



## PREVALENCE OF CULTURE NEGATIVE ASCITIC FLUID INFECTION AMONG PATIENTS WITH CHRONIC LIVER DISEASE.

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**ABSTRACT... Objectives:** To determine prevalence of patients with chronic liver disease having culture negative ascitic fluid infection. **Study Design:** Cross sectional study. **Setting:** Gastroenterology and medicine ward of DHQ Teaching Hospital Gujranwala. **Period:** January 2018 August 2018 having total duration of 8 months. **Material & Methods:** All patients irrespective of age and gender, having ascites due to chronic liver disease and showing signs and symptoms of ascitic fluid infection like fever, abdominal pain and tenderness, admitted in the medical unit of study hospital underwent ascitic tap and fluid was sent for culture examination to the hospital laboratory. Patients with chronic liver disease having no bacterial growth found on culture of ascitic fluid were placed in one group and who had culture positive ascites were placed in separate group. Patients who have taken any antibiotic in last one month or having any intra abdominal source of infection were excluded from the study. All cases in study group were already diagnosed with CLD. **Results:** There were 160 cases included in this study having chronic liver disease and ascitic fluid infection with 62.5% male and 37.5% female cases. Out of 160 cases, 22.5% were having culture positive ascites while 77.5% cases were having culture negative ascites among them 61% were male and 39% were female in positive group and 62.9% were male and 37.1% were female cases in negative group. Age range of patients was 25-75 years with mean age of  $50 \pm 25$  years. Mean duration of chronic liver disease was  $9.5 \pm 2.4$  months with minimum duration of 6 months and maximum duration of 15 months. There were 72.6% cases with culture negative ascites and 69.4% with positive culture were having age above 45 years. There was majority of male patients (62.9%) having culture negative ascites due to CLD. **Conclusion:** Ascitic fluid infection among patients with chronic liver disease is usually culture negative. In our study prevalence of culture negative ascitic fluid infection was 77.5%, more common among male patients having age above 45 years.

**Key words:** Ascitic Fluid Infection, Ascitic Tap, Chronic Liver Disease, Portal Hypertension.

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## INTRODUCTION

Chronic liver disease is a very common disease in our community with high prevalence rate with high mortality rate. This disease leads to liver cirrhosis and portal hypertension producing typical signs and symptoms of upper gastrointestinal bleeding, hemorrhoids, and abdominal ascites. In liver cirrhosis scars and nodules are formed in liver parenchyma. Liver plays many roles in body but major role is detoxification and removal of bacteria from blood. Therefore in liver failure bactiremia and various bacterial infections occur.<sup>1</sup>

Ascites is defined as abnormal fluid collection in abdominal cavity. It occurs in 60% of cases with

compensated liver failure within 10 years after diagnosing the disease. Mortality rate is 40% in a year and 50% within 2 years. Patients having refractory ascites usually do not survive more than 6 months. Patients with ascites after liver cirrhosis have findings of hyponatremia, low urine sodium, ascitic fluid low protein content  $\leq 2\text{g/dl}$  and spontaneous bacterial peritonitis.<sup>2</sup>

Other complications of chronic liver disease include encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome, coagulopathy and hepatocellular carcinoma. Development of a bacterial infection in the peritoneum in the absence of obvious source of infection is called

spontaneous bacterial peritonitis (SBP). A model of end stage liver disease (MELD) score is very useful in predicting development of spontaneous bacterial peritonitis in future so this condition can be prevented in time and managed promptly using this scoring system.<sup>3</sup>

Albumin is a major blood protein maintaining oncotic pressure. In CLD total protein content of blood is decreased. Due to low oncotic pressure fluid from vessels comes out in peritoneal space and collects producing ascites. For treating ascites albumin is transfused to the patient to increase oncotic pressure in blood vessels.<sup>4</sup>

Enterobacter and Streptococci are most common bacteria causing spontaneous bacterial peritonitis in patients with chronic liver disease.<sup>5</sup>

Ascitic fluid infection is classified into three types spontaneous bacterial peritonitis, culture negative neutrocytic ascites (CNNA) and non-microbial non neutrocytic bacterascites (MNBA). Recent studies do not differentiate between SBP and CNNA for treatment purpose and recommend that if polymorphonuclear count is more than 250 cells/mm<sup>3</sup> immediate antibiotic treatment should be given and should not wait for bacterial culture report.<sup>6</sup>

In this study we studied culture negative neutrocytic ascites in patients with chronic liver disease. In spontaneous bacterial peritonitis antibiotics should be given according to the culture and sensitivity report of ascitic fluid otherwise antibiotic resistance is developed in patients and basic infection is not cured due to wrong antibiotic therapy.<sup>7,8</sup>

## MATERIAL & METHODS

First of all approval was taken from ethical committee of the study institution DHQ Teaching Hospital Gujranwala for conducting study in the hospital. Study was conducted in gastroenterology and medical wards of the hospital. A performa was designed in which all relevant data of each patient was documented such as name, age, address, duration of CLD, important points of history like previous treatment, history of previously done

ascitic tap or taking any antibiotic therapy and important points of physical examination.

There were 160 patients included in our study which were falling in our inclusion criteria. Patients having chronic liver disease as a cause of ascites and showing signs and symptoms of ascitic fluid infection like fever, abdominal pain and tenderness, respiratory distress without any intra abdominal source of infection were included in this study. These cases were not underwent ascitic tap previously.

All other patients having cause of ascites other than liver cirrhosis, having tuberculous peritonitis any intraabdominal source of infection or tuberculosis, pancreatitis, secondary peritonitis or malignancy or who had taken antibiotic therapy in last one month were not included in this study. Patients having ascitic fluid infection were divided into two groups one consisted on all cases with positive culture of ascitic fluid and other group having culture negative ascitic fluid infection. Diagnostic peritoneal tap was done using 20cc sterile syringe, 20 ml of ascitic fluid taken put into EDTA tube and examined within 3 hours. Total leucocyte count and differential leucocyte count and total protein content in sample was determined in laboratory.

Culture and sensitivity of ascitic fluid was also determined for each sample. Statistical analysis of data was done using SPSS software (version 25). Results were calculated in the form of percentages for qualitative data and means and standard deviation for quantitative data. P-value less than 0.05 was considered significant. Results were presented in tabular and graphical forms.

## RESULTS

There were total 160 patients in this study having clinically ascitic fluid infection. There were 100() male and 60() female cases. Out of total 160 cases 124() cases including 78() male and 46() female cases were having culture negative ascites and 36() patients including 22() male and 14() female patients were having culture positive ascites (Table-I).

Age range of patients was 25-75 years with mean age of 50±25 years. There were 12() cases between 25-35 years, 23() between 36-45 years, 35() between 46-55 years, 54() between 56-65 years and 36 patients were having age 66-75 years (Table-II).

Among patients with culture negative ascites 34(27.4%) cases were having age less than 45 years and 90(72.6%) having age above 45 years and out of those having culture positive ascites 11(30.6%) cases were having age below 45 years and 25(69.4%) above 45 years of age (Table-III).

Duration of chronic liver disease among cases having culture negative ascites was less than 6 months in 40(32.2%) cases and more than 6 months in 84(67.7%) cases, among cases with

culture positive ascites duration of CLD was less than 6 months in 56(35%) cases and more than 6 months in 104(65%) cases (Table-IV).

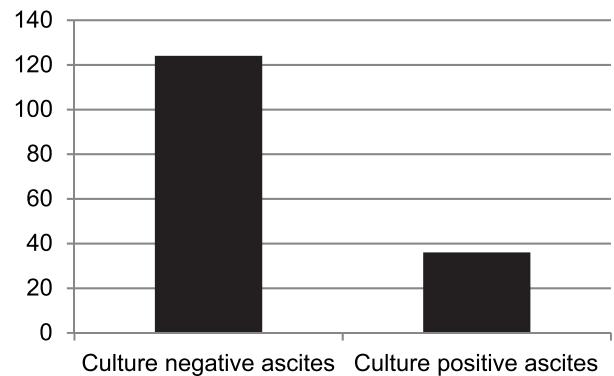


Figure-1. Frequency of culture positive and culture negative ascites in study group (n=160)

Gender	Culture Negative Ascites	Culture Positive Ascites	Total	P-Value
Male	78(62.9%)	22(61.1%)	100(62.5%)	0.542
Female	46(37.1%)	14(38.9%)	60(37.5%)	0.812
Total	124(100%)	36(100%)	160(100%)	

Table-I. Gender distribution of culture positive and negative ascites

Age (years)	Male	Female	Total
25-35	8	4	12 (7.5%)
36-45	16	7	23 (14.4%)
46-55	20	15	35 (21.9%)
56-65	25	29	54 (33.8%)
66-75	20	16	35 (21.9%)
Total	100	60	160 (100%)

Table-II. Age distribution of cases in study group (n= 160)

Age (Years)	Culture Negative Ascites	Culture Positive Ascites	Total	P-Value
<45	34 (27.4%)	11 (30.6%)	100 (62.5%)	0.992
>45	90 (72.6%)	25 (69.4%)	60 (37.5%)	0.732
Total	124 (100%)	36 (100%)	160 (100%)	

Table-III. Comparison of age among patients having culture positive and negative ascites in study group

Duration of CLD (months)	Culture Negative Ascites	Culture Positive Ascites	Total	P-Value
<6	40 (32.2%)	16 (44.4%)	56 (35%)	0.856
>6	84 (67.7%)	20 (55.5%)	104 (65%)	0.664
Total	124 (100%)	36 (100%)	160 (100%)	

Table-IV. Comparison of duration of CLD among patients with culture positive and negative ascites

## DISCUSSION

Bacterial infections in patients with liver cirrhosis are main threat of developing spontaneous bacterial peritonitis (SBP). It is associated with high mortality rate in patients with liver cirrhosis even after resolution of SBP, life expectancy was not good in such chronically ill patients. Patients with decompensated liver cirrhosis have weak immune system so making them susceptible to various infections particularly SBP which leads to development of hepatic encephalopathy, upper GIT bleeding and acute kidney injury. If SBP is acquired in hospitals (Nosocomial SBP) then mortality rate is very high up to 30%.<sup>9,10</sup> A study conducted in Nepal on 81 cases out of them 20(24.7%) cases were having SBP comprising on its variants, 65% cases with CNNA, 20% having classical SBP and 15% having bacterascites.<sup>11</sup> In our study 160 cases were included having SBP and out of them Culture negative SBP was present in 124(77.5%) cases and culture positive SBP was found in 22.5% cases.

A study conducted in Karachi, a city of Pakistan, reported culture positive SBP in 21.5% while culture negative SBP was present in 78.5% cases. Patients having culture negative SBP were consisted of 54.7% male and 45.2% female cases. Age range in their study was 18-67 years.<sup>12</sup> This is compared to our study in which age range was 25-75 years and cases with culture negative ascites were consisted of 62.9% and 37.1%. To prevent ascitic fluid infection after ascitic tap first line antibiotic therapy should be given to the patients immediately. Children having ascites are more prone to get ascitic fluid infection therefore special care should be given to children and if there is no signs and symptoms of ascitic fluid infection then ascitic tap should be avoided to prevent development of nosocomial peritonitis.<sup>13,14</sup>

Diagnosis of spontaneous bacterial peritonitis is made by culture of ascitic fluid but sometimes culture is negative inspite of ascitic fluid infection and increased neutrophil count in ascitic fluid so culture alone is not sufficient to diagnose SBP hence a study conducted in Egypt studied Amyloid-A in serum and ascitic fluid as a diagnostic marker for SBP. They reported sensitivity and

specificity 90% and 60% respectively of ascitic fluid Amyloid-A level for diagnosing SBP. Serum Amyloid-A level has high sensitivity and specificity than ascitic fluid level.<sup>15</sup> A study conducted on patients having culture negative neutrocytic ascites mentioned that it is a variant of SBP and having mortality rate same as SBP. The term culture negative neutrocytic ascites was used in 1984 by Runyon and it is described as increased neutrophil count in ascitic fluid greater than 250 cells/mm<sup>3</sup>, negative ascitic fluid culture and absence of antibiotic therapy in last one month, no intra abdominal source of infection which can be treated surgically or pancreatitis.<sup>16</sup> A study conducted in Korea concluded that patients with SBP were having high MELD score, higher rate of positive culture of ascitic fluid and also higher 7-days mortality rate as compared to patients having culture negative neutrocytic ascites (CNNA), while 30-days and 90-days mortality rate was equal in both groups. According to their study prevalence of SBP was 48.6% and CNNA was 51.4%.<sup>17</sup>

## CONCLUSION

Our study concluded that most of the patients presenting to teaching hospitals in our community with ascites due to liver cirrhosis have culture negative ascites while they have clinically ascitic fluid infection. So patients showing clinically infection of ascitic fluid should be treated with empirical antibiotics immediately without waiting for culture report. In our study ascitic fluid infection was mostly seen in male patients and patients having age above 45 years and duration of CLD more than 6 months. Early diagnosis of the disease and immediate treatment can reduce morbidity and mortality rate.




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### AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Muhammad Ayub	Topic selection and data collection.	
2	Sagheer Hussain	Data analysis, Data collection.	
3	Salman Ahmed	Found additional literature for information, Data composing.	
4	Muhammad Adnan Iqbal	Abstract and recording.	