followed by Pedal edema 89 (95.70%), Hepatic encephalopathy 39 (41.94%), UGI Bleed 29 (31.18%), Icterus 27 (29.03%), Abdominal pain 20 (21.51%), Gynaecomastia 18 (19.35%), Testicular atrophy 10 (10.75%), Spider naevi 7 (7.53%), Palmar erythema 1 (1.08%). Similar findings were found in the studies conducted by Trimukhe et al.[35], Suthar et al.[36] Ascites is the one of the main complication of cirrhosis[37], and the mean time period to its development is approximately 10 years.[2] Ascites is a sign that cirrhosis is progressing into the decompensated phase and is associated with a poor prognosis and quality of life; mortality is estimated to be 50% in two years.[38] In our study ascites was the most common presentation, it indicates most of the patients presented in the decompensated phase of cirrhosis of liver.

In our study, it can be seen that in patients with bacterial infections in cirrhosis of liver, 28 (30.11%) patients had SBP, followed by UTI 23 (24.73) and, 18 (19.25%) patients had pneumonia, 14 (15.05%) patients had skin and soft tissue infection, Septicemia with positive blood culture comprising of 5 (5.38%) cases. No cause could be found in 6 (6.45%) patients. Similar findings were found in the studies conducted by Fernandez et al.[19], Borzio et al.[18] Regardless of the

cause, bacterial infection, is a serious complication of decompensated cirrhosis that, despite being often asymptomatic, leads to longer hospital stays and higher mortality rates.[18]

In our study, it can be seen that 41.93% of cirrhosis of liver with sepsis patients developed encephalopathy, whereas 33.3% had renal involvement as Hepatorenal syndrome and Acute kidney injury. 18 (19.35%) patients had respiratory involvement in the form of Hepatopulmonary syndrome. 29 (31.18%) patients developed Coagulopathy in the form of UGI Bleed. Similar findings were found in the studies conducted by Trimukhe et al.[35] Multiorgan failure in patients with cirrhosis of the liver necessitates a unique medical therapy because multiple organ dysfunction has a detrimental impact on the prognosis.[39]

In our study it can be seen that patients with cirrhosis of liver with sepsis with PTAR SCORE <0.55 (LOW RISK) were 28 (30.10%), and PTAR SCORE 0.55-1.00 (INTERMEDIATE RISK) were 39 (41.95%), PTAR SCORE >1 (HIGH RISK) was 26 (27.95%). Similar findings were found in the studies conducted by Gao et al.[14] In our study, it can be seen that, Out of 28 (30.10%) LOW RISK PATIENTS, 24 (85.71%) patients survived and discharged from the hospital whereas 4 (14.29%) patients died during the hospital stay. Out of 39 (41.95%) INTERMEDIATE RISK PATIENTS, 30 (76.92%) survived and discharged from the hospital whereas 9 (23.08%) patients died during the hospital stay. Out of 26 (27.95%) HIGH RISK PATIENTS, 6 (23.07%) survived and discharged from the hospital whereas 20 (76.93%) patients died during the hospital stay. PTAR was an independent and significant prognostic factor of poor prognosis. The higher the PTAR score, the worse the patient prognosis.

Conclusion

The prognostic value of INR to albumin ratio patients with cirrhosis of liver with sepsis is highlighted in this study. This study found that bacterial infections are more common in patients with cirrhosis of liver. Prevalence of alcohol as an etiology of cirrhosis has increased over the decade, especially in this part of the country, as average consumption of alcohol has increased, and the average age of consumption has decreased.

As prevalence of alcohol consumption continues to rise in this part of country thereby increasing the burden of alcohol induced cirrhosis of liver and death, especially in a productive age group, which is really an alarming situation.

Sepsis has one of the important causes of mortality in patients with cirrhosis of liver. SBP has the commonest source of sepsis in this study. Our study showed high mortality in patients presenting with cirrhosis of liver with sepsis, which warrants prompt recognition of this condition and q SOFA score can be useful bedside assessment tool.

PTAR score is an independent and significant prognostic factor of poor prognosis. This study found that higher the PTAR SORE, the worse the patient prognosis. This study was conducted in a single centre with some limitations, but it may still be considered as a curtain riser for a large multicentric study to draw a conclusive remark.

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