# Incidence of spontaneous bacterial peritonitis among asymptomatic cirrhosis patients undergoing outpatient paracentesis: a systematic review and meta-analysis

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**Introduction** Spontaneous bacterial peritonitis (SBP) is a common complication of decompensated cirrhosis with high morbidity and mortality rate. There is a paucity of evidence regarding the incidence of SBP in asymptomatic liver cirrhosis patients undergoing routine out-patient large-volume paracentesis (LVP). The aim of this study was to perform a systematic review and meta-analysis to determine the incidence of SBP among asymptomatic decompensated cirrhosis patients undergoing routine outpatient LVP.

**Methods** A systematic search of Ovid Medline, Embase, Web of Science and CENTRAL electronic databases was performed in January 2021, along with a manual search of reference lists of retrieved articles. Data were extracted to determine the incidence of SBP [polymorphonuclear cells (PMNs) greater than 250 PMNs/mm$^3$ with or without positive culture] and the incidence of all positive paracentesis (SBP or bacterascites-positive ascitic culture but no elevation in PMNs).

**Results** A total of 504 studies were retrieved with 16 studies being included in the review. A total of 1532 patients were included with a total of 4016 paracentesis performed. The incidence of a positive paracentesis (SBP and/or bacterascitis) was 4% [95% confidence interval (CI), 3–6%]. However, the incidence of definite SBP was 2% (95% CI, 1–3%).

**Conclusion** The incidence of SBP in asymptomatic outpatients with decompensated cirrhosis requiring LVP is low. The benefit of routine analysis of all paracentesis samples in this population is questionable. Further studies are required to determine the cost-effectiveness of routine analysis and to determine if certain subgroups are at higher risk of SBP that require routine analysis. Eur J Gastroenterol Hepatol XXX: 00–00


## Introduction

Ascites are the most common complication of decompensated cirrhosis. More than one-half of compensated cirrhosis patients will develop ascites within 10 years [1]. Large-volume paracentesis (LVP) has been recommended as treatment for the patient with ascites that is refractory or intolerant to dietary and medical treatments [2,3]. Decompensated cirrhosis patients with ascites are prone to spontaneous bacterial peritonitis (SBP). It has been reported that one-third of hospitalized patients have SBP and two-thirds will have a recurrence of SBP in the first year. Moreover, SBP is associated with worse outcomes in decompensated cirrhosis as it can lead to septic shock, renal failure, gastrointestinal bleeding and hepatic encephalopathy with mortality rates up to 50% [4–6].

SBP is diagnosed when ascitic fluid neutrophils (PMN) are >250/mm$^3$ which shows high sensitivity while PMN >500/mm$^3$ has high specificity. However, positive bacterial culture found in the ascitic fluid is observed in <40% of cases. Patients with high PMNs and culture-negative have similar outcomes to patients with positive ascitic fluid cultures. Also, patients with bacterascitis in which ascitic fluid cultures are positive and PMN <250/mm$^3$ are usually asymptomatic, likely representing transient ascitic fluid colonization, but in symptomatic patients, this could indicate early stage of SBP. For that reason, most guidelines recommended using PMN >250/mm$^3$ (in the absence of secondary bacterial peritonitis) as the diagnostic criteria for SBP [7–11].

Analysis of the ascitic fluid for cell counts, differential and culture to detect early SBP has been recommended in all symptomatic and hospitalized patients. The American Society of the Study of Liver Disease (AASLD)

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practice guidelines for ascites management and European Association for the Study of the Liver guidelines for decompensated cirrhosis recommend fluid analysis for new-onset or hospitalized patients with ascites [10,11]. The AASLD practice guidelines indicate that patients undergoing serial outpatient therapeutic paracenteses probably should be tested only for cell count and differential. Although there are several studies on the routine analysis of ascitic fluid on asymptomatic decompensated cirrhosis patients undergoing LVP, there has been no systematic review or meta-analysis examining the incidence of SBP among asymptomatic decompensated cirrhosis patients undergoing routine LVP.

## Methods

### Search strategy

From an a priori protocol, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses reporting guidelines were followed. A systematic search was conducted by a clinical librarian with experience in conducting electronic literature searches (A.L.) in collaboration with two other authors (A.A. and M.A.). To identify relevant literature, we searched Medline, Embase, Web of Science and CENTRAL electronic databases from inception to 6 January 2021. In addition, grey literature search was performed in two popular web engines Google.ca and Google Scholar, conference proceedings, and clinical trial registry 'clinicaltrials.gov'. Furthermore, reference lists of relevant papers and reviews were reviewed. The sensitive search strategies were created using a combination of keywords and standardized index terms using alternative spellings and word endings such as but not limited to the terms: 'Spontaneous bacterial peritonitis', 'SBP', 'Asymptomatic SBP', 'End Stage Liver Disease', 'Liver Cirrhosis', 'Peritonitis', 'Paracentesis', 'Ascitic Fluid', 'Ascites', 'Asymptomatic', 'Ambulatory Care', 'Outpatient clinics', 'Hospital', and 'Outpatients'. All searches were restricted to English language. The electronic search strategies for each database are available in the Appendix, Supplemental digital content 1, *http://links.lww.com/EJGH/A717*. All relevant studies after removal of duplication were exported to EndNote X9 bibliographic software (Clarivate Analytics, Philadelphia, Pennsylvania, USA).

### Study selection

We included any randomized controlled trials and prospective or retrospective cohort studies that reported on the prevalence of SBP among asymptomatic decompensated cirrhosis patients undergoing LVP. We excluded: (1) symptomatic patients, (2) paracentesis in the inpatient setting or hospitalized patients, (3) pediatric population with age <18 and (4) studies published in the non-English language. Conference abstracts that provided the same outcome and met inclusion criteria were included in our review.

### Data abstraction

All identified articles were screened independently by two reviewers (A.A. and M.A.), first through title and abstract screening, then full-text screening. In the case of failure to achieve consensus, a third reviewer adjudicated and made the final determination (M.B.). Data were extracted from eligible studies independently by two reviewers (A.A. and M.A.) and preceded by piloting the data collection document. Disagreements were resolved by consensus and a third reviewer (M.B.). Study quality assessments tool is not applicable in our analysis due to the nature of our study. Data extraction included the following variables: publication information (EndNote reference number, name of first author, year of publication, country study conducted in), sample size, age, etiology of cirrhosis, sex, number of patients with SBP or Bacterascitis. There was no protocol deviation.

### Outcomes assessed

Our primary outcome of interest was the proportion of paracentesis positive for SBP, defined as absolute neutrophilic count >250 with/without positive ascitic culture, formally known as culture-negative neutrophilic ascites among asymptomatic decompensated cirrhosis patients undergoing routine LVP. Secondary outcome for the present study was to evaluate the proportion of all positive paracentesis (SBP+Bacterascitis).

### Statistical analysis

The proportion of positive tests was pooled and meta-analyzed to obtain an average estimate and 95% confidence interval (CI). Meta-analyses were conducted in Stata 13.0 using the *metaprop* command, exact CIs, the Freeman–Tukey double arcsine transformation, and random effect models to account for methodological and clinical heterogeneity (Nyaga *et al*., 2014) [12]. Statistical heterogeneity was assessed using the $I^2$ statistic (Higgins *et al*., 2003) [13]. Lastly, publication bias was evaluated using funnel plots for proportions in SAS 9.4 (Higgins *et al*., 2007) [14]; specifically, the plot was visually inspected for asymmetry around the average proportion (Spiegelhalter, 2008) [15].

## Results

A total of 499 studies were identified through electronic database searches and an additional five records through supplementary sources from reviewing citing papers and reference lists of selected relevant studies; 419 titles and abstracts were screened after duplicate articles were removed; 38 full-text articles and conference abstracts were reviewed for eligibility and 16 were included [16–31]. Two articles [31,32] had similar results and data; the author and journal were contacted but did not respond. To avoid data duplication, we included the results of the first article [31] and excluded the second article [32] as a duplicate (Fig. 1).

Table 1 represents a summary of the studies included and patient characteristics. Included studies were published between 1994 and 2019. Three publications were retrospective studies (16, 19 and 27). Six of the publications were conference abstracts (16, 17, 22, 25, 27 and 28). The age range for the patients was 29–92 years based on the available data. The total number of patients was 1532. The most common etiology of cirrhosis was alcohol and viral hepatitis. Patients were predominantly males.

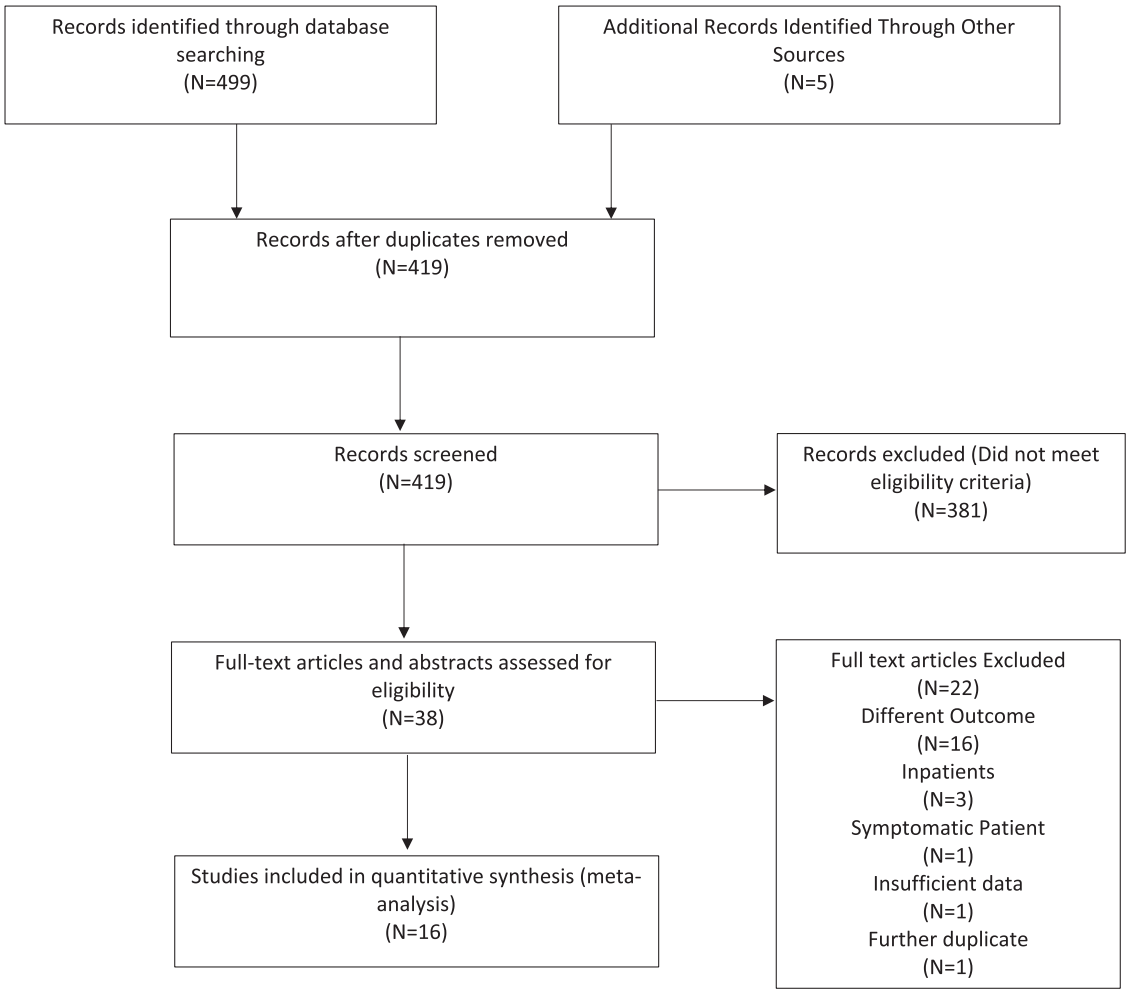


**Fig. 1.** Flowsheet of study selection.

The total number of paracentesis included was 4016. There were 141 patients with SBP and 42 patients with bacterascitis. Of the identified studies, the proportion of SBP positive paracentesis ranged from 0 to 12%, and the proportion of SBP and/or bacterioascitis positive paracentesis ranged from 0 to 24%. Combining the studies, the overall incidence of SBP was 2% (95% CI, 1–3%), and the overall incidence of all positive fluid analysis (SBP or bacterascitis) was 4% (95% CI, 3–6%) (Fig. 2). Results were similar when studies published in abstract form only were excluded (2%, 95% CI, 1–4% and 5%, 95% CI, 3–7%, respectively). There was considerably heterogeneity in the results ($I^2 = 80$ and 79%, respectively) and funnel plots (Fig. 3) did not suggest the presence of publication bias.

## Discussion

SBP is a common complication among decompensated cirrhosis patients and can present with symptoms (abdominal pain, tenderness, nausea and vomiting), hepatic encephalopathy, acute on chronic liver failure, shock and/or gastrointestinal bleeding [19,33,34]. Previously, the mortality rate from SBP was up to 90% but with early diagnosis and treatment, survival has improved significantly [35]. The rate of asymptomatic SBP among decompensated cirrhosis patients has been reported to be low, and to our knowledge, this is first systematic review and meta-analysis looking at the rate of SBP among asymptomatic decompensated cirrhosis patients undergoing LVP [9].

Several studies have shown the rate of SBP among decompensated cirrhosis patients undergoing outpatient paracentesis to be low (0–4%). Other studies have reported higher rates of SBP (8–10%) but this could be affected by the low rates and non-consecutive number of paracentesis (37, 80 and 86, respectively) [24,30,31]. Our analysis included more than 4000 paracenteses in 1532 patients, and the reported rate of SBP among asymptomatic decompensated cirrhosis patients undergoing routine LVP was 2% (95% CI, 1–3%). Bacterascitis with PMN <250/mm$^3$ might be transient or represent early SBP. Positive paracentesis (bacteriascitis and/or SBP) among the decompensated cirrhosis patients in our analysis was still low (4%). Conversely, the rate of SBP among hospitalized patients has been reported in previous studies to be up to 30% [36–38]. However, these are inherently different populations and the differences in the reported incidence of SBP can be explained by selection bias relating to the need for hospitalization due to factors such as worsening liver disease, gastrointestinal bleeding and previous SBP, which all increase the risk of SBP [4–6].

Multiple societies recommend using antibiotics prophylaxis in decompensated cirrhosis patients with acute gastrointestinal bleeding, primary prophylaxis in the patients with low total protein content in the ascitic fluid and in

**Table 1.** Characteristics of the articles included in the study

| Study | Year | Country | Type of study | Type | Age, years (SD) [Range] | No. patients | Etiology (number; percentage) | Gender: number of male (% male) |
|---|---|---|---|---|---|---|---|---|
| Stern *et al*. [16] | 1994 | USA | Retrospective | Abstract | 56 [29–88] | 26 | Not provided | 19 (73%) |
| Kolle *et al*. [17] | 1996 | Spain | Prospective | Abstract | Not provided | 51 | Not provided | Not provided |
| Jeffries *et al*. [18] | 1999 | USA | Prospective | Full | 55 (11) [37–76] | 29 | Alcohol (12; 41.4%) | 23 (79.31%) |
| | | | | | | | Alcohol and HCV (6; 20.7%) | |
| | | | | | | | HCV (5; 17.2%) | |
| | | | | | | | Cryptogenic (2; 6.9%) | |
| | | | | | | | Other (4; 13.8%) | |
| Evans *et al*. [19] | 2003 | USA | Retrospective | Full | 58 | 427 | Alcohol (132; 31%) | 316 (74%) |
| | | | | | | | Viral hepatitis (± alcohol use) (162; 38%), cholestatic liver disease (PBC, PSC) (51; 12%), Other (82; 19%). | |
| Romney *et al*. [20] | 2005 | France | Prospective | Full | 59 (9) [38–92] | 67 | Alcohol (59) | 48 (71.6%) |
| | | | | | | | HCV (4) | |
| | | | | | | | HBV (1) | |
| | | | | | | | Hemochromatosis (1) | |
| | | | | | | | Other (2) | |
| Castellote *et al*. [21] | 2007 | Spain | Prospective | Full | 63 (14) | 40 | Alcohol (16) | 23 (57.5%) |
| | | | | | | | HCV (14) | |
| | | | | | | | Alcohol and HCV (5) | |
| | | | | | | | HBV (2) | |
| | | | | | | | Autoimmune (2) | |
| | | | | | | | Cryptogenetic (1) | |
| Sersté *et al*. [22] | 2010 | France | Prospective | Abstract | 58 (10) | 31 | Alcohol (41.9%) | 25 (80.6%) |
| | | | | | | | HCV (25.8%) | |
| | | | | | | | Cryptogenic (6.2%) | |
| Mohan and Venkataraman [23] | 2011 | India | Prospective | Full | 47.1 | 110 | Alcohol (61; 56%) | Not provided |
| | | | | | | | HBV (24; 22%) | |
| | | | | | | | HCV (10; 9%) | |
| | | | | | | | Others (15; 14%) | |
| Kasztelan-Szczerbinska *et al*. [24] | 2011 | Poland | Prospective | Full | 56.2 | 37 | Not provided | 31 (83.3%) |
| Major *et al*. [25] | 2011 | UK | Prospective | Abstract | Median: 54 [35–83] | 45 | Alcoholic liver disease (ALD) in 32 (71%), HCV in 5 (11%), HCV/ALD in 1, PBC in 1, NASH in 1 and other/cryptogenic in 5 | 39 (86.6%) |
| Cadranel *et al*. [26] | 2013 | France | Prospective | Full | 61 (11) | 355 | Alcohol (83.7%) | 748 (71.9) |
| Sugumaran *et al*. [27] | 2014 | UK | Retrospective | Abstract | Not provided | Not provided | Not provided | Not provided |
| Albert *et al*. [28] | 2015 | USA | Prospective | Abstract | 66 (13) | 23 | Cirrhosis (94%) | Not provided |
| | | | | | | | Malignant (6%) | |
| Haddad *et al*. [29] | 2015 | Brazil | Prospective | Full | 57 (11) | 148 | Alcohol (33; 22.3%) | 90 (60.8%) |
| | | | | | | | Viral hepatitis (HBV or HCV) (40; 27%) | |
| | | | | | | | Other (33; 22.3%) | |
| Khalid *et al*. [30] | 2015 | Pakistan | Prospective | Full | 61 | 80 | HBV in 10 (12.5%) and HCV in 70 (81.5%) patients | 80 (100%) |
| Ather *et al*. [31] | 2019 | Pakistan | Prospective | Full | 50.91 (4.08) | 86 | Not provided | Not provided |

HBV, hepatitis B virus; HCV, hepatitis C virus; NASH, nonalcoholic steatohepatitis; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis.

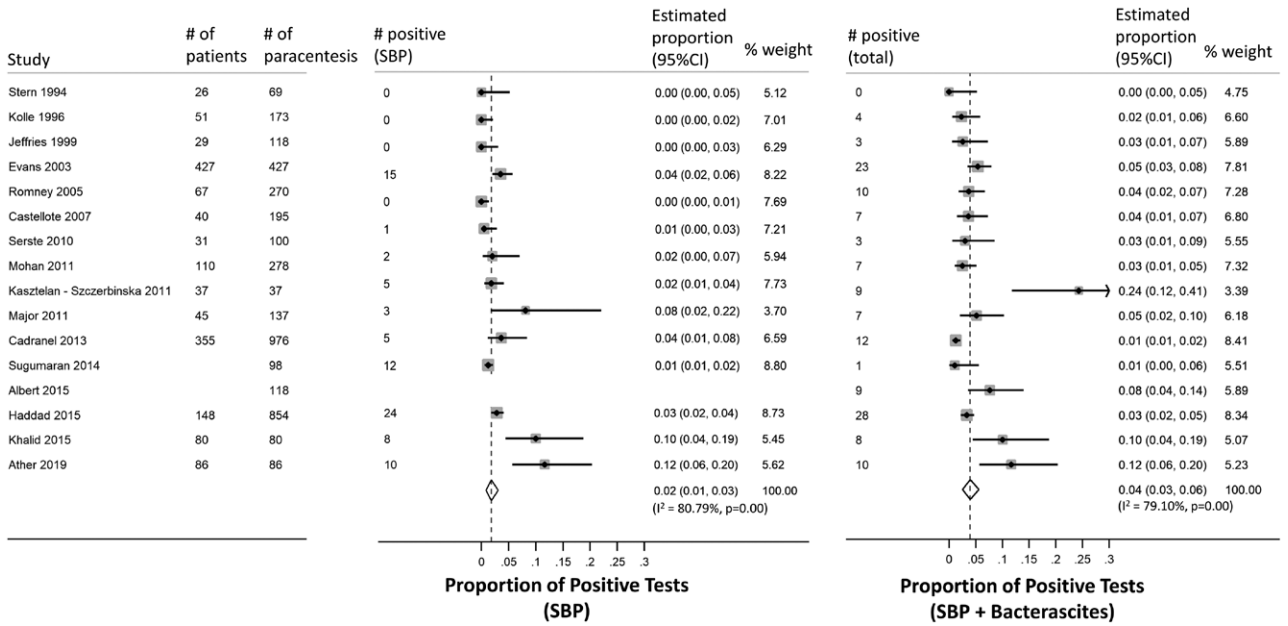


**Fig. 2.** Proportion of patients with positive fluid analysis. SBP, spontaneous bacterial peritonitis.

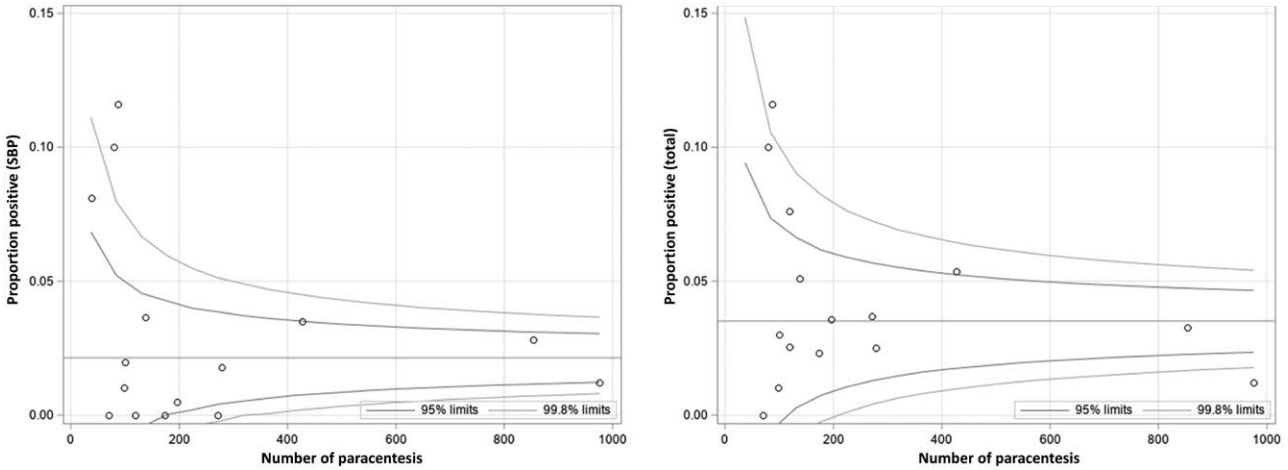


**Fig. 3.** Funnel plot of publication bias.

the patient with previous SBP as secondary prophylaxis [10,11]. Primary prophylaxis in patients with low ascitic fluid protein and advanced liver disease or impaired renal faction has shown to improve survival by 3 months and reduces the risk of SBP and hepatorenal syndrome up to 1 year [39]. Patients with an episode of SBP have a recurrence rate up to 70% in 1 year with a survival rate of 30% at 2 years [10]. Using prophylactic antibiotics after an episode of SBP has been shown to reduce the recurrence of SBP in many studies [40,41]. Most of the studies in our analysis excluded patients on prophylactic antibiotics; however, the two studies which included a proportion (37%) of patients on prophylactic antibiotics did not show a statistically difference between those who were on antibiotics versus those who were not [20,28]. Therefore, most asymptomatic decompensated cirrhosis patients undergoing routine outpatient LVP may not require routine fluid analysis regardless of their antibiotic prophylaxis exposure unless clinical factors (fever, abdominal pain, etc.) and laboratory markers (increasing WBC, declining renal function, etc.) would result in a change in management.

Another important consideration is cost-effectiveness of obtaining routine cell counts in asymptomatic patients with ascites. Although there is no additional procedural risk for the patient. in the USA, reimbursement through Medicare and Medicaid, fluid analysis for cell counts costs 5.6 US dollar (USD) and aerobic and anerobic fluid culture costs 8.62 and 9.47 USD, respectively [42]. Based on the rate of SBP in our analysis, 100 ascitic fluid paracentesis would be needed to detect one episode of SBP which would cost around 560 USD. The detection of one positive ascitic fluid (bacteriostatic and/or SBP) would require 25 ascitic fluid paracentesis at a cost of 614.75 USD. These direct laboratory reimbursement costs do not account for additional costs, for example, related to location (for example, hospital-based ambulatory care), staff and equipment. Furthermore, patients refractory or intolerant to diuretics often have frequent repeat paracentesis and have fluid analysis requested as a routine. Our findings suggest that fluid analysis for SBP could be deferred in most cases, and continue to be based on clinical assessment or appearance of the ascites fluid (such as cloudy or

bloody appearance) in otherwise asymptomatic patients. A formal cost-effectiveness analysis accounting for these factors would help address this issue.

Our study has many strengths. This is the first systematic review and meta-analysis of outpatient LVP among decompensated cirrhosis patients. Our literature search was broad and inclusive with clearly defined inclusion and exclusion criteria. Given the large sample size, we were able to provide a precise estimate of SBP in outpatients undergoing LVP. However, within this context, we must also highlight several limitations. First, due to the incidence nature of our study and the inclusion of conference abstracts, there was a lack of quality assessment tools. Second, important laboratory variables (i.e. MELD score, total protein in ascitic fluid, etc.) were difficult to pool in this analysis due to heterogeneity in reporting in the included studies. Lastly, although there was statistical heterogeneity in the studies included there was no clinical heterogenicity with clear inclusion and exclusion criteria. However, there is insufficient data for us to extrapolate our findings to certain higher-risk groups such as patients with prior SBP and upper gastrointestinal bleeding.

### *Conclusion*

This meta-analysis shows that the rate of SBP among asymptomatic decompensated cirrhosis outpatients undergoing LVP is very low and questions the clinical utility of obtaining routine ascitic fluid analysis among asymptomatic patients. Moreover, it is likely not cost-effective, but this requires further modeling.

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A.A., M.A., M.B. and K.P.: study concept and design. A.A., M.A. and A.I.: literature search. A.A., M.A. and K.P.: analysis and interpretation of data; drafting of the article. A.A., M.A., O.A., K.P., D.R., M.S., M.B. and K.P.: critical revision of the article for important intellectual content. K.P.: statistical analysis.

### *Conflicts of interest*

There are no conflicts of interest.

## References

1 Ginés P, Quintero E, Arroyo V, Terés J, Bruguera M, Rimola A, *et al*. Compensated cirrhosis: natural history and prognostic factors. *Hepatology* 1987; 7:122–128.
2 Kuiper JJ, van Buuren HR, de Man RA. Ascites in cirrhosis: a review of management and complications. *Neth J Med* 2007; 65:283–288.
3 Moore KP, Wong F, Gines P, Bernardi M, Ochs A, Salerno F, *et al*. The management of ascites in cirrhosis: report on the consensus conference of the International Ascites Club. *Hepatology* 2003; 38:258–266.
4 Thévenot T, Briot C, Macé V, Lison H, Elkrief L, Heurgué-Berlot A, *et al*.; CFEHTP, ANGH and the PerDRISLA study group. The periscreen strip is highly efficient for the exclusion of spontaneous bacterial peritonitis in cirrhotic outpatients. *Am J Gastroenterol* 2016; 111:1402–1409.
5 Ichou L, Carbonell N, Rautou PE, Laurans L, Bourcier S, Pichereau C, *et al*. Ascitic fluid TREM-1 for the diagnosis of spontaneous bacterial peritonitis. *Gut* 2016; 65:536–538.
6 Coral G, Mattos AA, Damo DF, Viégas AC. Spontaneous bacterial peritonitis: prevalence and prognosis. Experience from a general hospital in Porto Alegre, RS, Brazil (1991-2000). *Arquivos de Gastroenterologia* 2002; 39:158–162.
7 Pelletier G, Salmon D, Ink O, Hannoun S, Attali P, Buffet C, Etienne JP. Culture-negative neutrocytic ascites: a less severe variant of spontaneous bacterial peritonitis. *J Hepatol* 1990; 10:327–331.
8 Terg R, Levi D, Lopez P, Rafaelli C, Rojter S, Abecasis R, *et al*. Analysis of clinical course and prognosis of culture-positive spontaneous bacterial peritonitis and neutrocytic ascites. Evidence of the same disease. *Dig Dis Sci* 1992; 37:1499–1504.
9 Aithal GP, Palaniyappan N, China L, Härmälä S, Macken L, Ryan JM, *et al*. Guidelines on the management of ascites in cirrhosis. *Gut* 2021; 70:9–29.
10 European Association for the Study of the Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. *J Hepatol* 2010; 53:397–417.
11 Runyon BA. Introduction to the revised American Association for the Study of Liver Diseases Practice Guideline management of adult patients with ascites due to cirrhosis 2012. *Hepatology* 2013; 57:1651–3.
12 Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. *Arch Public Health* 2014; 72:39.
13 Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; 327:557–560.
14 Higgins J, Green S, editors. *Cochrane handbook for systematic reviews of interventions, version.* 5th ed. The Cochrane collaboration; 2011.
15 Spiegelhalter DJ. Funnel plots for comparing institutional performance. *Stat Med* 2005; 24:1185–1202.
16 Stern MA, Chalasani N, Strauss RM. Is it cost-effective or necessary to routinely, analyze ascitic fluid in an asymptomatic outpatient population of cirrhotics. *Hepatology* 1994;19:I127. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399: WB SAUNDERS CO.
17 Kolle L, Ortiz J, Ricart E, Sabat M, SolaVera J, Minana J, *et al*. Ascitic fluid culture is not necessary in asymptomatic cirrhotic outpatients undergoing repeated therapeutic paracentesis. *Hepatology* 1996;24:1274. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399: WB SAUNDERS CO.
18 Jeffries MA, Stern MA, Gunaratnam NT, Fontana RJ. Unsuspected infection is infrequent in asymptomatic outpatients with refractory ascites undergoing therapeutic paracentesis. *Am J Gastroenterol* 1999; 94:2972–2976.
19 Evans LT, Kim WR, Poterucha JJ, Kamath PS. Spontaneous bacterial peritonitis in asymptomatic outpatients with cirrhotic ascites. *Hepatology* 2003; 37:897–901.
20 Romney R, Mathurin P, Ganne-Carrié N, Halimi C, Medini A, Lemaitre P, Gruaud P, *et al*. Usefulness of routine analysis of ascitic fluid at the time of therapeutic paracentesis in asymptomatic outpatients: results of a multicenter prospective study. *Gastroentérol Clin Biol* 2005; 29:275–279.
21 Castellote J, Girbau A, Maisterra S, Charhi N, Ballester R, Xiol X. Spontaneous bacterial peritonitis and bacterascites prevalence in asymptomatic cirrhotic outpatients undergoing large-volume paracentesis. *J Gastroenterol Hepatol* 2008; 23:256–259.
22 Sersté T, Bert F, Leflon-Guibout V, Chauveau C, Asselah T, Francoz C, Durand F, *et al*. 854 bacterial DNA is rarely detected in the serum and the ascitic fluid of noninfected outpatients with cirrhosis and ascites treated by paracentesis. *J Hepatol* 2010; 52:S332–S333.
23 Mohan P, Venkataraman J. Prevalence and risk factors for unsuspected spontaneous ascitic fluid infection in cirrhotics undergoing therapeutic paracentesis in an outpatient clinic. *Indian J Gastroenterol* 2011; 30:221–224.
24 Kasztelan-Szczerbinska B, Słomka M, Celinski K, Serwacki M, Szczerbinski M, Cichoz-Lach H. Prevalence of spontaneous bacterial peritonitis in asymptomatic inpatients with decompensated liver cirrhosis – a pilot study. *Adv Med Sci* 2011; 56:13–17.
25 Major GA, Ingram R, Chivinge A, James M. How can risk reduction and early detection of SBP in cirrhotic ascites be improved? *Gut* 2011; 60(Suppl 1):A239.
26 Cadranel JF, Nousbaum 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.
27 Sugumaran A, Martin D, Czajkowski M, Yeoman A. PWE-126 spontaneous bacterial peritonitis (SBP) is rare among routine elective day-case therapeutic paracentesis: is routine fluid analysis justified? *Gut* 2014; 63(Suppl 1):A180.

28 Albert D, Singla M, Cheng F, Sjogren M, Torres D. Is prevalence of spontaneous bacterial peritonitis different among inpatients or outpatients with ascites? *Hepatology* 2015; 285:62.

29 Haddad L, Conte TM, Ducatti L, Nacif L, D'Albuquerque LA, Andraus W. MELD score is not related to spontaneous bacterial peritonitis. *Gastroenterol Res Pract* 2015; 2015:270456.

30 Khalid M, Samiullah R, Khalid SR. Frequency of asymptomatic spontaneous bacterial peritonitis in outdoor patients with liver cirrhosis. *Pakistan Armed Forces Med J* 2015; 65:278–281.

31 Ather MM, Arif MM, Qadir M, Khan HR, Khaliq SA, Rasheeq T. Frequency of asymptomatic spontaneous bacterial peritonitis in outdoor patients with liver cirrhosis. *Med Forum Monthly* 2019; 30:2–5.

32 Ali M, Bukhari T, Qasim O. Asymptomatic spontaneous bacterial peritonitis in patients with liver cirrhosis. *World J Pharm Med Res* 2020; 6:347–349.

33 Nousbaum JB, Cadranel JF, Nahon P, Khac EN, Moreau R, Thévenot T, *et al*.; Club Francophone pour l'Etude de l'Hypertension Portale; Association Nationale des Hépato-Gastroentérologues des Hôpitaux Généraux de France. Diagnostic accuracy of the Multistix 8 SG reagent strip in diagnosis of spontaneous bacterial peritonitis. *Hepatology* 2007; 45:1275–1281.

34 Plessier A, Denninger MH, Consigny Y, Pessione F, Francoz C, Durand F, *et al*. Coagulation disorders in patients with cirrhosis and severe sepsis. *Liver Int* 2003; 23:440–448.

35 Garcia-Tsao G. Current management of the complications of cirrhosis and portal hypertension: variceal hemorrhage, ascites, and spontaneous bacterial peritonitis. *Gastroenterology* 2001; 120:726–748.

36 Fernández J, Navasa M, Gómez J, Colmenero J, Vila J, Arroyo V, Rodés J. Bacterial infections in cirrhosis: epidemiological changes with invasive procedures and norfloxacin prophylaxis. *Hepatology* 2002; 35:140–148.

37 Piano S, Fasolato S, Salinas F, Romano A, Tonon M, Morando F, *et al*. The empirical antibiotic treatment of nosocomial spontaneous bacterial peritonitis: results of a randomized, controlled clinical trial. *Hepatology* 2016; 63:1299–1309.

38 Fasolato S, Angeli P, Dallagnese L, Maresio G, Zola E, Mazza E, *et al*. Renal failure and bacterial infections in patients with cirrhosis: epidemiology and clinical features. *Hepatology* 2007; 45:223–229.

39 Fernández J, Navasa M, Planas R, Montoliu S, Monfort D, Soriano G, *et al*. Primary prophylaxis of spontaneous bacterial peritonitis delays hepatorenal syndrome and improves survival in cirrhosis. *Gastroenterology* 2007; 133:818–824.

40 Ginés P, Rimola A, Planas R, Vargas V, Marco F, Almela M, *et al*. Norfloxacin prevents spontaneous bacterial peritonitis recurrence in cirrhosis: results of a double-blind, placebo-controlled trial. *Hepatology* 1990; 12:716–724.

41 Bauer TM, Follo A, Navasa M, Vila J, Planas R, Clemente G, *et al*. Daily norfloxacin is more effective than weekly rufloxacin in prevention of spontaneous bacterial peritonitis recurrence. *Dig Dis Sci* 2002; 47:1356–1361.

42 Centers for Medicare and Medicaid Services. Clinical laboratory fee schedule files. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Clinical-Laboratory-Fee-Schedule-Files. Accessed 21 March 2021.