# Risk Factors for Spontaneous Bacterial Peritonitis in Patients with Liver Cirrhosis and Ascites

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**ABSTRACT**

*Spontaneous bacterial peritonitis (SBP) is one of serious complication of liver cirrhosis. Most of the patient with SBP have severe reduced liver function that clasified as Child Plugh class C. There are other risk factors for SBP such as poor nutritional status, GI bleeding, intravascular catheter insertion, ascites fluid protein concentration of less than 1 g/L, large volume paracentesis, urinary tract infection and respiratory tract infection. The management of SBP is mainly the administration of proper antibiotics. The antibiotic of choice for the emperial treatment is cefotaxim.*

***Key Words**: SBP,liver cirrhosis, risk factor, ascites*

## INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is a serious complication in patients with liver cirrhosis and ascites. Spontaneous bacterial peritonitis is defined as infection of ascites fluid due to prolonged bacteremia with the absence of a local infection within the abdomen.[1,2,3,4,5,6,7,8,9]

Spontaneous bacterial peritonitis is usually caused by prolonged bacteremia, supported by reduced activity of the rethiculoendothelial phagocytosis system and serum complement deficiency, as well as reduced opsonin activity.[1,10,11,12,13] Spontaneous bacterial peritonitis practically only occurs in severe liver disease. Spontaneous bacterial peritonitis often occurs after a patient with liver cirrhosis and ascites is admitted to the hospital, and is very probable in patients with gastrointestinal bleeding, renal failure, or those undergoing invasive diagnostic or therapeutic procedures.[1,2] Ninety percent of infection from the blood is caused by one kind of microorganism, 60-80% of which is caused by negative-gram bacteria.[2] Infection that occurs due to more than one microorganism may be due to paracentesis, colon perforation, colon dilatation, or the presence of other intra-abdominal sources of infection.[2] Over 95% of patients with spontaneous bacterial peritonitis are found with increased serum bilirubin levels, while 81% of patients demonstrate clinical jaundice, and 98% are found with abnormal prothrombine time (PT).[1] Infection usually occurs in patients with liver cirrhosis with a large volume of ascites fluid. Ascites in patients with nephrotic syndrome may result in spontaneous bacterial peritonitis prior to antibiotic therapy, but with the use of diuretics and antibiotics, such conditions are rarely encountered. Cardiac and chromatosis peritonial ascites never develop into spontaneous bacterial peritonitis.[1,14] Spontaneous bacterial peritonitis differs from secondary bacterial perito-

nitis, laboratory wise or in therapy.[1,15] Surgical procedures conducted in spontaneous bacterial peritonitis has a mortality rate of 90%.[15] Ninety percent of patients with liver cirrhosis and infected ascites will develop spontaneous bacterial peritonitis, while the remaining 10% will develop secondary bacterial peritonitis. Even though theoretically spontaneous bacterial peritonitis can be found in several patients with ascites, infection usually only occurs in patients with liver cirrhosis accompanied by ascites.[3]

## EPIDEMIOLOGY

The prevalence rate for spontaneous bacterial peritonitis in patients with liver cirrhosis is estimated to range between 8% and 27%, with a mortality rate ranging from 48% to 57%.[4,16] The incidence rate of spontaneous bacterial peritonitis in hospitalized patients is estimated to range from 10% to 25%.[5]

Abdominal paracentesis, a routine hospital procedure for patients with liver cirrhosis and ascites, with or without signs of infection, found 10% to 27% with spontaneous bacterial peritonitis.[1,5]

Between 12% and 15% of patients with liver cirrhosis and ascites who are hopitalized suffer from spontaneous bacterial peritonitis.

Paracentesis must be repeated during hospitalization if there is a deterioration in the patient's condition, characterized by the presence of abdominal discomfort, fever, mental state changes, renal failure, peripheral blood leukocytosis, acidosis, or gastrointestinal bleeding.[1]

In the previous year, the incidence of spontaneous bacterial peritonitis in patients with liver cirrhosis was approximately 11%. Reduced liver function accompanied by increased serum billirubin (approximately 2.5 mg/100 ml) and low protein concentration in ascites fluid (<1 g/100 ml) facilitate spontaneous bacterial peritonitis, increasing the rate to 29% to 33% in 1 year.[15] Approximately 60% of spontaneous bacterial peritonitis cases are caused by environmental factors, while the rest occur during hospitalization.

## RISK FACTORS

The greatest risk factor for spontaneous bacterial peritonitis attack is reduced liver function. Seventy percent of patients with spontaneous bacterial peritonitis are classified into Child-Pugh class C. Seventy one percent of Class C Child-Pugh patients are expected to suffer from an attack of spontaneous bacterial peritonitis within one year. Poor nutritional status, serum bilirubin concentration of less than 2.5 mg/100 ml, prothrombine time comparison of less than 40%, and the presence of hepatic encephalipathy increase the possibility of spontaneous bacterial peritonitis up to 20% to 36%.[15] Gastrointestinal bleeding causes bacteremia, especially if sclerotherapy is conducted. Over 20% of patients with liver cirrhosis, ascites, and gastrointesinal bleeding have been infected at the time of admission, while 30% are infected during hospitalization. Out of 90% of patients with Child-pugh class C undergoing emergency sclerotherapy, 3% will suffer from spontaneous bacterial peritonitis. Ascites fluid protein concentration of less than 1 g/L increases the incidence of spontaneous bacterial peritonitis as much as 20% within one year. A prospective study conducted in Barcelona found that 46% of 187 patients with liver cirrhosis are infected in various forms during hospitalization, from asymptomatic urinary tract infection to sepsis. Bacteria that infect the urinary tract of patients with liver cirrhosis are the same as those causing spontaneous bacterial peritonitis.[1]

Risk factors for spontaneous bacterial peritonitis.[15]

1. Child-Pugh class C.
2. Gastrointestinal bleeding in Child-Pugh clas C, with or without sclerotherapy.
3. Ascites fluid protein concentration of less than 1 g/L.
4. Urinary tract or respiratory tract infection.
5. Intravascular catheter insertion.
6. Previous spontaneous bacterial peritonitis attack.
7. Large volume paracentesis.

Factors that do not increase the incidence of spontaneous bacterial peritonitis:

1. Diagnostic paracentesis.
2. Elective or prophylactic sclerotherapy or ligation.
3. Hepatocellular carcinoma.

## PATHOPHYSIOLOGY

Portal hypertension that occurs due to liver cirrhosis, and extensive liver deterioration due to acute hepatitis and ascites, indirectly cause bacterial translocation from the bowel through the mesenteric lymph nodes.[15,17] This process is facilitated by intestinal congestion, increased permeability of the intestinal mucosa, excessive bacterial growth in the intestines, and reduced intestinal defense function.[15,18] Bacterial translocation from the bowel directly into the abdominal cavity is not possible, thus spontaneous bacterial peritonitis is usually caused by one type of bacteria. The bacteria spread from the infected

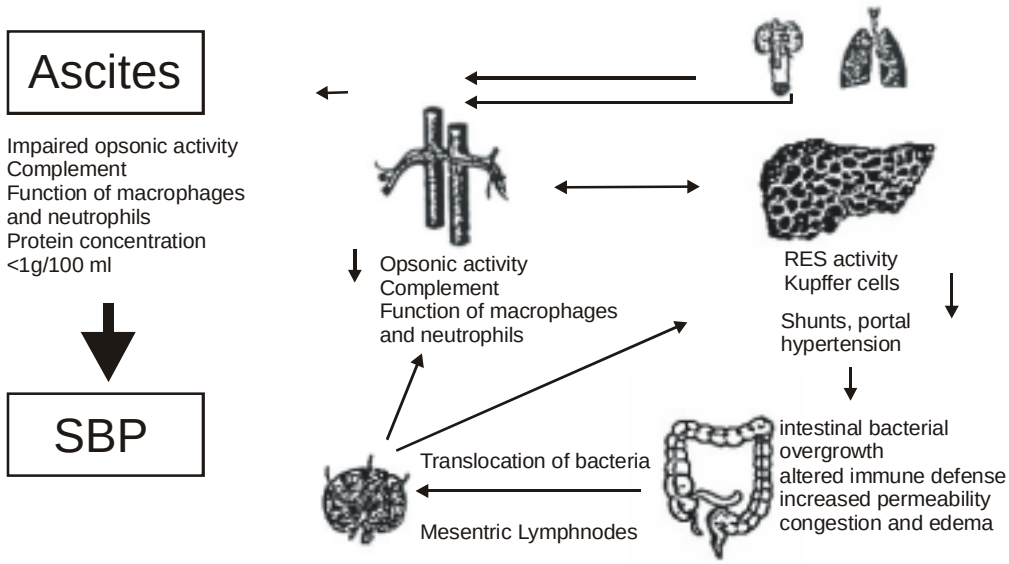


Figure 1. Scheme for the Pathophysiology of Spontaneous Bacterial Peritonitis

lymph node into the bloodstream, causing bacteremia. Prolonged bacteremia causes reduced rethiculoendothelial system function, portosystemic shunting, and reduced opsonin and serum phagocytosis activity. Low ascites fluid protein and reduced opsonin and complement concentration, as well as reduced polymorphonuclear (PMN) leukocyte function facilitate bacterial colonization (bacterascites), which could develop into spontaneous bacterial peritonitis. Other sources of prolonged bacteremia are urinary tract infections, respiratory tract infections, and invasive medical instrumental intervention.

## ETIOLOGY

Bacteria that cause infection of the ascites fluid mostly come from the bowel. Ninety-two percent of spontaneous bacterial peritonitis is caused infection by one kind of bacteria.[5,15,19] In 50% to 70% of cases, spontaneous bacterial peritonitis is caused by negative-gram bacteria.[10] In 25% to 30%, it is caused by positive-gram bacteria, while the remaining 3% to 5% is caused by anaerobic bacteria, and 2% are caused by a combination of bacteria (miscellaneous).

Patients receiving prophylactic therapy demonstrate a change in the pattern of microorganism spectrum, where 70% of cases are caused by positive gram cocci, and 14.3% are caused by negative gram bacteria.[15]

## CLINICAL SYMPTOMS

Classic signs of spontaneous bacterial peritonitis include stiff abdomen, which is often reduced or hard to detect. Recurrent abdominal tenderness may be reduced by ascites, and is found in 30% to 47% of cases, usually in a mild form.[15] Ten percent of spontaneous bacterial peritonitis cases are asymptomatic. In 25% to 40% of spontaneous bacterial peritonitis cases, hepatic encephalopathy or deterioration of disease is found. Twenty percent of spontaneous bacterial peritonitis cases suffer from gastrointestinal bleeding. Thirty to 46% of spontaneous bacterial peritonitis are accompanied by a decline in renal function.[15]

Signs and symptoms commonly encountered in spontaneous bacterial peritonitis are as follows: [1,3,5,15]

1. Abdominal discomfort
2. Malaise
3. Nausea and vomiting
4. Mental state changes
5. Fever
6. Chills

## DIAGNOSIS

Almost all peritonitis attacks in patients with liver cirrhosis and ascites take the form of spontaneous bacterial peritonitis. According to the latest study, if no persistent sign or symptom of infection is found, the patient usually does not develop spontaneous bacterial peritonitis.

Clinical manifestations may take one form or a combination of several different forms. Diarrhea, reduced liver function, encephalopathy, and hypothermia, are clues leading to the diagnosis of spontaneous bacterial peritonitis.[5]

Evaluation of ascites fluid, blood, and urine, should be conducted on all patients with suspected spontaneous bacterial peritonitis prior to the administration of antibiotics. Evaluation of ascites fluid as an initial predictor of spontaneous bacterial peritonitis is based on one of the following criteria: [1,4,15]

| Infection of ascites fluid | Culture of ascites fluid |
|---|---|
| 1. PMN cell count > 250/mm$^3$ | 1. Positive |
| 2. PMN cell count > 250/mm$^3$ or PMN cell=500/mm$^3$ | 2. Negative Negative |
| 3. PMN cell count < 250/mm$^3$ | 3. Positive |

Spontaneous bacterial peritonitis management is mainly the administration of proper antibiotics. More immediate administration of antibiotics demonstrated improved survival rates. Due to the high morbidity and mortality rate, as well as high risk of recurrent spontaneous bacterial peritonitis, studies are conducted with simultaneous prevention.[5]

If during initial examination, there is a great suspicion for the development of spontaneous bacterial peritonitis, antibiotics may be administered empirically to the patient, if one of the following criteria is met: [2,5]

1. There are typical clinical manifestations of spontaneous bacterial peritonitis.
2. PMN cell count > 250 / mm3 accompanied by persistent signs and symptoms.
3. PMN cell count > 500 / mm3.

The antibiotic of choice for the empirical treatment of spontaneous bacterial peritonitis is cefotaxim as a first line treatment. Cefotaxim is a third generation cefalosporine, with and activity spectrum covering positive and negative gram as well as anaerobic bacteria.[4] Cefotaxim has satisfactory efficacy and safety rate and is not nephrotoxic.[2,7,8,20,21] The dose for administration is 2 g/8 hours or 1 g/6 hours, administered intravenously for 10 to 14 days. Amoxycillin – clavulonic acid is just as effective as the first line treatment, with a recovery rate of 85%.[2,4,10] The dose for administration is 1 g Amoxycillin with 0.2 gram of clavulonic acid/6 hours intravenously for 14 days.

## PREVENTION

Recurrent spontaneous bacterial peritonitis often develops in patients with liver cirrhosis and ascites, often resulting in death.[4]

Primary prevention is the prevention of spontaneous bacterial peritonitis in high-risk patients with liver cirrhosis and ascites. Secondary prevention is prevention of recurrent spontaneous bacterial peritonitis. A method of prevention is by eliminating the development of ascites, by administering diuretics.

Administration of prophylactic antibiotics is aimed to cut-off the chain of translocation of intestinal microbes and bacteremia, which is known to cause infection of ascites fluid.[4]

Runyon, et al, demonstrated that the administration of diuretics in patients with liver cirrhosis and ascites increases total protein concentration of ascites fluid, as well as increase complement and opsonin activity of ascites fluid. According to this data, the administration of diuretic agents most probably would be able to prevent the development of spontaneous bacterial peritonitis.[14] Diuretic treatment has been known to reduce the incidence of spontaneous bacterial peritonitis and increase opsonin and complement C3 activity in the ascites fluid. Paracentesis therapy reduces total protein concentration, as well as complement, and opsonin activity, thus would quite probably increase the risk of spontaneous bacterial peritonitis in patients with liver cirrhosis and ascites.[14]

Spironolacton may be used as a diuretic, with a dose of 100 mg / day. Amilorid may also be used, with a dose of 10 mg/day. Administration of prophylactic antibiotics such as Cyprofloxacin with a dose of 750 mg / week is adequately effective for the long-term prevention of spontaneous bacterial peritonitis. Bacteriological study do not demonstrate the development of resistancy towards Cyprofloxacin after 6 months administration.[22,23]

Both oral administration of norfloxacin and cyprofloxacin in patients with liver cirrhosis and ascites demonstrate effectivity and safety in preventing recurrent spontaneous bacterial peritonitis due to enterobacteria.[11,18,24]

## PROGNOSIS

The prognosis depends on the severity of the primary liver disease and acute reduction of liver function due to infection.[2]

Complications that occur due to spontaneous bacterial peritonitis, such as septic shock, gastrointestinal bleeding, encephalopathy, and renal failure, have very poor prognosis.[3,13,19]

Reduced liver function is characterized by increased serum billirubin, serum creatinine, and increased peripheral blood leukocyte count.

Fifty percent of patients with spontaneous bacterial peritonitis will die during hospitalization, while 69% of patients suffer from a recurrent spontaneous bacterial peritonitis attack within the following year, in which 50% would die.

## CONCLUSION

1. High risk factors for the development of spontaneous bacterial peritonitis in patients with liver cirrhosis and ascites are gastrointestinal bleeding, intravascular catheter insertion, ascites fluid protein concentration of less than 1 g/L, large volume paracentesis, urinary tract infection, and respiratory tract infection.
2. Spontaneous bacterial peritonitis is an infection of ascites fluid in Child-Pugh class C.
3. As much as 92% of spontaneous bacterial peritonitis cases are infected by one kind of bacteria (monomicrobe).
4. Because of the high morbidity and mortality rate due to infection of ascites fluid, diuretic therapy and therapy of prophylactic antibiotic therapy is highly recommended.
5. Cefotaxim is the first choice drug for its ability to deal with positive-gram, negative-gram, and anaerobic bacteria.
6. Culture of ascites fluid, blood, and urine should be performed in patients suspected with spontaneous bacterial peritonitis prior to the administration of antibiotics.

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