

Prevalence and Risk Factors for Unsuspected Spontaneous Ascitic Fluid Infection in Cirrhotics Undergoing Therapeutic Paracentesis in an Outpatient Clinic

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ABSTRACT

Background and Aim: Ascites is a common complication of liver cirrhosis, making patients more vulnerable to infectious diseases such as spontaneous bacterial peritonitis. There hasn't been much research done on infectious ascitic fluid in asymptomatic patients. The purpose of the study was to find out the infectious asymptomatic ascitic fluid incidence and risk factors in liver cirrhotic patients.

Materials and Methods: This cross-sectional study was conducted on 76 cirrhotic patients who underwent therapeutic paracentesis between September 2020 and February 2021 in an outpatient department of Jinnah Medical College, Peshawar. An 18-G catheter was used to collect ascitic fluid under strict aseptic conditions. Total and differential leucocyte counts, as well as total protein and albumin levels, were measured. The fluid was injected for bacterial culture of aerobic type and anaerobic blood culture bottles (10 mL each) under strict aseptic conditions. Individuals with abdominal pain, recent gastrointestinal bleeding, fever, SBP previous history, hepatic encephalopathy, impaired renal function, and treatment with antibiotics were excluded. Written informed consent and ethical approval were taken prior to study conduction. Demographic details, liver disease severity, and etiology were noted along with laboratory technique-based biochemical tests, ascitic fluid count, and culture. SPSS version 20 was used for data analysis.

Results: A total of 192 paracenteses were done on 76 liver cirrhosis patients with an average of 2.53 per patient. The overall mean age was 43.65±8.7 years. Of the total 76 patients, 55 (72.4%) were male and 21 (27.6%) were female. The ascites duration for study inclusion was 3 to 12 months. Hepatitis B, fatty liver disease, hepatitis C, and drugs were the major causes of cirrhosis among study patients. The prevalence of Hepatitis B, fatty liver disease, hepatitis C, and drugs was 27 (35.5%), 23 (30.3%), 11 (14.5%), and 15 (19.7%) respectively. The hepatic encephalopathy and variceal bleeding history were present in 16 (33.3%) and 32 (66.7%) respectively in a total of 48 (63.2%) cirrhotic patients. The class C and child Pugh class had 23 (30.3%) and 53 (69.7%) respectively. Null mortality was found in patients due to infection caused by spontaneous ascitic fluid.

Conclusion: Our study found that hepatitis B, fatty liver disease, hepatitis C, and drugs were the major causes of cirrhosis. Asymptomatic ascitic fluid infection was extremely rare in cirrhotic patients who attended an outpatient clinic and underwent therapeutic paracentesis. Additionally, our study found that the peritoneal fluid asymptomatic spontaneous infection is rare among cirrhotic patients undergoing outpatient base therapeutic paracentesis. Further investigation for ascitic fluid analysis's role in such infection without treatment is to be carried out.

Keywords: Ascitic fluid; Cirrhosis; Infection; Therapeutic paracentesis; Spontaneous bacterial peritonitis

INTRODUCTION

Ascites is a common complication of liver cirrhosis, making patients more vulnerable to infectious diseases such as spontaneous bacterial peritonitis. The obstinate, intolerant, and resistive ascitic patients have been treated with abdominal paracentesis [1]. Numerous cirrhotic patients are admitted on a regular basis for AP. As per Liver Diseases Association clinical practice strategies [2], neutrocytic ascites and bacterial peritonitis are the two major complications should be investigated through analysis of ascitic fluid [3, 4]. This approach has been evidently recognized for inpatients, but it is still dubious for outpatients. Several studies have shown that spontaneous bacterial peritonitis (SBP) is rare [59]. The differences in severity of liver disease between inpatients and outpatients may explain the SBP lower prevalence in patients. Though,

only a few investigations have been piloted to determine these differences. Spontaneous bacterial peritonitis (SBP) diagnosis with urinary strips has been investigated by numerous researchers [10]. But lower sensitivity of these urinary strips makes it the least preferred choice for SBP diagnosis. On the other hand, a Periscreen strip is an innovative stripe that effectively diagnoses spontaneous bacterial infections [11].

Cirrhotic and ascitic patients are more vulnerable to bacterial infections, the most common and potentially fatal of which is spontaneous bacterial peritonitis (SBP) [12]. It has typically been described in hospitalized patients with cirrhotic ascites, with 7–27% of patients showing evidence of occult peritoneal fluid infection at the time of hospital admission [13]. At the time of initial presentation, one-third of patients with infected peritoneal fluid has no overt signs or symptoms such as fever or abdominal pain [14]. The

peritoneal fluid infection could be diagnosed with ascitic fluid analysis conducted on the cirrhotic and ascitic patients of both outpatients and inpatients settings. The analysis of ascitic fluid in asymptomatic cirrhotic patients who underwent paracentesis is still unclear [15]. Very limited research has been done regarding asymptomatic cirrhotic patients [16]. The purpose of the study was to find out the infectious asymptomatic ascitic fluid incidence and risk factors in liver cirrhotic patients.

MATERIALS AND METHODS

This cross-sectional study was conducted on 76 cirrhotic patients who underwent therapeutic paracentesis between September 2020 and February 2021 in an outpatient department of Jinnah Medical College, Peshawar. An 18-G catheter was used to collect ascitic fluid under strict aseptic conditions. Total and differential leucocyte counts, as well as total protein and albumin levels, were measured. The fluid was injected for bacterial culture of aerobic type and anaerobic blood culture bottles (10 mL each) under strict aseptic conditions. Individuals with abdominal pain, recent gastrointestinal bleeding, fever, SBP previous history, hepatic encephalopathy, impaired renal function, and treatment with antibiotics were excluded. Written informed consent and ethical approval were taken prior to study conduction. Demographic details, liver disease severity, and etiology were noted along with laboratory technique-based biochemical tests, ascitic fluid count, and culture. Cirrhosis was diagnosed based on clinical, biochemical findings, and imaging. Baseline demographic information such as age, literacy, gender, and socioeconomic status were gathered. A thorough investigation into the cause of cirrhosis was carried out. The Child-Pugh class was used to assess disease severity.

An elevated ascitic fluid positive culture and absolute polymorph nuclear count (at least 250 cells/mm³), but without any source of infection for intra-abdominal surgically treatable, SBP were diagnosed. SBP Patients were hospitalized and intravenous cefotaxime was given for 5 days. A second paracentesis was performed to endorse that the contagion had been resolved. The quantitative data were expressed as mean and standard deviation, while the qualitative data were expressed as frequencies.

RESULTS

A total of 192 paracenteses were done on 76 liver cirrhosis patients with an average of 2.53 per patient. The overall mean age was 43.65±8.7 years. Of the total 76 patients, 55 (72.4%) were male and 21 (27.6%) were female as shown in Figure-1. The ascites duration for study inclusion was 3 to 12 months. Hepatitis B, fatty liver disease, hepatitis C, and drugs were the major causes of cirrhosis among study patients. The prevalence of Hepatitis B, fatty liver disease, hepatitis C, and drugs was 27 (35.5), 23 (30.3%), 11 (14.5%), and 15 (19.7%) respectively as demonstrated in Figure-II. The hepatic encephalopathy and variceal bleeding history were present in 16 (33.3%) and 32 (66.7%) respectively in a total of 48 (63.2%) cirrhosis patients as shown in Figure-III. The class C and child Pugh class had 23 (30.3%) and 53 (69.7%) respectively as

shown in Figure-IV. Null mortality was found in patients due to infection caused by spontaneous ascitic fluid.

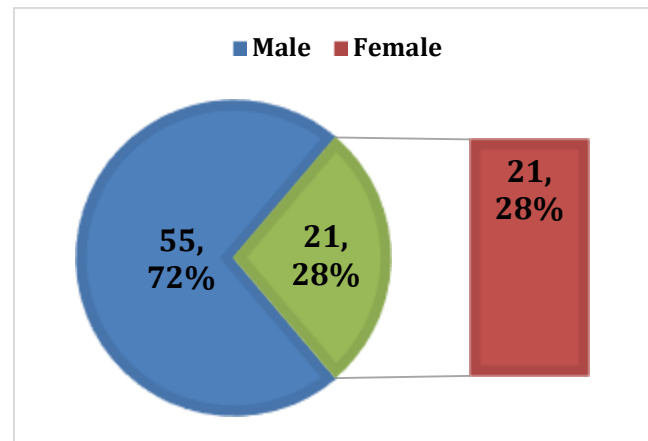


Figure-I Gender distribution n= (76)

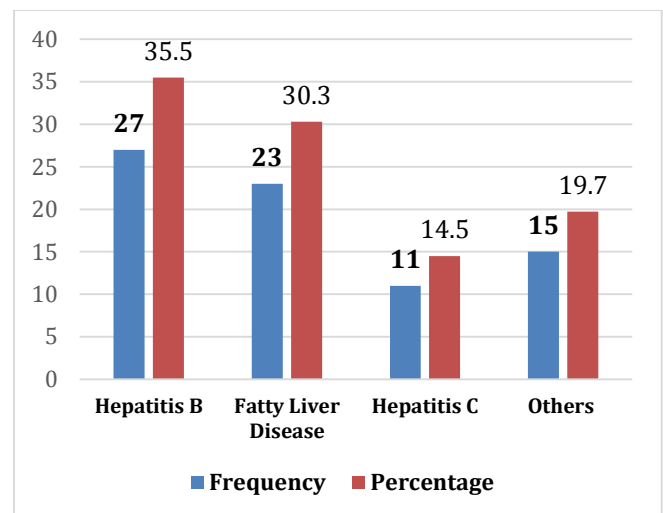


Figure-II Prevalence of various causes of Cirrhosis

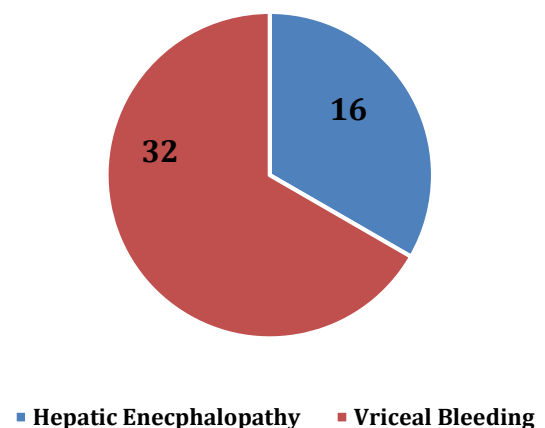


Figure-III The hepatic encephalopathy and variceal bleeding history prevalence (n=76)

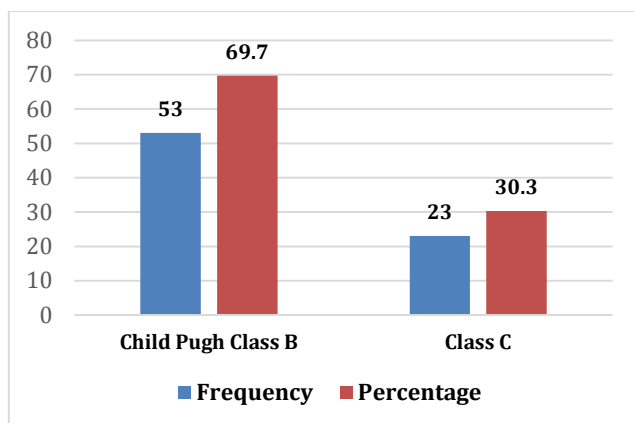


Figure-IV Prevalence of Class B and Child Pugh Class C (n=76)

DISCUSSION

In the present study, cirrhotic ascites patients who underwent large-volume paracentesis were examined and found a low rate of peritoneal fluid infection. Kawaratani et al. [17] reported a 1.4% prevalence of spontaneous bacterial peritonitis and 2.1% of culture-negative neurolyticascites among cirrhotic patients of outpatient setting whereas risk factors or symptoms for SBP were none. Also, monomicrobial nonneutrocytic bacterascites (MNB) prevalence was 3%. Another prospective study [18] obtained ascitic fluid cell counts and cultures in outpatients with refractory ascites undergoing large-volume paracentesis; 2.5% had MNB and none had SBP. It has been reported that SBP in 2% study population over a 2-year period [19]. United based study conducted on 37 cirrhotic patients underwent paracentesis were hospitalized, no peritoneal infection observed based on cultures and ascitic fluid cell counts among patients [20]. Likewise, a Spanish study analyzed 51 asymptomatic patients with 173 ascitic fluid samples whereas all the patients had cirrhotic refractory ascites [21]. The bacteria growth and cell count were 2.3% and <250PMN/mm3 respectively and categorized as asymptomatic.

SBP differs between asymptomatic patients and hospitalized patients. Gram-positive bacteria grow more frequently in ascitic fluid from former patients [16], rather than *E. coli* and *K. pneumoniae*, which prevail in hospitalized patients. Furthermore, co-existing type I hepatorenal syndrome is uncommon in these patients, reappearance of infection peritoneal fluid is uncommon and lower mortality rate was found within a year (33% vs. 50 to 70%) [22, 23].

Asymptomatic patients, the prevalence of SBP ranges from 0% to 3.5 % [24]. Kawaratani et al. [17] examined 427 investigative paracenteses accomplished over a 6-years duration. The exclusion criteria matched to those used in Kuo et al [25]'s study. In a multicenter study no case of SBP was reported among 67 patients and 270 paracentesis [26]. SBP was found to be present in 0.5% of people in a more recent study by Cadranet et al. [27]. A large-scale study of 976 outpatient paracentesis found a prevalence of SBP of 1.2%. In a large series, the SBP prevalence was <.5%, while it was beyond 8% in symptomatic outpatients. In contrast, the SBP prevalence was considerably lesser in outpatients compared to

inpatients (2.1% vs.11.2%; p 0.001). Thevenot et al. [28] revealed differences in SBP prevalence, reporting that in inpatients, the cirrhosis cause was more often hepatitis B, fatty liver, and Hepatitis C. SBP is more common in patients with low ascitic protein concentrations and cirrhotic patients with gastrointestinal bleeding requiring antibiotic prophylaxis [29]. Cirrhotic patients with hypernatremia or renal failure have also been shown to be at a higher risk of SBP [30].

The current study focused on the role and utility of ascitic fluid analysis in patients undergoing paracentesis with a lower prevalence of 2.5%. Though spontaneous bacterial infection with natural history without treatment was not investigated, obtaining an ascitic fluid count in such patients may be difficult. Despite the fact that the SBP outcome has been enhanced recently, but the mortality rate remains high [31]. SBP early diagnosis may aid in the early treatment implementation. For patients undergoing serial outpatient therapeutic paracentesis, testing ascitic fluid for cell count and differential count [32]. In asymptomatic patients, a bacterial culture is not required.

CONCLUSION

Our study found that hepatitis B, fatty liver disease, hepatitis C, and drugs were the major causes of cirrhosis. Asymptomatic ascitic fluid infection was extremely rare in cirrhotic patients who attended an outpatient clinic and underwent therapeutic paracentesis. Additionally, our study found that the peritoneal fluid asymptomatic spontaneous infection is rare among cirrhotic patients undergoing outpatient base therapeutic paracentesis. Further investigation for ascitic fluid analysis's role in such infection without treatment is to be carried out.

REFERENCES

1. Ramadan HK, Kamel SI, Rashed HA, Georgy AA, Ahmed AO. Antibiotic susceptibility of asymptomatic spontaneous bacterial peritonitis in decompensated liver cirrhosis: A prospective study. *Journal of Current Medical Research and Practice*. 2021 Jul 1;6(3):291.
2. Kuftinec G, Estrada JR, Bhamidimarri KR. Spontaneous Bacterial Peritonitis and Secondary Bacterial Peritonitis—a Comprehensive Review. *Current Hepatology Reports*. 2020 Nov 6:1-3.
3. Aharwar S, Shaikh RG. A Study to Estimate Spontaneous Bacterial Peritonitis in Chronic Liver Disease. *Indian Journal of Clinical Practice*. 2020 Jul;31(2).
4. Sehgal R, Singh IP, Mittal J. Associated Risk Factors and the Laboratory Parameters of Liver Cirrhosis after Spontaneous Bacterial Peritonitis (SBP). *Journal of Advanced Medical and Dental Sciences Research*. 2020 Oct 1;8(10):1-1.
5. Zhang L, Li X, Qi Y, Zhao Y, Wang F, Ma H, Qin X, Kong X, Qi Z, Zhang XY. Characteristics and influence of type 2 diabetes in cirrhosis ascites with spontaneous bacterial peritonitis. *medRxiv*. 2020 Jan 1.
6. Xiaoyu Z. Analysis and application of routine parameters in diagnosis of cirrhotic ascites complicated with asymptomatic spontaneous bacterial peritonitis. *JOURNAL OF NEW MEDICINE*. 2020 Mar 15;51(3):222.
7. Shizuma T. Spontaneous bacterial and fungal peritonitis in patients with liver cirrhosis: A literature review. *World journal of hepatology*. 2018 Feb 27;10(2):254.
8. Lahmer T, Brandl A, Rasch S, Schmid RM, Huber W. Fungal Peritonitis: Underestimated Disease in Critically Ill Patients

- with Liver Cirrhosis and Spontaneous Peritonitis. *PLoS One*. 2016;11:e0158389.
9. Fiore M, Leone S. Spontaneous fungal peritonitis: Epidemiology, current evidence and future prospective. *World J Gastroenterol*. 2016;22:7742–7747.
 10. Alexopoulou A, Agiasotelli D, Vasilieva LE, Dourakis SP. Bacterial translocation markers in liver cirrhosis. *Ann Gastroenterol*. 2017;30:486–497.
 11. Gómez-Hurtado I, Such J, Sanz Y, Francés R. Gut microbiota-related complications in cirrhosis. *World J Gastroenterol*. 2014;20:15624–15631.
 12. Guarner C, Soriano G. Bacterial translocation and its consequences in patients with cirrhosis. *Eur J Gastroenterol Hepatol*. 2005;17:27–31.
 13. Gentile I, Buonomo AR, Scotto R, Zappulo E, Borgia G. Infections worsen prognosis of patients with cirrhosis irrespective of the liver disease stage. *Eur J Intern Med*. 2017;46:e45–e47.
 14. Pijls KE, Koek GH, Elamin EE, de Vries H, Masclee AA, Jonkers DM. Large intestine permeability is increased in patients with compensated liver cirrhosis. *Am J Physiol Gastrointest Liver Physiol*. 2014;306:G147–G153.
 15. Zhang J, Gong F, Li L, Zhao M, Wu Z, Song J. The diagnostic value of neutrophil gelatinase-associated lipocalin and hepcidin in bacteria translocation of liver cirrhosis. *Int J Clin Exp Med*. 2015;8:16434–16444.
 16. Harputluoglu MM, Dertli R, Otlu B, Demirel U, Yener O, Bilgic Y, Erdogan MA, Atayan Y, Cagin YF. Nucleotide-Binding Oligomerization Domain-Containing Protein 2 Variants in Patients with Spontaneous Bacterial Peritonitis. *Dig Dis Sci*. 2016;61:1545–1552.
 17. Kawaratani H, Fukui H, Yoshiji H. Treatment for cirrhotic ascites. *Hepatol Res*. 2017;47:166–177.
 18. Usui S, Ebinuma H, Chu PS, Nakamoto N, Yamagishi Y, Saito H, Kanai T. Detection of bacterial DNA by in situ hybridization in patients with decompensated liver cirrhosis. *BMC Gastroenterol*. 2017;17:106.
 19. Bunchorntavakul C, Chamroonkul N, Chavalitdhamrong D. Bacterial infections in cirrhosis: A critical review and practical guidance. *World J Hepatol*. 2016;8:307–321.
 20. Schwab S, Lehmann J, Lutz P, Jansen C, Appenrodt B, Lammert F, Strassburg CP, Spengler U, Nischalke HD, Trebicka J. Influence of genetic variations in the SOD1 gene on the development of ascites and spontaneous bacterial peritonitis in decompensated liver cirrhosis. *Eur J Gastroenterol Hepatol*. 2017;29:800–804.
 21. Piotrowski D, Boroń-Kaczmarek A. Bacterial infections and hepatic encephalopathy in liver cirrhosis-prophylaxis and treatment. *Adv Med Sci*. 2017;62:345–356.
 22. Waidmann O, Kempf VA, Brandt C, Zeuzem S, Piiper A, Kronenberger B. Colonisation with multidrug-resistant bacteria is associated with increased mortality in patients with cirrhosis. *Gut*. 2015;64:1183–1184.
 23. Pouriki S, Vrioni G, Sambatakou H, Alexopoulou A, Vasilieva L, Mani I, Tsakris A, Dourakis SP. Intestinal colonization with resistant bacteria: a prognostic marker of mortality in decompensated cirrhosis. *Eur J Clin Microbiol Infect Dis*. 2018;37:127–134.
 24. Jalan R, Fernandez J, Wiest R, Schnabl B, Moreau R, Angeli P, Stadlbauer V, Gustot T, Bernardi M, Canton R, et al. Bacterial infections in cirrhosis: a position statement based on the EASL Special Conference 2013. *J Hepatol*. 2014;60:1310–1324.
 25. Kuo CH, Changchien CS, Yang CY, Sheen IS, Liaw YF. Bacteremia in patients with cirrhosis of the liver. *Liver*. 1991;11:334–339.
 26. Karvellas CJ, Abalde JG, Arabi YM, Kumar A; Cooperative Antimicrobial Therapy of Septic Shock (CATSS) Database Research Group. Appropriate and timely antimicrobial therapy in cirrhotic patients with spontaneous bacterial peritonitis-associated septic shock: a retrospective cohort study. *Aliment Pharmacol Ther*. 2015;41:747–757.
 27. Cadranet JF, Noursbaum JB, Bessaguet C, Nahon P, Nguyen-Khac E, Moreau R, et al. Low incidence of spontaneous bacterial peritonitis in asymptomatic cirrhotic outpatients. *World J Hepatol*. 2013; 5: 104–108.
 28. Thevenot T, Briot C, Mace V, Lison H, Elkrief L, Heurgue-Berlot A, et al. The periscreen strip is highly efficient for the exclusion of spontaneous bacterial peritonitis in cirrhotic outpatients. *Am J Gastroenterol*. 2016; 111: 1402–1409.
 29. Bartoletti M, Giannella M, Lewis R, Caraceni P, Tedeschi S, Paul M, Schramm C, Bruns T, Merli M, Cobos-Trigueros N, et al. A prospective multicentre study of the epidemiology and outcomes of bloodstream infection in cirrhotic patients. *Clin Microbiol Infect*. 2017 Epub ahead of print.
 30. Dionigi E, Garcovich M, Borzio M, Leandro G, Majumdar A, Tsami A, Arvaniti V, Roccarina D, Pinzani M, Burroughs AK, et al. Bacterial Infections Change Natural History of Cirrhosis Irrespective of Liver Disease Severity. *Am J Gastroenterol*. 2017;112:588–596.
 31. Shi L, Wu D, Wei L, Liu S, Zhao P, Tu B, Xie Y, Liu Y, Wang X, Liu L, et al. Corrigendum: Nosocomial and Community-Acquired Spontaneous Bacterial Peritonitis in patients with liver cirrhosis in China: Comparative Microbiology and Therapeutic Implications. *Sci Rep*. 2017;7:46868.
 32. Alexopoulou A, Vasilieva L, Agiasotelli D, Siranidi K, Pouriki S, Tsiriga A, Toutouza M, Dourakis SP. Extensively drug-resistant bacteria are an independent predictive factor of mortality in 130 patients with spontaneous bacterial peritonitis or spontaneous bacteremia. *World J Gastroenterol*. 2016;22:4049–4056.