

## ORIGINAL ARTICLE

# Prevalence of Culture Negative Ascitic Fluid Infection among Chronic Liver Disease Patients

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## ABSTRACT

**Background and Aim:** Ascitic fluid infection is pre-existing ascites infection of both symptomatic and asymptomatic types without abdominal source in chronic liver disease patients. Culture negative ascites are common infections in patients with chronic liver disease. The aim of the recent study was to determine the prevalence of culture-negative ascitic fluid infection among chronic liver disease patients.

**Methodology:** This cross-sectional study was conducted on 134 patients with ascitic fluid infection due to chronic liver disease in the Department of Medicine and Gastroenterology, Pak International Medical College, Peshawar for six months duration from December 2020 to May 2021. All the ascitic infectious patients due to chronic liver disease regardless of their age and gender showing ascitic fluid infection symptoms such as tenderness, fever, and abdominal pain were admitted and underwent laboratory culture examination. Based on bacterial growth, all the chronic liver disease patients were grouped into two; Group-I of no bacterial growth and Group-II of positive bacterial growth. All the patients having an intra-abdominal infection or taking antibiotics were excluded.

**Results:** Of the total 134 patients, 84 (62.7%) were male and 50 (37.3%) were females. Overall mean age was 47.56±19.8 years with an age range of 20 years to 80 years. Of the total 134 cases, the prevalence of positive and negative culture ascites were 30 (22.4%) and 104 (77.6%) respectively. Out of 104 culture-negative patients, 65 (62.5%) were male patients whereas 39 (37.5%) were females. Chronic liver disease means duration was 8.9±2.6 months with a range of 6 months to 18 months. For all the patients above 40 years, the prevalence of culture-positive and negative ascitic infection was 20 (66.7%) and 77 (74.1%) respectively. The prevalence of male patients was higher (62.5%) among culture-negative patients due to chronic liver disease.

**Conclusion:** Our study found that the prevalence of culture-negative ascitic fluid was higher at 77.6% among male patients. Also, ascitic fluid infection due to chronic liver disease was higher in patients of age above 40 years.

**Keywords:** Ascitic fluid, Culture-negative ascitic fluid infections, Chronic liver disease

## INTRODUCTION

Chronic liver disease patients are especially vulnerable to infections, which are more common in cirrhotic [1]. Cirrhosis is frequently associated with ascites. Infections are a major cause of morbidity and mortality in patients with chronic liver disease (CLD). The mechanism underlying the increased susceptibility to infection is unknown [2]. Spontaneous bacterial peritonitis (SBP), dermatologic infections, community-acquired pneumonia, bacteremia, and urinary tract infection (UTI) are the most common bacterial infections in CLD patients [3]. Ascitic fluid culture is required for ascitic fluid infection diagnosis and classification [4]. Bacteriological culture of ascitic fluid is negative in approximately 40% of adult patients with spontaneous bacterial peritonitis suggestive clinical manifestations [5]. Based on ascitic fluid culture results, polymorph nuclear leucocyte counts (PMN), and the presence or absence of a surgical source of infection, ascitic fluid infection is classified into five categories (three of which are spontaneous) [6].

Spontaneous bacterial peritonitis and culture-negative ascites are the frequent infections reported in 29-43% chronic liver disease patients among five variants followed by acute liver failure 25% and acute viral hepatitis 11% [6]. Prompt detection of ascitic fluid infection aids in the use of

appropriate antibiotics for ascitic fluid infection treatment. Bacterial infection of ascitic fluid in cirrhotic patients may be symptomatic in 30% of cases [7]. The liver performs many functions in the body, the most important of which is detoxification and bacterial removal from the blood. Bacteremia and other bacterial infections occur as a result of liver failure [8]. Patients with refractory ascites rarely live longer than 6 months. Ascites after liver cirrhosis is associated with hypernatremia, spontaneous bacterial peritonitis, ascitic fluid with a low protein content of 2g/dl, and low urine sodium [9]. A major blood protein (Albumin) regulates blood pressure and blood total protein content reduced in CLD due to leakage of fluid from vessels into the peritoneal space where it collects leads to ascites [10]. Various studies conducted did not distinguish between culture-negative neurolytic ascites (CNNA) and spontaneous bacterial peritonitis but suggested treating patients with antibiotics in case of polymorph nuclear count >250 cells/mm<sup>3</sup>. The present study investigated the culture-negative neurolytic ascites in chronic liver disease patients.

## METHODOLOGY

This cross-sectional study was conducted on 134 patients with ascitic fluid infection due to chronic liver disease in the

Department of Medicine and Gastroenterology, Pak International Medical College, Peshawar for six months duration from December 2020 to May 2021. All the ascitic infectious patients due to chronic liver disease regardless of their age and gender showing ascitic fluid infection symptoms such as tenderness, fever, and abdominal pain were admitted and underwent laboratory culture examination. Based on bacterial growth, all the chronic liver disease patients were grouped into two; Group-I of no bacterial growth and Group-II of positive bacterial growth. All the patients having an intra-abdominal infection or taking antibiotics were excluded. Pre-designed proforma was used for gathering patients all the relevant data such as age, gender, and chronic liver disease duration, previous history of treatment, ascites tap, and antibiotic therapy. Patients other than liver cirrhosis, tuberculosis, intra-abdominal infections source, and malignancy were excluded. A diagnostic peritoneal tap with a 20cc sterile syringe and ascitic fluid (20 ml) was taken and placed in an EDTA tube, and the patient was examined within 3 hours. The total protein content, leucocyte differential count, and total leucocyte count of the sample were all determined in the lab.

For each sample, the sensitivity culture of ascitic fluid were also determined. SPSS software version 24 was used to perform statistical analysis on the data. For qualitative data, the results were calculated as percentages, and for quantitative data, the means and standard deviation were used. A p-value of < 0.05 was deemed significant. The findings were presented in both tabular and graphical formats.

**RESULTS**

Of the total 134 patients, 84 (62.7%) were male and 50 (37.3%) were females. Overall mean age was 47.56±19.8 years with an age range of 20 years to 80 years. Of the total 134 cases, the prevalence of positive and negative culture ascites were 30 (22.4%) and 104 (77.6%) respectively. out of 104 culture-negative patients, 65 (62.5%) were male patients whereas 39 (37.5%) were females. Chronic liver disease means duration was 8.9±2.6 months with a range of 6 months to 18 months. For all the patients above 40 years, the prevalence of culture-positive and negative ascitic infection was 20 (66.7%) and 77 (74.1%) respectively.

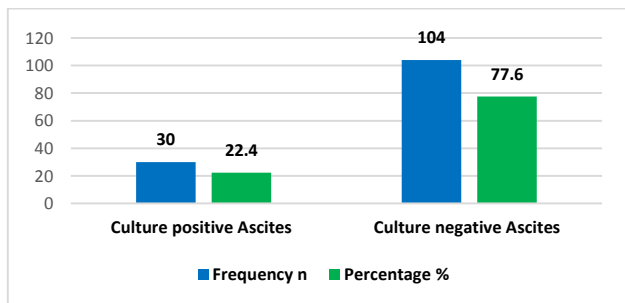


Figure 1: Prevalence of culture-negative and positive ascites (n=134)

The prevalence of male patients was higher (62.5%) among culture-negative patients due to chronic liver

disease. The prevalence of culture negative and positive ascitic infections are shown in Figure-1. Figure-2 demonstrate the gender distribution of all the patients. Age-wise distribution of patients are shown in Tale-I. Figure -3 illustrates the ascitic fluid infection prevalence among patients having age >40 years. Chronic liver disease duration are compared for both culture negative and positive infections in Figure-4.

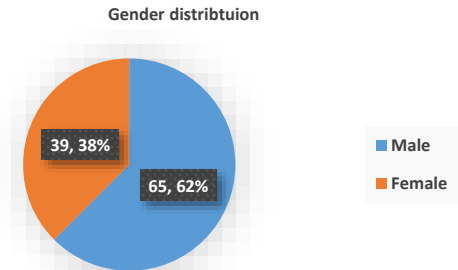


Figure 2: Gender's distribution (n=104)

Table 1: Age-wise distribution (n=134)

Age group (years)	Male n (%)	Female's n (%)	Total n (%)
20-30	9 (6.7)	5 (3.7)	14 (10.4)
31-40	13 (9.7)	5 (3.7)	18 (13.4)
41-49	15 (11.2)	10 (7.5)	25 (18.7)
50-60	16 (11.9)	11 (8.2)	27 (20.1)
61-70	13 (9.7)	18 (13.4)	31 (23.1)
71-80	11 (8.2)	8 (6.1)	19 (14.3)
Total	77 (57.5)	57 (42.5)	134 (100)

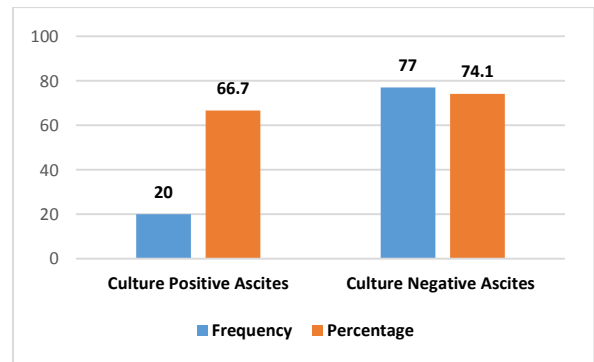


Figure 3: Prevalence of culture negative and positive ascites in patients >40 years

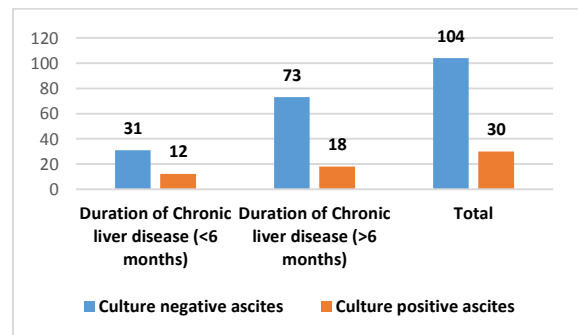


Figure 4: Chronic liver disease duration comparison in culture negative and positive ascites

## DISCUSSION

Bacterial infections are the most common cause of spontaneous bacterial peritonitis in patients with liver cirrhosis (SBP) which is substantially associated with liver cirrhosis patient's high mortality rate. Patients with damaged liver cirrhosis have a weakened immune system, in turn leads to infections, which causes upper GI bleeding, hepatic encephalopathy, and injuries related to acute kidney failure. The Nosocomial SBP increase the mortality rate that can reach 30% [11, 12]. A Nepalian study conducted on 81 cases found that 20 (24.7%) had SBP and its variants, 65% had CNNA, 20% had classical SBP, and 15% had bacteria ascites [13]. In our study, 134 SBP cases were included, and culture negative SBP was found in 104 (77.6%) of them, while culture positive SBP was found in 22.4% of them.

Patients with ascitic fluid total protein levels greater than 1gm/dl were more likely to develop ascitic fluid infection [14]. The ascitic fluid's opsonic activity was proportional to its protein concentration [15]. In a study conducted by Hossen, [16] mean ascitic fluid total protein levels were 0.360.23gm/dl in infected children and 1.28 1.13gm/dl in non-infected children ( $p=0.087$ ). Another study [17] of 35 adult patients with CLD and ascites found that the mean ascitic fluid total protein level was 1.53 0.61 g/dl in infected patients and 1.200.59 g/dl in no infected patients. In this study, the mean ascitic fluid total protein concentration was 1.210.633 gm/dl in infected (CNNA) children and 1.070.64 gm/dl in non-infected children. As a result, the mean value of ascitic fluid total protein of infected children in this study differs from that of the previous study [18], which could be due to age differences in the study populations of these two studies, besides their statistically insignificance ( $p>0.05$ ).

Ascitic fluid culture can diagnose spontaneous bacterial peritonitis, however, regardless of ascitic fluid increased neutrophil count and ascitic fluid infection, the culture is negative in ascitic fluid which revealed that SBP cannot be diagnosed with culture alone, so an Egyptian study found that diagnostic marker for SBP are serum Amyloid-A and ascitic fluid. They found that ascitic fluid has a sensitivity and specificity of 90% and 60%, respectively. Amyloid-A levels are used to diagnose SBP. The Amyloid-A level serum is more sensitive and specific than the levels of ascitic fluid [19].

In Korean based study, patients with SBP had a higher rate of ascitic fluid positive culture, and a higher mortality rate in 7-day against culture negative neutrocytic ascites (CNNA) patients, while the 30-day and 90-day mortality rates were equal in both groups. The prevalence of SBP was 48.6 percent in their study, and CNNA was 51.4% [20].

A study conducted in Karachi, Pakistan, found that 21.5% of cases had culture positive SBP, while 78.5% had culture negative SBP. The patients with culture negative SBP were 54.7% male and 45.2% female. Their study's age range was 18-67 years [21]. In our study, the age range was 20-80 years, and the cases with culture negative ascites were 77.5% and 22.5%, respectively. To prevent ascitic fluid infection after ascitic tap, patients should receive first-line antibiotic therapy right away [22, 23].

## CONCLUSION

Our study found that the prevalence of culture-negative ascitic fluid was higher at 77.6% among male patients. Also, ascitic fluid infection due to chronic liver disease was higher in patients of age above 40 years.

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