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## Do the clinical symptoms in cirrhotic patients with ascites indicate spontaneous bacterial peritonitis?

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### ABSTRACT

Spontaneous bacterial peritonitis (SBP) is the most common prevalent infection among patients with liver cirrhosis. Neglecting this infection in early time can be life threatening. The goal of this study was to determine physician clinical impression in confirming the diagnosis of Spontaneous bacterial peritonitis in patients for aspiration of abdominal fluid. In this study, 80 cirrhotic patients selected including: 32 person with Spontaneous bacterial peritonitis and 48 patients without Spontaneous bacterial peritonitis who referred for aspiration of ascites fluid during February 2012 to January 2014. The sensitivity, specificity, positive and negative predictive values of clinical signs and symptoms (such as abdominal pain, fever, tachycardia, hypotension and encephalopathy) in diagnosis of Spontaneous bacterial peritonitis were evaluated through check list. Of 80 patients with cirrhosis, 32 had Spontaneous bacterial peritonitis but the rest 48 did not have (N=48). The highest sensitivity amounts were abdominal pain 93.75 % (95%CI: 79.85-98.27) and the highest specificity amounts were for fever and tachycardia both 97.92 % (95%CI: 89.1-99.63). Cirrhotic patients with ascites in the absence of abdominal pain do not have spontaneous bacterial peritonitis. In cirrhotic outpatient, abdominal paracentesis can be performed without sending samples for diagnostic testing to rule out spontaneous bacterial peritonitis.

**Keywords:** Spontaneous Bacterial Peritonitis, Cirrhosis, Abdominal Paracentesis.

### INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is the most common infection in patients with liver cirrhosis which can be life threatening without prompt recognition and appropriate treatment.[1-3] SBP is caused by bacterial translocation across the intestinal wall to mesenteric lymph nodes, resulting in the bacteremic seeding of ascites. [4, 5] The infecting organisms are usually those found among the normal intestinal flora. When first described, its mortality exceeded 90% but this has been reduced to approximately 20% with early diagnosis and treatment.[6, 7]

All patients with cirrhosis and ascites are at risk of SBP and the prevalence of SBP in outpatients is 1.5%-3.5% and about 10%-30% in hospitalized patients. [8, 9] Approximately half of the episodes of SBP are present at the time of hospital admission. The 1-year probability for development of the first episode of SBP in cirrhotic patients with ascites is approximately 10%.<sup>[10]</sup> The outcome in cirrhotic patients with SBP has improved dramatically during the last 20 years. In studies published before 1980, the rate of SBP resolution ranged between 25% and 50%. [10-11]

Patients with SBP may have one of the following: (1) local symptoms and/or signs of peritonitis: abdominal pain, abdominal tenderness, vomiting, diarrhea, ileus; (2) signs of systemic inflammation: hyper or hypothermia, chills, altered white blood cell count, tachycardia, and/or tachypnea; (3) worsening of liver function; (4) hepatic encephalopathy; (5) shock; (6) renal failure; and (7) gastrointestinal bleeding. Yang and Lin,[10-11]recommended diagnosis of SBP as shown in Table 1.

Diagnosis of SBP	<ol style="list-style-type: none"> <li>1. Ascitic fluid polymorphonuclear neutrophil (PMN) count &gt; 250/mm<sup>3</sup>; in patients with bloody ascites, subtract 1 PMN per 250 red blood cells</li> <li>2. Cultures               <ul style="list-style-type: none"> <li>- Ascitic fluid cultures: bedside inoculation into blood culture bottles ( 10 mL)</li> <li>- Blood cultures: simultaneous to ascitic fluid cultures</li> </ul> </li> </ol>
Special conditions	<ol style="list-style-type: none"> <li>1. Bacterascites: positive ascitic fluid culture, ascites PMN &lt; 250/mm<sup>3</sup>, and no evidence of local or systemic infection               <ul style="list-style-type: none"> <li>- Repeat paracentesis once bacterascites is diagnosed and initiate antibiotic if:                   <ul style="list-style-type: none"> <li>• Ascites PMN &gt; 250/mm<sup>3</sup></li> <li>• Ascites PMN &lt; 250/mm<sup>3</sup>, but culture continues to be positive</li> </ul> </li> </ul> </li> <li>2. Secondary peritonitis: suspected when any of the following:               <ul style="list-style-type: none"> <li>- Lack of response to antibiotic treatment</li> <li>- Two or more organisms isolated (particularly anaerobes or fungi)</li> <li>- At least 2 of the following findings in ascitic fluid:                   <ul style="list-style-type: none"> <li>• glucose &lt; 50 mg/dL; protein &gt; 10 g/L; lactate dehydrogenase &gt; normal serum levels</li> </ul> </li> </ul>               Once secondary peritonitis is suspected:               <ul style="list-style-type: none"> <li>- Initiate appropriate radiologic investigation</li> <li>- Add antibiotics against anaerobes and enterococci</li> </ul> </li> </ol>

However, it is important to note that SBP may be asymptomatic in about 10%-32% of cases, particularly in outpatients.[8-12-13] The diagnosis of SBP is based on the detection of an elevated polymorph nuclear leukocyte count to more than 250 cells/mm in ascites fluid without an evident intra-abdominal origin of bacterial infection. [14] Although spontaneous bacterial peritonitis in cirrhotic patients can have symptoms such as abdominal pain, fever, Hypotension, tachycardia and encephalopathy, this disease may also be in a symptomatic patients. The aim of this study is to determine the sensitivity and specificity of clinical symptoms in diagnosis of spontaneous bacterial peritonitis in cirrhotic patients with ascites and with clinical symptoms, spontaneous bacterial peritonitis can be diagnosed or ruled out.

## MATERIALS AND METHODS

### Sampling

This is a study of diagnostic methods. Patients with liver cirrhosis who referred to emergency department referral center of Imam Khomeini hospital of Sari for aspiration of ascites fluid from February 2012 to January 2014 were included as a sample. Sample size was calculated based on the sample size calculation formula and prior studies. [3, 4, and 8] Therefore 80 patients selected through convenience sampling method. Exclusion criteria were patients who had ascites etiology other than cirrhosis. All included patients underwent paracentesis. In this study, no further invasive procedures were performed on patients. Informed consent was obtained for entry into the program and all costs for those who were included were free.

### Design testing

The selected patients were transferred to a reference laboratory for examination of spontaneous bacterial peritonitis. The results of laboratory examination associated with clinical symptoms such as abdominal pain, fever (body temperature above 37.8 ° C with an oral thermometer), Hypotension (systolic pressure less than 90 mmHg), tachycardia (heart rate higher than 100), and encephalopathy were then recorded by an emergency medicine specialist in prepared check list. The patients were divided into two groups: patients considered as positive in those with bacterial peritonitis Spontaneous (PMN greater than 250 or WBC more than 500 per cubic millimeter ascites fluid) and negative in those without bacterial peritonitis (PMN less than 250 or WBC less than 500 per cubic millimeter ascites fluid). [12] Presence of more than 250 polymorph nuclear (PMN) or more than 500 white blood cells (WBC) per cubic millimeter ascites fluid considered as a standard diagnostic test for the diagnosis of Spontaneous bacterial peritonitis. [2-12]The results were positive for 32 patients and 48 patients showed negative results.

**Statistic**

Gathered data was analyzed through SPSS software and the sensitivity, specificity and positive and negative predictive value of clinical symptoms (95% confidence interval) in the diagnosis of spontaneous bacterial peritonitis was measured.

**RESULTS**

This study was done on 80 patients with ascites who referred to Imam Khomeini hospital for paracentesis. Mean and standard deviation of patients age was  $56.25 \pm 12.21$ . Mean age of patients with spontaneous bacterial peritonitis was 57.09 and of those who were healthy was 55.68. 52.5% female and 47.5 male formed the study population. The youngest patient was 35 years old and the oldest patient in the study was 81 years old. Only 3 patients in the study had encephalopathy. The most common symptom of the patient was abdominal pain (48 patients). Abdominal pain had the highest sensitivity 93.75% (95% CI: 79.85-98.27) and the highest negative predictive value of 93.75% (95% CI: 79.85-98.27) in the diagnosis of Spontaneous bacterial peritonitis (Table 2 and 3).

**Table 2: Sensitivity Specificity and accuracy of clinical symptom in spontaneous bacterial peritonitis**

Sign's	(Accuracy) (CI: 95%)	(Specificity) (CI: 95%)	(Sensitivity) (CI: 95%)
<b>Abdominal Pain</b>	75%(95%CI:64.52-83.19)	62.50%(CI:48.36-74.78)	93.75%(95%CI:79.85-98.27)
<b>Fever</b>	65%(95%CI:54.8-74.55)	97.92%(95%CI:89.1-99.63)	15.63%(95%CI:6.86-31.75)
<b>Hypotension</b>	63.75%(95%CI:52.81-73.43)	95.83%(95%CI:86.02-98.85)	%(95%CI:6.86-31.75)16.63
<b>Tachycardia</b>	70%(95%CI:59.23-78.94)	97.92%(95%CI:89.1-99.63)	28.13%(95%CI:15.56-45.37)
<b>Encephalopathy</b>	61.25%(95%CI:71.18-50.29)	97.92%(95%CI:89.1-99.63)	6.25%(95%CI:1.73-20.15)

**Table 3: Positive and negative predictive values and LR + and LR-clinical symptom in diagnosis of spontaneous bacterial peritonitis**

Sign's	LR(CI: 95%) Likelihood ratio <sup>-</sup>	LR <sup>+</sup> (CI: 95%) Likelihood ratio <sup>+</sup>	Negative predictive values (CI: 95%)	Positive predictive values (CI: 95%)
<b>Abdominal Pain</b>	0.1 (95%CI:0.02-0.39)	2.5 (95%CI:1.71-3.64)	93.75%(95%CI:79.85-98.27)	62.50%(95%CI:48.36-74.78)
<b>Fever</b>	0.86 (95%CI:0.91-61.24)	7.5 (95%CI:0.91-11.13)	63.51%(CI:52.13-73.56)	83.33%(95%CI:43.65-96.99)
<b>Hypotension</b>	0.88 (95%CI:0.75-1.03)	3.75 (95%CI:0.77-18.16)	63.01%(95%CI:51.55-73.18)	71.43%(95%CI:35.89-91.78)
<b>Tachycardia</b>	0.73 (95%CI:0.58-0.91)	13.5 (95%CI:1.79-101.46)	67.14%(95%CI:55.5-77)	90%(95%CI:59.58-98.21)
<b>Encephalopathy</b>	0.95 (95%CI:0.86-1.05)	3 (95%CI:0.28-31.72)	61.04%(95%CI:49.87-71.16)	66.67%(95%CI:20.77-93.85)

The lowest specificity 62.50% (CI: 48.36-74.78) and positive predictive value of 62.50% (95% CI: 48.36-74.78) were associated with abdominal pain. From 10 patients who had tachycardia, only one patient did not have spontaneous bacterial peritonitis. Six patients who participated in the study had fever and 5 cases had spontaneous bacterial peritonitis. Highest specificity and positive predictive value of the clinical symptoms was for fever and tachycardia respectively. Specificity and positive predictive value of fever in the diagnosis of spontaneous bacterial peritonitis, was 97.92% (95% CI: 89.1-99.63) and 83.33% (95% CI: 43.65-96.99) respectively (Table 2 and 3). Specificity and positive predictive value of tachycardia in spontaneous bacterial peritonitis, was 97.92% (95% CI: 89.1-99.63) and 90% (95% CI: 59.58-98.21) respectively (Table 2 and 3). In this study, encephalopathy had the least sensitivity 6.25% (95% CI: 1.73-20.15) and negative predictive value of spontaneous bacterial peritonitis diagnosis, 61.04% (95% CI: 49.87-71.16).

**DISCUSSION**

Of 80 cirrhotic patients, 30 patients with Spontaneous bacterial peritonitis had abdominal pain, and it had the highest sensitivity in diagnosing spontaneous bacterial peritonitis (93.75%) but this symptom had low specificity (62.50%). According to the negative predictive value of abdominal pain (93.75%) it can be concluded that in cirrhotic patients without abdominal pain, likelihood of presence of spontaneous bacterial peritonitis is low. In the study of Mihaset al in 1992, from 35 patients with Spontaneous bacterial peritonitis (SBP), the most common symptom in 20 patients was abdominal pain (57%). [15] In this study hypothermia and encephalopathy had the lowest sensitivity. Many studies reported encephalopathy as the most prevalent symptom after abdominal pain, in patients with spontaneous bacterial peritonitis. [14-16] In this study, only 3 patients had encephalopathy, 2 of which have spontaneous bacterial peritonitis. It seems there is no significant relationship between spontaneous bacterial and encephalopathy. In many references, fever is the most common symptom of peritonitis after icterus and in 60% or even 80% of cases was reported. [14, 17] In our study, 5 cases of 6 patients who had fever, had spontaneous bacterial peritonitis. Fever has a high positive predictive value and specificity in diagnosis of bacterial peritonitis. Therefore, the presence of fever in

cirrhotic patients raises the probability of bacterial peritonitis. In this study, Tachycardia was also considered as a symptom of spontaneous bacterial peritonitis according to the high specificity and positive predictive value. In some studies routine examination of ascites fluids of all cirrhotic patients for rapid diagnosis of spontaneous bacterial peritonitis is suggested [18-19] In study conducted by Romney ET AL (2005) sixty-seven cirrhotic patients had 270 therapeutic paracenteses, preceded by an exploratory aspiration. No patient had spontaneous bacterial peritonitis nor culture-negative neutrocytic ascites; 10 cases of monomicrobial bacteras cites were observed, all with commensal germs. They believed that in the absence of obvious signs of infection, the prevalence of spontaneous bacterial peritonitis and culture-negative neutrocytic ascites in asymptomatic cirrhotic outpatients with ascites is near 0%. Moreover, for 100 large volume paracenteses, not performing exploratory paracentesis corresponds to a savings of 5,500 euros, without risk for these patients. [20]

Other similar studies also showed that spontaneous bacterial peritonitis in outpatients is very rare or even absent. [21, 22-23]

### CONCLUSION

In this study we conclude that in diagnosis of spontaneous bacterial peritonitis, fever and tachycardia have high positive predictive value and abdominal pain has high negative predictive value. So cirrhotic patients with ascites in the absence of abdominal pain do not have spontaneous bacterial peritonitis. In cirrhotic outpatient, abdominal paracentesis can be performed without sending samples for diagnostic testing to rule out spontaneous bacterial peritonitis. Conducting this study with a larger sample size in a multi-center is suggested.

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