

## Prevalence of Spontaneous Bacterial Peritonitis in Cirrhotic Patients with Ascites and Its Pattern in Aswan University Hospital

Mohammed Zain-Eldeen Hafez\*<sup>1</sup>, Hala Abdallah Mahmoud Abdallah<sup>2</sup>, Khalid Khairy Khalafalla Abdellatif<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, Faculty of Medicine, Assiut University,

<sup>2</sup>Department of Internal Medicine, Faculty of Medicine, Aswan University

\*Corresponding author: Khalid Khairy Khalafalla Abdellatif, Mobile: (+20)01000065925

### ABSTRACT

**Background:** Spontaneous bacterial peritonitis (SBP) is the most common infection and a lethal complication in patients with liver cirrhosis and ascites. It has high mortality and recurrence rates and poor long-term prognosis.

**Objective:** This study was done to determine the prevalence of spontaneous bacterial peritonitis and its variants in patients of liver cirrhosis with ascites.

**Patients and Methods:** This was a prospective, randomized, cross-sectional clinical study, included 100 adult patients of decompensated liver cirrhosis with ascites in Aswan University Hospital during the period from January 2019 to December 2019.

**Results:** Diagnosis of SBP is based on ascitic fluid analysis as well as culture and sensitivity. The diagnostic criteria are PMNL > 250/mm<sup>3</sup> and or positive culture. Mean of age of patients was 63.06 ± 9.67 years old. Majority of patients were males (63%) and 37 % were females. In Our study, 62% of patients were diagnosed SBP. Classic SBP in 30.6%, Culture Negative Neutrocytic Ascites (CNNA) in 59.7% and MNB in 9.7% of patients. Of 25 patients who have positive culture ascetic fluid, 60% were positive for gram-negative bacteria predominantly E. coli.

**Conclusion:** Spontaneous Bacteria Peritonitis is the most common and life-threatening infection in patients who have liver cirrhosis and ascites. It is diagnosed by a) Ascitic fluid PMNL > 250/mm<sup>3</sup>. b) Positive ascetic fluid culture. c) Both a and b. It is found that SBP has recently increased in prevalence with predominantly causative organism gram negative E Coli.

**Keywords:** Spontaneous Bacterial Peritonitis, Liver cirrhosis, Ascites.

### INTRODUCTION

Liver cirrhosis is a significant cause of health burden. It is the 14<sup>th</sup> most common cause of death worldwide <sup>(1)</sup>. In 2010, Egypt had the highest age-standardized cirrhosis mortality rates and almost one-fifth (18.1%) of all deaths occurred in males (45 to 54 years old) were due to liver cirrhosis <sup>(2)</sup>. Liver cirrhosis also leads to liver dysfunction (impaired synthetic and metabolic functions of the liver) up to liver cell failure. Both portal hypertension and liver cell failure contribute to serious complications e.g. hepatic encephalopathy <sup>(3)</sup>.

The disease can be compensated or decompensated. Significant morbidity and mortality are associated with decompensation. Complications include variceal hemorrhage, ascites, increased risk of bacterial infection, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome, umbilical hernia and hepatic hydrothorax <sup>(4)</sup>. Management should be focused on the prevention of recurrence of complications. Ascites is the most common complication of cirrhosis and is often the first sign of decompensation to appear <sup>(5)</sup>. It occurs within 10 years of diagnosis in half of patients with 5-year mortality of 44% <sup>(6)</sup>.

Cirrhosis is an immunocompromised state, which predisposes patients to various infections resulting from alterations in defense mechanisms and translocation of gut flora <sup>(7)</sup>. In advanced stages of liver cirrhosis with ascites, patients tend to develop

bacterial peritonitis without evidence of source of infection, a form of infection which has been termed spontaneous bacterial peritonitis (SBP) in 1963 <sup>(8)</sup>.

SBP is the most common and life-threatening infection in patients with advanced liver cirrhosis. Its prevalence is as high as 12% in hospitalized patients while it develops in up to 3.5% of patients that are treated as outpatients <sup>(9)</sup>. Hospital mortality in patients with SBP reaches 10-20 % with high recurrence rate and so that it has poor long-term prognosis, one-year survival after an episode of SBP is 30-40 % and 20 % at two years <sup>(10)</sup>. SBP is recognized as an important marker of liver disease progression, which might be the decisive watershed in the management of advanced liver disease <sup>(11)</sup>. So it is necessary to consider this diagnosis in every clinical decompensation of a cirrhotic patient, diagnose it early and treat it effectively <sup>(12)</sup>.

SBP is defined as the presence of an infection in a previously sterile ascites in the absence of an intra-abdominal source of infection or malignancy <sup>(13)</sup>. The clinical manifestation is nonspecific and variable, up to one third of patients might be asymptomatic (bacterascites) or it can quickly emerge as a fatal sepsis syndrome <sup>(10)</sup>. Presenting signs and symptoms can include fever, changes in mental status, abdominal tenderness, gastrointestinal (GI) bleeding, chills, nausea, or vomiting. Because of the tremendous variability in presentations, and also because such presentations may overlap with other conditions often



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seen in cirrhosis (e.g., encephalopathy), a proper assessment is essential in diagnosis <sup>(14)</sup>.

Abdominal paracentesis and ascitic fluid analysis is the gold standard test for diagnosis <sup>(14)</sup>. It is diagnosed by presence of more than 250 polymorphnuclear cells per mm<sup>3</sup> of ascitic fluid <sup>(13)</sup>. Bacteriological examination of ascites fluid detects causative agents at less than half of the cases <sup>(10)</sup>. It is usually monomicrobial infection and majority of cases are caused by enteric gram-negative organisms, mostly *Escherichia coli* <sup>(12)</sup>. Other causative organisms are *Klebsiella pneumoniae*, *Streptococci* spp, *Enterobacteriaceae* spp <sup>(8)</sup> and *Listeria monocytogenes* in a reported case. SBP is an endogenous infection, in general caused by transmigration of enteric bacteria to the ascites <sup>(15)</sup>.

The variants of Spontaneous bacterial peritonitis include: (i) Classic Spontaneous bacterial peritonitis where ascitic fluid polymorphnuclear leukocyte counts more than 250/mm<sup>3</sup> and positive culture. (ii) Culture Negative Neutrocytic Ascites (CNNA) but the ascitic fluid polymorphnuclear leukocyte counts more than 250/mm<sup>3</sup>. (iii) Bacterascites where a culture positive ascitic fluid but the polymorphnuclear leukocyte counts less than 250/ mm<sup>3</sup> <sup>(16)</sup>.

The result of bacteriological examination is available after a few days. However, empirical treatment should be initiated without delay so that the prognosis becomes better <sup>(10)</sup>. Third-generation cephalosporins or quinolones have been suggested as the empirical treatment for SBP. Early diagnosis and appropriate treatment can help in reducing mortality and morbidity in patients with chronic liver disease <sup>(17)</sup>.

This study was done to determine the prevalence of spontaneous bacterial peritonitis and its variants in patients of liver cirrhosis with ascites.

## PATIENTS AND METHODS

This prospective, randomized, cross-sectional clinical study included 100 adult patients of decompensated liver cirrhosis with ascites in Aswan University Hospital during the period from January 2019 to December 2019.

### Inclusion Criteria:

Adult patients >18 years old of both genders who have liver cirrhosis diagnosed on basis of clinical features suggestive of liver disease, biochemical features (modestly elevated liver enzymes, Hypoalbuminaemia, prolonged prothrombin time) and abdominal ultrasound showing features of cirrhosis of liver and portal hypertension.

### Exclusion criteria:

1. Patients who had received antibiotic within 3 weeks prior to admission.

2. Patients classified as having secondary peritonitis diagnosed when one of the following features is present:
  - a) Selective and persistent localized abdominal pain and tenderness.
  - b) Presence of following:
    - i- Ascitic fluid lactic dehydrogenase concentration more than 225 mg/dL.
    - ii- Ascitic fluid glucose concentration less than 50 mg/dL.
  - c) Isolation of more than one microorganism in the ascetic fluid culture.
  - d) An evidence of intra-abdominal surgically treatable source of infection.
3. Tuberculosis of the abdomen with ascites.
4. Malignancy with ascites.

### All patients were subjected to the following:

- Complete Blood Count (CBC).
- Liver function tests: serum level of liver enzymes [alanine transaminase (ALT) and aspartate transaminase (AST)] and serum albumin and bilirubin.
- Coagulation profile: Prothrombin time (PT) and international normalized ratio (INR).
- Kidney function tests.
- Ascitic fluid analysis: All patients underwent paracentesis as soon as the patient is admitted and diagnosed to be suffering from liver cirrhosis, before giving any antibiotic. Ascitic fluid was subjected to cytology, culture and biochemical examination.

### Ethical considerations:

- **Research statement:**
  1. **Ethics Committee, Faculty of Medicine, Aswan University approved the final protocol.**
  2. **Approval of the authority of Aswan University Hospital for final protocol and carrying out the study.**
  3. Written informed consent was taken from patients who were participating in the study.
  4. Before patients are admitted in the study, the purpose and nature of the study as well as the risks were explained to them.
  5. Patients must agree that:
    - a) They understand nature of the study, its inherent risks and benefits.
    - b) They have the right of refusal to participate in the study and the right of withdrawal from the study at any time without giving any reasons and without

affecting their right in having proper healthcare in the study site.

- c) They have the right to ask any questions regarding the study.
- d) They are freely giving informed consent to participate in this study.

- **Confidentiality:** The confidentiality of all participants admitted to the study was protected to the fullest extent possible. Analysis of data was demonstrated in a secured way without identifying patients' names.
- **Informed consent:** The signed informed consent form was a permanent part of the participant's study records and was maintained in the same manner as other records.

**Statistical analysis**

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage. The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x<sup>2</sup>) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%.

**RESULTS**

**Table (1):** Age and gender distribution for whole group

		N	%	Median
Age (years)	Mean ± SD	63.06 ± 9.67		63
	30-60	40	40%	
	> 60	60	60%	
Gender	Male	63	63%	
	Female	37	37%	

The table showed that mean age of patients was 63.06 ± 9.67. Majority of patients were males (63%) and female patients were 37 %.

**Table (2):** Prevalence of SBP in cirrhotic patients with ascites and variants of SBP

	Number of patients	Percentage
SBP	62	62%
Non SBP	38	38%
<b>Total</b>	<b>100</b>	<b>100%</b>
<b>Variants of SBP:</b>		
Classic SBP	19	30.6%
CNNA	37	59.7%
MNB	6	9.7%
<b>Total</b>	<b>62</b>	<b>100%</b>

This table showed that about 62% of studied patients were diagnosed as SBP with statistically significant result. This indicated high prevalence of SBP in cirrhotic patients with ascites.

Majority of patients were CNNA meaning that they have PMNL > 250/mm<sup>3</sup> in ascitic fluid and negative culture with percentage about 59.7%.

Classic SBP patients who had both culture positive ascitic fluid and PMNL > 250/mm<sup>3</sup> were the next being about 30.6% of total SBP patients. The remaining SBP patients were diagnosed as MNB meaning that they had only culture-positive ascitic fluid with PMNL < 250/mm<sup>3</sup>. They were about 9.7% of total SBP patients.

**Table (3):** Classification of SBP patients according to culture and sensitivity of ascitic fluid and to gram stain

		Number of Patients	Percentage
Culture and sensitivity of ascitic fluid	Culture positive	25	40.3%
	Culture negative (CNNA)	37	59.7%
Gram stain	Gram Positive	10	40%
	Gram Negative	15	60%
<b>Total</b>		<b>87</b>	<b>100%</b>

This table showed that majority of SBP patients (59.7%) had culture-negative ascitic fluid. Majority of culture-positive SBP patients had gram-negative bacteria of about 60% and gram positive were about 40%.

**Table (4):** Classification of culture positive SBP according to microorganisms

Micro-organism		Number of Patients	Percentage
Gram Negative	E. Coli	10	40%
	Klebsiella SPP	5	20%
Gram positive	Staph. Aureus	6	24%
	Streptococcus SPP	4	16%
<b>Total</b>		<b>25</b>	<b>100%</b>

This table showed that most of culture-positive SBP patients had E Coli (40%) followed by Staphylococcus aureus (24%), Klebsiella SSP (20%) and Streptococcus SPP (16%).

**Table (5):** Microorganisms in gram negative and gram-positive group

		Number of patients	Percentage
Gram Negative	E.coli	10	66.6%
	Klebsiella SPP	5	33.3%
Gram positive	Staphylococcus Aureus	6	60%
	Streptococcus SPP	4	40%
<b>Total</b>		<b>25</b>	<b>100%</b>

This table showed that majority of gram-negative culture SBP patients had E.coli (66.6%) and Klebsiella patients were the least of about 33.3%. Majority of gram-positive culture SBP patients had Staphylococcus aureus (60%) and Streptococcus SPP patients were the least of about 40%.

### DISCUSSION

In this study that was conducted on 100 patients having decompensated liver cirrhosis, mean age was  $63 \pm 9$  years with 63 male patients (63%) and 37 female patients (37%).

In our study, we found a high prevalence of SBP in 62 patients (62%). This agrees with a study by **Abeer et al.** (18) who found the prevalence of SBP was about 57% in a study was conducted on 100 cirrhotic, ascetic patients presented to the Internal Medicine Department, Kasr Elaini Hospital, Cairo University, Egypt. Another study by **El Gharabawy et al.** (19) found that prevalence of spontaneous bacterial peritonitis was about 76% in 400 patients with liver cirrhosis and ascites admitted to Hepatology Unit at Mansoura Specialized Medical Hospital, Mansoura University, Egypt. In a study by **Oladimeji et al.** (20) SBP developed in 67.7% of 31 patients with liver cirrhosis and ascites who were admitted into the Medical Ward of the Ekiti State University Teaching Hospital (EKSUTH), Ado-Ekiti, Nigeria.

According to results of ascitic fluid culture of SBP patients, we found that 37 patients (59.7 %) among 62 SBP had CNNA with PMNL  $> 250/\text{mm}^3$ , while 25 (40.3%) patients had culture-positive ascitic fluid. Our study agrees with **Purohit et al.** (12) who studied 217 clinically suspected cases of SBP. They concluded that 71 (43.80%) had ascitic fluid polymorph nuclear cells (PMN) count  $\geq 250/\text{mm}^3$ , 31 (43.6%) cases were culture-positive and 40 (56.4%) cases were culture-negative neutrocytic ascites.

Also, we agrees with **El Gharabawy et al.** (19) who found that 179 patients (58.3 %) among 400 SBP patients had CNNA while 128 (41.7%) patients had positive cultures. It was also found that positive cultures were gram-negative in 77 patients (60.2%) and gram-positive in 51 patients (39.8%). But, **Oladimeji et al.** (20) found that in patients who

developed culture-positive SBP was present in 66.7%, while CNNA was found in 33.3%.

In our study, of 25 culture-positive patients, 19 patients (30.6% of SBP patients) were classic SBP being had PMNL  $> 250/\text{mm}^3$  and 6 patients (9.7% of SBP patients) were Monobacter Non-Neutrocytic bacterascites (MNB) being had PMNL  $< 250/\text{mm}^3$ . This disagrees with **Oladimeji et al.** (20) who found that in patients who developed SPB, the prevalence of MNB was 26%.

In our study, we found that positive cultures were gram-negative in 15 patients (60%) predominantly E Coli (66.6%) and Klebsiella (33.3%) and gram-positive in 10 patients (40%) predominantly Staphylococcus aureus (60%) and streptococcus SPP (40%). This agrees with **Oladimeji et al.** (20) who found that in those with SBP, 93% had gram-negative bacilli being responsible in 66.7% of the cases with E coli (70%) was the predominant organism followed by Klebsiella species. Gram-positive organisms accounted for 33.3% with Streptococcal species (60%) was the predominant organism followed by Staphylococcus aureus (40%).

For all of 25 culture-positive patients, the causative microorganism was found to be E coli in 10 patients (40%) followed by Staphylococcus aureus in 6 patients (24%) and then Klebsiella SPP in 5 patients (20%) and lastly Streptococcus SPP.

In this study as well as some recent studies, Spontaneous bacterial peritonitis showed increased prevalence in patients who have liver cirrhosis and ascites with predominantly culture-negative variant (CNNA) and causative organisms were predominantly gram-negative bacteria.

### CONCLUSION

Spontaneous bacterial peritonitis is the most common and life threatening infection in patients who have liver cirrhosis and ascites. It is diagnosed by a) Ascitic fluid PMNL  $> 250/\text{mm}^3$ . b) Culture positive ascetic fluid. c) Both a and b. It is found that SBP has recently increased in prevalence with predominantly causative organism gram-negative E Coli.

### RECOMMENDATIONS

We recommend to consider SBP in deteriorating patients with decompensated liver cirrhosis with ascites and to obtain ascitic fluid samples for analysis and cultures and sensitivity at the time of hospitalization. In addition, it is recommended to early initiate empirical treatment with appropriate antibiotic to get better outcome and reduce mortality and morbidity from spontaneous bacterial peritonitis (SBP) in patients with liver cirrhosis.

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