International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 02 Issue 11 November 2022

Page No: 1211-1215

DOI: https://doi.org/10.47191/ijmscrs/v2-i11-04, Impact Factor: 5.365

Spontaneous Bacterial Peritonitis in Alcohoolic Cirrhosis

Liri Cuko [1], Irgen Tafaj[2], Alma Idrizi [3], Eva Shagla[4], Arlinda Hysenj[5], Ledi Mullaj[6]

[1]Department of Clinical Semiolgy and Imaging

[2,4,5,6]Department of Gastro-Hepatology

[3]Department of Nefrology and Dialysis

ABSTRACT

Background: Spontaneous bacterial peritonitis (SBP) is one of the most common complications in cirrhosis with ascites, which is associated with a high mortality. Various studies have shown that the prevalence of PBS ranges from 20-30% in patients with cirrhosis and ascites. Not in all cases it is accompanied by obvious symptoms, which makes early diagnosis difficult.

Aim: The aims of this study were to assess the prevalence and the risk factors of PBS in alcoholic liver cirrhosis.

Methodology: This is a retrospective study, which considers all cases diagnosed with PBS admitted to our hospital during 2018-2021. Diagnosis is based on the European Association for the Study of Liver (EASL) guidelines. The patients were divided into two groups, alcohoolic cirrhosis with PBS, and without PBS. Data collection consists of filling out a standard form for each patient,which contained information about the diagnosis, the degree of liver function damage evaluated by Child-Pough score and MELD score, clinical and laboratory indicators and complications associated with cirrhosis with PBS, ascitic fluid analyses. All categorical variables were analised by using SPSS version 25, and t-test were used for continuous date.

Results: The average age of the patients included in the study was 54.15 ± 12.5 years, while according to gender, there were 112 males (97.3%) and 3 females (2.7%). According to the evaluation of MELD, it was seen to be higher in the group with PBS than those without PBS ($p < 0.05$). The most frequent complications accompanying PBS were Encephalopathy ($p < 0.004$), hepatorenal syndrome ($p< 0.004$), gastro\intestinal hemorrhage ($p < 0.004$). From laboratory data, platelets ($p < 0.015$), creatinine ($p < 0.006$), bilirubin ($p < 0.002$), INR ($p < 0.049$) and prothrombin level ($p < 0.002$) were seen as predictive factors.

Conclusions: The most probable predictive factors in the case of PBS in alcoholic cirrhosis were found the low level of platelets, prolonged level of INR and prothrombin, increased level of creatinine. While the most frequent associated complications were hepatic encephalopathy, HRS, G\I hemorrhage, jaundice.

ARTICLE DETAILS

Published On:
09 November 2022

Available on:
https://ijmscr.org/

KEYWORDS: Cirrhosis, PBS, complications, predict

INTRODUCTION

Spontaneous Bacterial Peritonitis (PBS) is defined as the infection of ascitic fluid in patients with decompensated liver cirrhosis with ascites from various bacteria, without previous intra-abdominal surgical history (1,2). The course of decompensated cirrhosis can be aggravated by the development of some other complications such as: a) bacterial infections, especially ascitic fluid infection "spontaneous bacterial peritonitis" (PBS) as well as other bacterial infections, b) gastrointestinal hemorrhage (GI) c) renal involvement, such as acute kidney injury (AKI) with or without features of hepatorenal syndrome (HRS), d) cardio-pulmonary effects such as cardiomyopathy, portopulmonary hypertension (PPHT), hepatopulmonary syndrome (HPS), e) pleural fluid accumulation (1 ,3,4). It is known that cirrhosis is the main cause of ascites in up to 80% of cases. Initially, ascites is "uncomplicated", that is, it responds well to treatment with diuretics and is not infected. But with the

advancement of cirrhosis and the change of physio pathological mechanisms, ascites does not respond equally to medication, and we are dealing with "refractory ascites". Further, as a result of the change in the intestinal microbiota due to dysbiosis, bacteria can infect the ascitic fluid, an entity known as Spontaneous Bacterial Peritonitis that occurs mostly in hospital conditions with aggravated liver pathology (4). During or after an episode of spontaneous bacterial peritonitis, patients often present with signs of decompensation such as the development or progressive worsening of ascites or hepatic encephalopathy, gastrointestinal bleeding, and other organ compromise such as acute kidney injury (AKI), with or without hepatorenal syndrome (HRS) (4,5). In fact, the most frequent cause of death in patients with PBS is the development of acute hepatic failure over a chronic injury characterized by a high mortality rate as a result of multiorgan failure (5,6). In daily practice, the diagnosis of PBS and other infections can be complicated by the fact that typical signs and symptoms such as temperature and leukocytosis are often absent in cirrhotic patients, and the liquid culture in most cases up to 60% results negative. However, early suspicion is very important for the diagnosis and treatment of PBS without delay in order to achieve the best possible treatment results, since being treated and continuing antibiotic prophylaxis has reduced the mortality rate by up to 20% per year after the first episode of PBS (7,8,9,11).All patients with cirrhosis and ascites are at risk of developing PBS, and it has been seen that the prevalence of PBS in outpatients ranges from 1.5-3.5%, while in hospitalized patients up to 10% of cases. PBS in some patients could be present from the beginning of admission to the hospital, while other patients are discovered during the staying in the hospital (3,4,10,12).

METHODS

This is a retrospective study to all patients diagnosed with PBS in our hospital during 2018-2021 at Service of Gastro-Hepatology, University Hospital Center “Mother Teresa” Tirana, Albania. In this study, are included 115 patients diagnosed with decompensated alcoholic cirrhosis, divided into two groups, 83 cases with PBS and 32 cases without PBS. Diagnosis is based on the European Association for the Study of Liver (EASL) guidelines. All patients included in this study were over 18 years old. Data collection consists of filling out a standard form for each patient,which contained information about the diagnosis, the degree of liver function damage evaluated by Child-Pough score and MELD score (Model End Stage Liver Disease), clinical and laboratory indicators and complications associated with cirrhosis with PBS, ascitic fluid analyses. All categorical variables were analised by using SPSS version, and t-test were used for continuous date. Patients with secondary bacterial peritonitis, viral cirrhosis B, C or cirrhosis with hepatocarcinoma (HCC) were not included in the study.

For statistical analysis, use the package **SPSS** ((Statistical Package for Social Sciences, version 25). For all the data, the mean ± standard deviation (SD) was calculated. In all cases, P values ≤ 0.05 were considered statistically significant (negligible).

RESULTS

The average age of the 115 participants in the study was 54.15 ± 12.5 years, 112 males (97.3%) and 3 females (2.7%). According to the distribution according to the age group in years, it was observed that the largest number of alcohoolic cirrhosis with PBS was after the age of 40 (44.6%). Regarding the amount and time of alcohol use (fig. 1), 111 cases (96.5%) had used alcohol > 200 ml per day, > 10 years, while only 5 cases (4.3%) < 200 ml per day < 10 years.

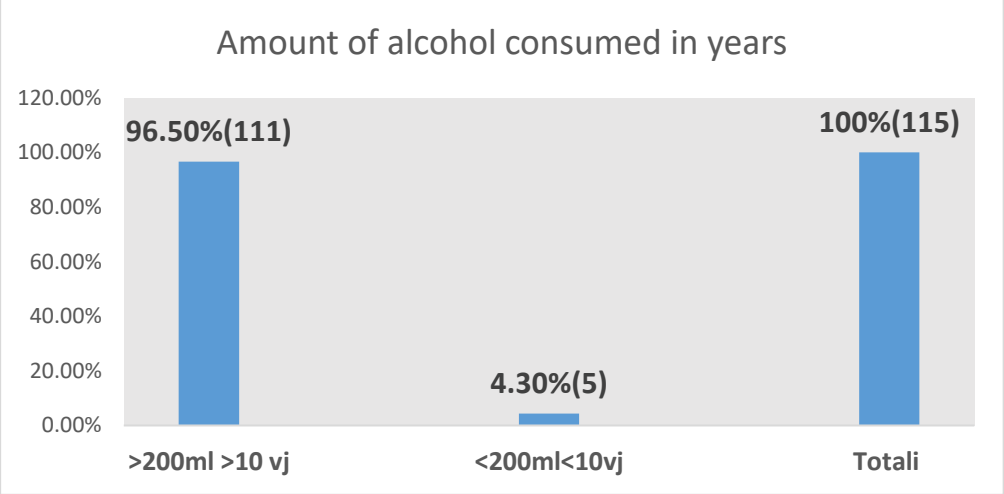

Fig. 1. Data regarding the amount and time in years of alcohol use in alcoholic cirrhosis with PBS and without PBS

MELD-score in patients with PBS and those without PBS were (19 ± 3.2, 16 ± 2.86, $p < 0.05$), and most of patients with were > 19 score (fig.2)

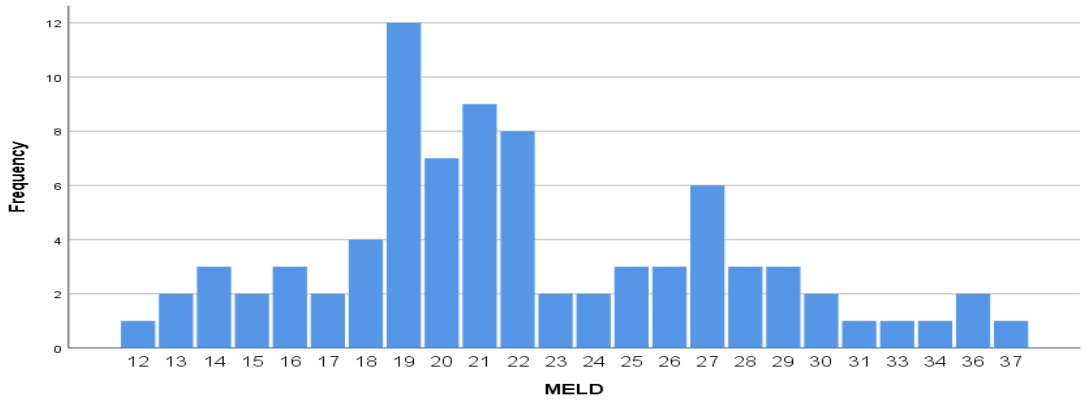

Fig 2. Alcoholic cirrhosis according to MELD-score

There was no significant difference between the two groups with PBS and without PBS (54.12 ± 9.6, vs 53.78 ± 11.3, p = 0.8). The most frequent in the group with PBS were EH (40.9% vs 15.6%, p < 0.04), HRS (27.7% vs 12.5%, p < 0.004), hemorrhage g/i (34.3% vs 10.8%, p < 0.04) jaundice (93.9% vs 78.1%, p < 0.002) (fig .3).

Table 1. Evaluation of demographic data and complications in patients with PBS and without PBS

Data	With PBS	Without PBS	p
Age (mean ± SD)	54.12 ± 9.6	53.78 ± 11.3	0.872
Jaundice (%)	93.9%	78.1%	**0.002**
Fever (%)	40.6%	31.75%	0.701
Hemorrhage (%)	34.3%	10.8%	**0.004**
Encephalopathy (%)	40.96%	15.625%	**0.004**
HRS (%)	27.7%	12.5%	**0.004**

P < 0.05 for comparison between two groups

Laboratory data in the group with PBS and without PBS (table 2), it was observed that INR had a significant difference in patients with PBS than those without PBS (2.02 ± 0.58 vs 1.7 ± 0.6, p < 0.049). Also, patients with PBS had a lower level of platelets compared to those without PBS (137 ± 81 vs 142 ± 94 mm ^{3}, p < 0.015), serum creatinine level was higher in the group with PBS (1.3 ± 0.8 vs 0.9 ± 0.4, p < 0.006). Significant difference between the group with PBS and without PBS was also seen in the level of prothrombin (39 ± 12, vs 48.3 ± 18.5, p 0.002).

Table 2. Biochemical data in patients with PBS and without PBS, in alcoholic cirrhosis.

Characteristics	With PBS	Without PBS	p
Leukocytes (mean ± SD)	9154.22 ± 5985.599	6371.25 ± 3750.25	0.016
Platelets (mean ± SD)	137698 ± 816123.54	142156.25 ± 94054.586	**0.015**
Hemoglobin (mean ± SD)	10.481 ± 2.0869	10.713 ± 2.0517	0.593
Creatinine (mean ± SD)	1.370 ± 0.8172	0.945 ± 0.4288	**0.006**
AST (mean ± SD)	85.78 ± 64.845	86.63 ± 41.166	0.950
ALT (mean ± SD)	73.46 ± 52.988	71.93 ± 33.304	0.192
Ascites albumin (mean ±SD)	0.676 ± 0.4695	0.706 ± 0.4250	0.750
INR (mean ± SD)	2.0227 ± 0.58033	1.7784 ± 0.60952	**0.049**
Prothrombin (mean±SD)	39.0622 ± 12.09659	48.3406 ± 18.50348	**0.002**
Natremia (mean ± SD)	129.98 ± 5.310	130.69 ± 5.146	0.517

The culture of the liquid, which was carried out only in 40 cases with PBS, and only 8 patients (25%) resulted in a positive culture, 6 patients with E.Coli and 2 patients with staphylococcus aureus.

DISCUSSION

Spontaneous bacterial peritonitis is one of the most frequent complications of cirrhosis, regardless of its nature, and has a high mortality rate if diagnosis and treatment are not in time. Most of the patients taken in the study were men 80 (96.4%), women 3 (3.6%), where it is known that men drink more alcohol in our Country. Age according to the distribution in years, most were over 40 years old, this is explained by the fact that before cirrhosis develops, it goes through several stages of disease, steatosis of the liver, alcoholic hepatitis which is associated with signs of necroinflammation of the

liver, and finally cirrhosis (14). The main age of presentation of cirrhosis is 40-50 years old, and this happens when they systematically consume 30-40 grams of alcohol a day in a systematic manner (15,16). The mean age of our patients was 54.12 ± 11.3, and most of them were > 40 years old. Most of the cases had jaundice (93%), encephalopathy (40%), upper gastrointestinal bleeding (34%), fever (40%), HRS (27.7%). The data of the study are similar to those of Sort et al, which demonstrates that renal function impairment occurs in about 30-40% of patients with PBS and is considered a predictive factor of deaths in PBS (17). In this study, abdominal pain was encountered in 48.2%, bloating in 69.9%, similar to other studies (18). The classification according to MELD score in this study resulted > 19 points in the majority of patients with PBS, which was slightly higher than the group without PBS (20). The level of bilirubin, serum albumin, and transaminases did not have any significant changes in our study, which is similar to other authors (21,22). In our study, it was seen that the group of patients with PBS had lower number of platelets ($p < 0.015$), higher creatinine level ($p < 0.006$), prolonged level of INR ($p < 0.049$), lower prothrombin level (0.002). The level of albumin in ascites did not have any significant difference between the group with PBS and without PBS, but when albumin in low levels in ascites is a known risk factor for PBS (<1.5 g), especially when associated with any of the following characteristics Child-Pough score > 9, bilirubin level > 3 mg/dl, creatinine 1.2 mg/dl, uremia > 25 mg/dl, or hyponatremia (23,24). A study by Filik et al from the analysis of all factors in patients with chronic liver diseases such as fatigue, hepatitis, encephalopathy, leukocytosis, impairment of renal function (creatinemia >2 mg/dl), coagulopathy (PTI >2.5 INR) and the level of decreased protein levels (< 1 mg/dl) were statistically associated with poor prognosis ($p< 0.005$) (18). The liquid culture was positive only in 8 patients out of 40 who had it done, where E.coli dominated (75%). Piroth et al. (25) in a retrospective study conducted in France in five different hospitals during the year 2006-2007 in 114 cases observed that the most frequent pathogens were Staphylococcus and E.Coli. While in a study by Ardolino et al. (26) conducted in the United States of America during 2005-2015 in 160 cases with PBS, it was seen that the main cause was E.Coli. In this case, it was seen that the sensitivity to the treatment with ceftriaxone was about 71%, which shows a very good result. While gram-positives in this study such as Enterococci, Streptococci and Staphylococci were found in up to 37.5% of cases. In conclusion, we can say that associated complications such as HRS, upper gastrointestinal bleeding, encephalopathy and intrahepatic cholestasis were more frequent in the group with PBS. As a result of this study, we can say that patients with alcoholic cirrhosis and PBS, who have a reduced number of platelets, increased creatinine levels, prolongation of the INR time, are more predisposed to suffer from PBS, especially when they are associated with levels of decrease in serum albumin. The MELD score was higher in the PBS group, but is considered indepedent factor. It is very important to emphasize the fact that early diagnosis and treatment, even in cases where they are asymptomatic, will lead to an increase in the quality and survival of patients.

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