

## ORIGINAL

# Spontaneous Bacterial Peritonitis in Decompensated Liver Cirrhosis. A Retrospective Study

*Peritonitis bacteriana espontánea en la cirrosis hepática descompensada.  
Un estudio retrospectivo.*

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## Abstract

**Background:** Spontaneous bacterial peritonitis (SBP) is a frequent and severe complication in patients with liver cirrhosis, which is associated with high mortality. Various studies have shown that the prevalence of SBP varies from 20-40% 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 determine several clinical and laboratory features and risk factors in bacterial spontan peritonitis.

**Methodology:** In this study, are included 137 patients diagnosed with decompensated cirrhosis, divided into three groups 83 cases with SBP and alcoholic cirrhosis, 22 cases with SBP and viral cirrhosis, and 32 cases with cirrhosis without SBP. All patients included in this study were over 18 years old. This is a retrospective study, where are analyzed clinical and laboratory characteristics of patients with SPB and liver cirrhosis, admitted to the Service of Gastro-Hepatology, University Hospital Center, Tirana, Albania during 2018-2022. Diagnosis of SBP is based on the European Association for the Study of Liver (EASL) guidelines. The degree of liver function damage is evaluated by the Child-Pough score and MELD score, clinical and laboratory indicators, and complications associated with cirrhosis with PBS, and ascitic fluid analyses. All categorical variables were analyzed by using SPSS version 25, and t-tests were used for continuous data.

**Results:** The average age of the 137 participants in the study was  $54.15 \pm 12.5$  years, 132 males (96.4%) and 5 females (3.6%), where 105 patients were with SBP. According to the evaluation of MELD, it was seen to be higher in the group with PBS than those without PBS ( $p < 0.05$ ). From the laboratory data, in this study seen the level of platelets ( $p < 0.015$ ), serum creatinine level ( $p < 0.001$ ), serum bilirubin level ( $p < 0.002$ ), INR ( $p < 0.049$ ), and prothrombin level ( $p < 0.002$ ) were seen as predictive factors. The most frequent complications accompanying SBP were Encephalopathy ( $p < 0.004$ ), hepatorenal syndrome ( $p < 0.002$ ), and gastrointestinal hemorrhage ( $p < 0.002$ ).

**Conclusions:** The most probable predictive factors in the case of PBS in liver decompensated cirrhosis were found the low level of platelets, prolonged levels of INR and prothrombin, increased levels of creatinine, increased levels of bilirubin, and low ascetic protein. While the most frequent associated complications were hepatic encephalopathy, HRS, GI hemorrhage, and jaundice.

**Keywords:** SBP, cirrhosis, complications, predictive, alcohol.

## Resumen

**Antecedentes:** La peritonitis bacteriana espontánea (PBE) es una complicación frecuente y grave en pacientes con cirrosis hepática, que se asocia a una elevada mortalidad. Diversos estudios han demostrado que la prevalencia de la PBE oscila entre el 20-40% en pacientes con cirrosis y ascitis. No en todos los casos se acompaña de síntomas evidentes, lo que dificulta el diagnóstico precoz.

**Objetivo:** Los objetivos de este estudio fueron determinar diversas características clínicas y de laboratorio y factores de riesgo en la peritonitis espontánea bacteriana.

**Metodología:** En este estudio, se incluyen 137 pacientes diagnosticados de cirrosis descompensada, divididos en tres grupos 83 casos con PAS y cirrosis alcohólica, 22 casos con PAS y cirrosis vírica, y 32 casos con cirrosis sin PAS. Todos los pacientes incluidos en este estudio tenían más de 18 años. Se trata de un estudio retrospectivo, donde se analizan las características clínicas y de laboratorio de los pacientes con SBP y cirrosis hepática, ingresados en el Servicio de Gastro-Hepatología, Centro Hospitalario Universitario, Tirana, Albania durante 2018-2022. El diagnóstico de SPB se basa en las directrices de la Asociación Europea para el Estudio del Hígado (EASL). El grado de daño de la función hepática se evalúa mediante la puntuación Child-Pough y la puntuación MELD, indicadores clínicos y de laboratorio, y complicaciones asociadas a la cirrosis con PBS, y análisis de líquido ascítico. Todas las variables categóricas se analizaron mediante el programa SPSS versión 25, y para los datos continuos se utilizaron pruebas t.

**Resultados:** La edad media de los 137 participantes en el estudio fue de 54,15±12,5 años, 132 varones (96,4%) y 5 mujeres (3,6%), donde 105 pacientes presentaban PBE. Según la evaluación del MELD, se observó que era mayor en el grupo con SBP que en los que no tenían SBP ( $p<0,05$ ). De los datos de laboratorio, en este estudio se observaron como factores predictivos el nivel de plaquetas ( $p<0,015$ ), el nivel de creatinina sérica ( $p<0,001$ ), el nivel de bilirrubina sérica ( $p<0,002$ ), el INR ( $p<0,049$ ) y el nivel de protrombina ( $p<0,002$ ). Las complicaciones más frecuentes que acompañaron al SBP fueron la encefalopatía ( $p<0,004$ ), el síndrome hepatorenal ( $p<0,002$ ) y la hemorragia gastrointestinal ( $p<0,002$ ).

**Conclusiones:** Los factores predictivos más probables en el caso de TBP en la cirrosis hepática descompensada se encontraron el bajo nivel de plaquetas, los niveles prolongados de INR y protrombina, el aumento de los niveles de creatinina, el aumento de los niveles de bilirrubina y la baja proteína ascítica. Mientras que las complicaciones asociadas más frecuentes fueron la encefalopatía hepática, el SHR, la hemorragia GI y la ictericia.

**Palabras clave:** PAS, cirrosis, complicaciones, predictivo, alcohol.

## Introduction

Spontaneous Bacterial Peritonitis (SBP) 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<sup>1,2</sup>. SBP is one the most common and important complications in cirrhotic patients with ascites because of significant morbidity and mortality<sup>3,4</sup>. The reason of SBP in liver cirrhosis is multifactorial and is associated with a defective immune system, gut dysmotility, alterations in microbiome, increased intestinal permeability, and bacterial translocation<sup>5,6</sup>. 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 (HE), gastrointestinal bleeding (GI), and another organ compromise such as acute kidney injury (AKI), with or without hepatorenal syndrome (HRS)<sup>7,8</sup>. 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<sup>9,10</sup>. 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 SBP<sup>11,12,13,14</sup>. All patients with cirrhosis and ascites are at risk of developing PBS, and it has been seen that the prevalence of PBS in outpatient's 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<sup>5,14</sup>. Risk factors associated with SBP development include ascitic fluid total protein less than 1gr\dl, total serum bilirubin greater than 2.5 mg\dl, variceal hemorrhage and a previous episode of SBP<sup>7,15</sup>. Therefore, we conducted a retrospective study in cirrhotic patients with ascites fulfilling the diagnosis of SBP. Our aim was to study the epidemiological, clinical, laboratory and risk factors in SBP.

## Patients and methods

This is a retrospective study to all patients diagnosed with PBS in our hospital during 2018-2022 at Service of Gastro-Hepatology, University Hospital Center "Mother Teresa" Tirana, Albania. In this study, are included 137 patients diagnosed with decompensated cirrhosis, divided in three groups 83 cases with SBP and alcoholic cirrhosis, 22 cases with SBP and viral cirrhosis and 32

cases with cirrhosis without SBP. All patients included in this study were over 18 years old. Data recorded included patient demographics, clinical information including presenting symptoms, medical comorbidities, cirrhosis etiology, time from decompensation to SBP development, gastrointestinal bleeding and MELD score, laboratory work-up (ascitic fluid neutrophils, albumin and culture, serum creatinine, albumin). Detailed data on chronic administration of b-blockers, proton pump inhibitors (PPIs) and antibiotic prophylaxis for SBP were also recorded. On admission, all patients are analyzed for biochemical evaluation, liver imaging (ultrasound or computed tomography) to exclude malignancy or other source of infection. SBP was diagnosed as an infection of ascetic fluid without any intra-abdominal surgically treatable source of infection, and was based on a neutrophil count >250/mm<sup>3</sup> in ascetic fluid, as determined by microscopy or positive culture of the ascetic fluid according to the guidelines of the European Association for the Study of the Liver (EASL)<sup>1</sup>.

For statistical analysis, use the package SPSS (Statistical Package for Social Sciences, version 25) and t-test were used for continuous date. For all the data, the mean ± standard deviation (SD) was calculated. P values ≤ 0.05 were considered statistically significant (negligible).

## Results

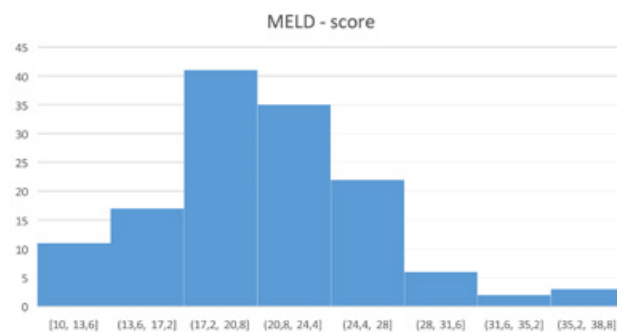
The average age of the 137 participants in the study was 54.15±12.5 years, 132 males (96.4%) and 5 females (3.6%), where 105 patients were with SBP. According to the distribution according to the age group in years, it was observed that the largest number of patients with decompensated cirrhosis was after the age of 40 (44.6%). The leading etiology of cirrhosis was alcohol-related 115 (80.5%), followed by viral 22 (16%). Most of cases were first episode of SBP, only 13 cases were another episode. Before the first episode 92 (80%) cases were on PPI treatment (Table I). Most of patients were Child-Pough C (66.4%).

The most of patients were MELD-score > 19 (Figure 1).

Table I: Baseline characteristics (n 137).

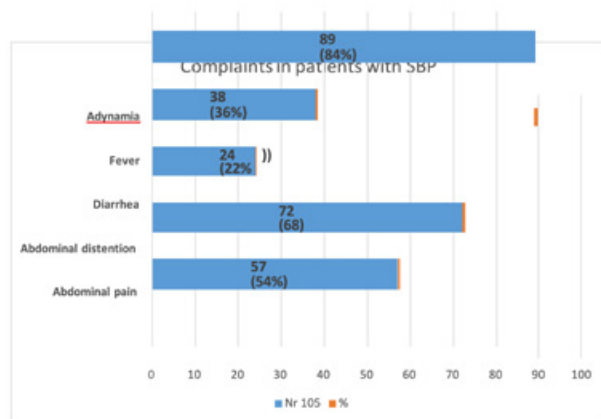
Caracteristics	N 137 (%)	
Age (years)	54.15 ± 12.5 years	
Gender	Male	132 (96.4%)
Etiology of cirrhosis	Alcohol	115 (80.5%),
	Viral hepatitis	22 (16%).
PPI	With SBP	90 (85%)
First episode of SBP	92 (87%)	
MELD score	With SBP	19 ± 9.2
	Without SBP	16 ± 4.86
Child-Pough score	A	9 (6.6%)
	B	37(27%)
	C	91 (66.4%)

Figure 1: Cirrhosis according to MELD-score.



In this study it was seen that the main complaint was adynamic (84%), abdominal distention 68%, and diffuse abdominal pain 54% (48.2%) and fever 36%.

Figure 2: Complaints in patients with SBP at the first moment of admitted to the hospital.



There was no significant difference between the two groups with SBP and without SBP about the age (55.12±9.7, vs 54.68±12.1, p=0.8). The most frequent in the group with SBP were EH (41.9% vs 16.6%, p < 0.04), HRS (29% vs 13.1%, p < 0.002), hemorrhage g/i (37.3% vs 11.6%, p<0.002) jaundice (92.8% vs 77%, p<0.002) (Table II).

Table II: Evaluation of complications in patients with SBP.

Data	With SBP	Without SBP	p
Age (mean ± SD)	55.12 ± 9.7	54.68 ± 12.1	0.872
Jaundice (%)	92.8 %	77 %	<b>0.002</b>
Fever (%)	36%	29.74%	0.701
Hemorrhage (%)	37.3%	11.6%	<b>0.002</b>
Encephalopathy (%)	41.96%	16.6%	<b>0.004</b>
HRS (%)	29 %	13.1%	<b>0.002</b>

P<0.05 for comparison between two groups.

Laboratory data in the group with SBP and without SBP (Table III), it was observed that INR had a significant difference in patients with SBP (p<0.049). Also, patients with SBP had a lower level of platelets compared to those without SBP (p<0.015), serum creatinine level was higher in the group with SBP (p<0.001). Significant difference between the group with PBS and without PBS

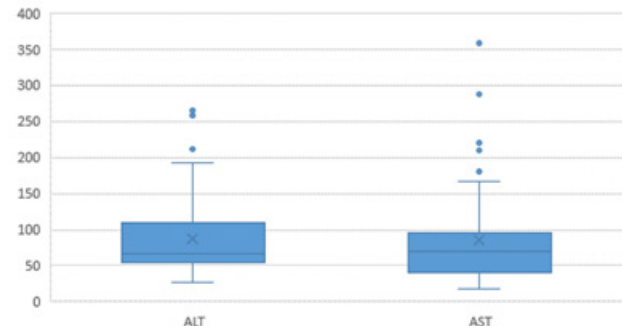
was also seen in the level of prothrombin ( $p < 0.002$ ). No significant difference was seen on level of ascitic albumin in both groups.

Comparison of SBP in cirrhosis of two groups, with alcoholic and viral etiology are seen no significant changes in relation to age, MELD-score, and other complications such as EH, HRS, and GI hemorrhage and laboratory data, except transaminases (Table IV). Regarding the laboratory data in the SBP of the two groups, in alcoholic cirrhosis the AST level was higher than ALT level ( $89.7 \pm 64$  vs  $64 \pm 52$  U/L).

Regarding the laboratory data in the SBP of the two groups, in alcoholic cirrhosis the AST level was higher than ALT level ( $89.7 \pm 64$  vs  $64 \pm 52$  U/L) (Figure 3).

The culture of the liquid, which was carried out only in 45 cases with SBP, and only 10 patients (22%) resulted in a positive culture, 7 patients with *E. coli* and 3 patients with *staphylococcus aureus*.

**Figure 3:** Level of transaminases ALT and AST in patients with SBP in two groups of cirrhosis (alcoholic and viral).



**Table III:** Biochemical data in patients with SBP.

Variable	With PBS	Without PBS	p
Leukocytes (mean $\pm$ SD)	6054.22 $\pm$ 2985.59	4371.25 $\pm$ 1750	0.316
Platelets (mean $\pm$ SD)	127698 $\pm$ 6161.54	14215.25 $\pm$ 94054.58	0.015
Hemoglobin (mean $\pm$ SD)	10.471 $\pm$ 2.076	10.613 $\pm$ 2.041	0.691
Creatinine (mean $\pm$ SD)	1.470 $\pm$ 0.918	0.745 $\pm$ 0.427	0.001
AST (mean $\pm$ SD)	86.78 $\pm$ 64.84	66.63 $\pm$ 41.175	0.950
ALT (mean $\pm$ SD)	73.45 $\pm$ 62.98	71.93 $\pm$ 23.302	0.192
Ascites albumin (mean $\pm$ SD)	0.76 $\pm$ 0.46	0.706 $\pm$ 0.524	0.750
INR (mean $\pm$ SD)	2.0216 $\pm$ 0.67	1.7784 $\pm$ 0.609	0.049
Prothrombin (mean $\pm$ SD)	38.056 $\pm$ 11.08	47.3506 $\pm$ 19.503	0.002
Natremia (mean $\pm$ SD)	128.97 $\pm$ 6.210	130.68 $\pm$ 4.145	0.515

**Table IV:** Comparison between alcoholic cirrhosis with SBP and viral cirrhosis with SBP.

Variable	Alcoholic with SBP	Viral with SBP	p
Leukocyte (mean $\pm$ SD)	9154.22 $\pm$ 5985.599	6295.45 $\pm$ 4315.020	0.034
Thrombocyte (mean $\pm$ SD)	157698.80 $\pm$ 50612.54	100909.09 $\pm$ 49097.482	0.103
Hemoglobin (mean $\pm$ SD)	10.481 $\pm$ 2.086	10.80 $\pm$ 2.082	0.525
Creatinine (mean $\pm$ SD)	1.370 $\pm$ 0.8172	1.066 $\pm$ 0.5431	0.103
AST (mean $\pm$ SD)	89.78 $\pm$ 64.845	50.37 $\pm$ 35.253	0.025
ALT (mean $\pm$ SD)	73.46 $\pm$ 52.988	75.67 $\pm$ 18.475	0.103
Albumin ascites (mean $\pm$ SD)	0.676 $\pm$ 0.4695	0.532 $\pm$ 0.3908	0.190
INR (mean $\pm$ SD)	2.0227 $\pm$ 0.8033	2.0314 $\pm$ 0.43023	0.948
Prothrombin (mean $\pm$ SD)	39.0622 $\pm$ 12.09659	40.5773 $\pm$ 10.94083	0.596
Natremia (mean $\pm$ SD)	129.98 $\pm$ 5.310	130.77 $\pm$ 4.730	0.006

## Discussion

Spontaneous bacterial peritonitis (SBP) is a frequent and severe complications in patients with liver cirrhosis. Various studies have shown that the prevalence of SBP varies from 20-40% in patients with cirrhosis and ascites. Not in all cases it is accompanied by obvious symptoms, which makes early diagnosis difficult<sup>1,2,15</sup>. An appropriate diagnosis and correct treatment are the first option in SBP management as untreated patients' mortality is much higher and approaches 50%<sup>1,16</sup>. Our study investigated adherence to the guidelines for diagnosis, and predictive factors in patients with SBP in decompensated cirrhosis. The average age of the 137 participants in this study was  $54.15 \pm 12.5$  years, 132

males (96.4%) and 5 females (3.6%), where 105 patients were with SBP. Most of patients were male because of alcoholic cirrhosis, 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<sup>14</sup>. 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<sup>15,16</sup>. The mean age of our patients was  $54.15 \pm 12.5$  years

and most of them were > 40 years old. At the moment of hospitalization, most of patients with SBP had jaundice (92.8%), encephalopathy (41.9%), upper gastrointestinal bleeding (37%), fever (36%), HRS (29%). 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<sup>20</sup>. This study show that abdominal pain was encountered in 54%, abdominal distention in 68%, similar to other studies<sup>21</sup>. The classification according to MELD score in this study resulted > 19 points in the majority of patients with SBP, which was slightly higher than the group without SBP<sup>20</sup>. In our study, it was seen that the group of patients with SBP had lower number of platelets ( $p < 0.015$ ), higher creatinine level ( $p < 0.002$ ), prolonged level of INR ( $p < 0.049$ ), lower prothrombin level (0.002). Regarding the laboratory data in the SBP of the two groups, in alcoholic cirrhosis the AST level was higher than ALT level ( $89.7 \pm 64$  vs  $83.4 \pm 52$  U/L).

The level of albumin in ascites did not have any significant difference between the group with SBP and without SBP, but low levels of albumin in ascites is a known risk factor for SBP (<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<sup>22,23</sup>. A study by *Fillik 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 ( $p < 0.005$ )<sup>21</sup>.

The culture of the liquid, which was carried out only in 45 cases with SBP, and only 10 patients (22%) resulted in a positive culture, 7 patients with *E. coli* and 3 patients with *staphylococcus aureus*. *Piroth et al*.<sup>22</sup> 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*.<sup>23</sup> 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*. While gram-positives in this study such as *Enterococci*, *Streptococci* and *Staphylococci* were found in up to 37.5% of cases. The role of proton pump inhibitors as a risk factor for spontaneous bacterial peritonitis is controversial, so that its use should be restricted to those with a clear indication<sup>1</sup>. Our study has limitations, including being a single - center retrospective study, and not represented other hospitals. Some patients had a lack of data in their documentation.

## Conclusions

The most probable predictive factors in the case of SBP in liver decompensated cirrhosis were found the increased level of creatinine, increased level of bilirubin, low level of platelets, prolonged level of INR and low level of prothrombin. While the most frequent associated complications were hepatic encephalopathy, HRS, GI hemorrhage, and jaundice. As a result of this study, we can say that patients with alcoholic cirrhosis and SBP had not difference with viral cirrhosis with SBP, about the predictive factors. The MELD score was higher in the SBP group, but is considered independent 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.

## Conflicts of Interest

None

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