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Research Article

**INCIDENCE OF CULTURE NEGATIVE NEUTROCYTIC  
ASCITES IN PATIENTS WITH CHRONIC LIVER DISEASE**<sup>1</sup>Dr Qudsia Mujeeb, <sup>2</sup>Dr Rana Sajid Ali, <sup>3</sup>Dr Maheen Rana<sup>1</sup>King Edward Medical University Lahore<sup>2</sup>Assistant Professor Pharmacology, Rashid Latif Medical & Dental College Lahore<sup>3</sup>Assistant Professor Pathology, Rashid Latif Medical & Dental College Lahore**Article Received:** November 2019 **Accepted:** December 2019 **Published:** January 2020**Abstract:**

Higher morbidity and mortality occur in patients with liver cirrhosis as a result of ascitic fluid infection. There are two types of ascitic fluid infections, namely spontaneous bacterial peritonitis (SBP) and negatively cultured neutrocytic ascites (CNNA). By definition, in the culture negative neutrocytic ascites (CNNA), the number of polymorphonuclear cells is equal to or greater than 250/mm<sup>3</sup> and there are no source of infection in the abdomen. Secondary causes such as pancreatitis, peritoneal cancer, tuberculous peritonitis must be omitted. CNNA is a type of ascitic fluid infection first described in 1984. SBP has been shown to have the same prognostic, clinical and therapeutic properties. However, CNNA has been shown to have lower mortality compared to spontaneous bacterial peritonitis. Third-generation cephalosporin is considered the most effective drug in the treatment of SBP. The following measures are helpful used for the CNNA diagnosis (1) neutrophil count above 250/mm<sup>3</sup> (2) culture negative ascetic fluid (3) absence of any intra-abdominal infection (4) no antibiotic received in the last one month (5) no clinical evidence of pancreatitis. Due to the increase in mortality, it is recommended that CNNA be treated with antibiotics as soon as possible.

**Aim:** The purpose of our research was to determine the occurrence of CNNA in patients with chronic liver disease.

**Place and Duration:** In the Department of Gastroenterology, Mayo Hospital Lahore for one-year duration from January 2018 to December 2018.

**Methods:** Patients with EPC presenting ascites at the Lady Reading Hospital, Gastroenterology Department, Medical Education Institutions. In most cases, cirrhosis is caused by hepatitis C followed by hepatitis B and so on. Most patients were in the Child-Pugh class C stage and sampling was performed using the non-probability consecutive sampling technique. The study involved two hundred and fifty patients (150 men and 100 women). Culture negative neutrocytic ascites was detected in 150 (60%) patients. There were no significant differences in CNNA prevalence in age, sex and duration of CLD.

**Conclusion:** 60% (150 of 250) of patients with chronic liver disease who were admitted in the hospital were found to have negative neutrocytic ascites.

**Key words:** culturally negative neutrocytic ascites, chronic liver disease, portal hypertension.

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**INTRODUCTION:**

Chronic liver disease develops into cirrhosis characterized by nodule formation, fibrosis and scarring. SBP is considered to be a major complication in patients with cirrhosis. Patients with cirrhosis have a high risk of many complications and have a lower survival rate<sup>1-2</sup>. Major complications among patients with CLD include portal hypertension, abnormal synthetic functions, or both, portosystemic encephalopathy, hepatopulmonary syndrome, hepatorenal syndrome, SBP, coagulopathy, hepatocellular carcinoma and the like<sup>3</sup>. Ascites are the most common complications of liver cirrhosis with hepatic encephalopathy and bleeding due to rupture of the esophageal varices. In patients with liver cirrhosis, the most common complication is ascites with variceal bleeding and portosystemic encephalopathy. These patients are increasingly susceptible to infection, mainly due to weak defense mechanisms. The most common and serious complication was SBP, then UTI, lower respiratory tract infections and so on. Controversy still exists regarding the clinical relevance and prognosis of CNNA in patients with cirrhosis<sup>4</sup>. There should be a low threshold for the SBP to be tested and treatment should be started as soon as possible without waiting for the breeding and susceptibility report, but it is necessary to drink ascites for routine tests and for culture and susceptibility tests. SBP was defined in 1970, after that SBP-related mortality was significantly reduced from 80% to 30%, mainly due to early diagnosis and emergency treatment. SBP is an ascitic fluid infection that transpires in the visceral perforation absence and without an inflammatory attention within the abdomen, such as an acute pancreatitis, cholecystitis and abscess. In patients with SBP, it is very important to isolate the minimum one germ in the C / S test if it is positive<sup>5-6</sup>. However, multi-bacterial infections in C / S tests will increase the secondary peritonitis suspicion. CNNA is another ascitic fluid infection in which the C / S test is negative, but the other diagnostic criteria are the same as the causes of SBP and other neutrophil ascitic (pancreatitis, peritonitis, tuberculosis and carcinogenicity peritoneal) should be excluded<sup>7-8</sup>.

**MATERIALS AND METHODS:**

This Study was held in In the Department of Gastroenterology, Mayo Hospital Lahore for one year duration from January 2018 to December 2018. The study included 250 patients meeting the criteria for inclusion. The study included patients with asymptomatic infection and clinical presentation of ascitic fluid infection. The patient's age, gender, clinical course, complications and laboratory results were collected and the Child-Pugh class was calculated. The study involved 250 patients with ascitic infection who met the criteria for SBP or CNNA. Patients with cirrhosis, secondary peritonitis / tuberculosis peritonitis or malignancy were excluded, or patients who received antibiotics within one month. Diagnostic tap was performed using a sterile method on the side of the bed using a 20 cc disposable syringe, and in an EDTA tube the sample was placed and within three hours must be analyzed. Then for 3 minutes, the sample was centrifuged in the laboratory for the total number and difference in the number of total proteins. Gram staining and 10 ml C / S testing of ascitic fluid were also carried out with aerobic and anaerobic culture flasks containing trypticase soy broth and then processed. Blood was also collected in anaerobic and aerobic C / S culture bottles prior to the start of antibiotics. Using the SPSS 21.0, statistical analysis was done. For clinical features, a descriptive analysis was done and the results were presented as standard deviation/ mean and percentages for qualitative and quantitative variables, respectively. In addition, Chi square and t tests were used to find the difference between qualitative and continuous data, respectively. The P value less than 0.05 was taken significant statistically.

**RESULTS:**

The average age of patients was  $40.0 \pm 30.0$  years. There were 150 (60%) men and 100 (40%) women. The average duration of CLD was  $8.50 \pm 1.40$  months. The majority of patients were 114 (57%) who have duration of CLD > 8 months. Culture negative neutrocytic ascites was detected in 150 (60%) patients. A comparison was made to see the effect of age, gender and duration of CLD on the result. The chi-square test was carried out. The results are shown in the following tables.

**The age distribution of patients is given in table 1**

Mean $\pm$ SD	Minimum	Maximum
40.0 $\pm$ 30.0	22	75

**The duration of CLD in months given in Table 2(n=250)**

Mean $\pm$ SD	Minimum	Maximum
8.50 $\pm$ 1.40	7	12

**The Comparison of Culture Negative Neutrocytic Ascites & Age (n=250) given in Table 3**

Age (Years)	Culture-Negative Neutrocytic Ascites		Total	P- Value
	Yes	No		
Age ≤40	60(40%)	35(35%)	95(38%)	0.99
Age > 40	90(60%)	65(65%)	155(62%)	
<b>Total</b>	<b>150(100%)</b>	<b>100(100%)</b>	<b>250(100%)</b>	

**Comparison of Culture Negative Neutrocytic Ascites & Gender distribution given in Table 4**

Duration of CLD (in Months)	Culture-Negative Neutrocytic Ascites		Total	P- Value
	Yes	No		
Male	80(53%)	60(40%)	140(56%)	0.73
Female	70(46.7%)	40(40%)	110(44%)	
<b>Total</b>	<b>150(100%)</b>	<b>100(100%)</b>	<b>250(100%)</b>	

**Culture-Negative Neutrocytic Ascites and Duration of CLD (in Months) n = 250 Table 5**

Duration of CLD (in Months)	Culture-Negative Neutrocytic Ascites		Total	P- Value
	Yes	No		
< 8	55(36.7)	45(45%)	140(56%)	0.88
> 8	95(63.3)	55(55%)	110(60%)	
<b>Total</b>	<b>150(100%)</b>	<b>100(100%)</b>	<b>250(100%)</b>	

**DISCUSSION:**

The risk of complications increases and the life expectancy decreases in patients with liver cirrhosis. One of the main complications of cirrhosis with ascites is SBP, and its prevalence is 6-30%. In our study, negatively cultured neutrophil ascites was detected in 150 (60%) patients. In another study, positive results seen in 64 (34.01%) and negative cultures in 124 (66.5%) were obtained in culture samples suspected of SBP<sup>9-10</sup>. In a local study involving CLD patients, classic SBP was present in 50 (39.06%), bacterial ascites (4.68%) in 6, and a culture of negative neutrophil ascites (CNNA) in 72 (56.25%). Another local study found that 22 patients were SBP; 11 of them were negative for culture, and the rest were positive for culture. Of the 50 patients, 28 (56%) had SBP or type, but classic SBP was only found in 11 (39.28%), 16 (57.14%) had CNNA, one (3.57%) of bacteriocytes. In patients with cirrhosis SBP pathogenesis was the main result of translocation<sup>11-12</sup>.

In bacterial translocation, bacteria or products enter the lumen of the intestine and then pass to the mesenteric lymph nodes or additional segment of the intestine, causing an inflammatory response and ultimately an infection. In addition, BT should be involved in the exacerbation of hemostasis disorders and hyperdynamic state<sup>13-14</sup>. Recommended BT

mechanisms in patients with cirrhosis include structural and functional changes in mucosal barriers, local immune response deficiencies, and intestinal bacterial hyperplasia. Intestinal bacterial hyperplasia is considered to be the main factors associated with BT. It is thought that there are other factors that reduce intestinal motility, sympathetic adrenal stimulation, increased NO formation, and oxidative stress. Remember that usually the activity of the small intestine is significantly reduced compared with the activity of the colon; However, in patients with cirrhosis, the reverse is possible. The clinical picture of SBP is very variable, especially for fever, abdominal pain and gastrointestinal motility, while others may have hepatic encephalopathy or renal failure, and even SBP patients may be asymptomatic, causing significant SBP episodes<sup>15</sup>. Diagnostic ascites puncture is recommended in all patients with cirrhosis and ascites that have significantly decreased. Amrapurkar DN et al. Reported a similar incidence of SBP (23%) in admitted patients. However, the SBP incidence be contingent on the degree of liver disease and is considered advanced in severe liver disease. Jain et al reported SBP incidence was 35.02% in 64 patients (Child-Pugh class C) reported by. 63 patients. All SBP patients were in the child class.

**CONCLUSION:**

Our study concludes that most of the CLD patients who go to tertiary hospital have negative cultured neutrocytic ascites, so that the patient who meets the criteria for spontaneous bacterial peritonitis needs to be treated empirically without waiting for the culture and sensitivity report. Cefotaxime is still the drug of choice for the treatment of SBP.

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