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Prevalence of Spontaneous Ascitic Fluid Infection and its Microbiological Profile in Decompensated Cirrhotic Liver Disease Patients in a Tertiary Health Care Hospital in Puducherry

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ABSTRACT

Background: Spontaneous ascitic fluid infection (SAI) is common in cirrhotic patients. Third-generation cephalosporins are currently recommended as first-line therapy. We conducted a study to determine bacterial etiology, susceptibility patterns.

Objective: To estimate the prevalence of spontaneous ascitic fluid infection in cirrhotic decompensated liver disease patients, and to analyse microbiological profile in cirrhotic ascites.

Method: We prospectively collected clinical data and laboratory values. Diagnostic paracentesis was performed in all patients of decompensated cirrhotic liver disease with ascites to investigate the presence of SAI.

Result: Among total 45 patients the leading cause of cirrhosis was alcohol consumption. SAI was diagnosed in 27 patients (60%). Of these, 19 patients (70 %) had culture negative neutrocytic ascites (CNNA), 5 (18.5%) had Spontaneous bacterial peritonitis (SBP), and 3 (11.1%) had mono microbial non neutrocytic bacterascites (MNB). CNNA and SBP did not differ in terms of clinical characteristics. Organisms found are - two Streptococci and two coagulase negative staphylococci, two E. coli, one klebsiella pneumonia, one candida growth. Gram positive cocci (50%) were predominant among culture positive SAI, gram negative bacilli (37.5%), fungus (12.5%). Among the commonly used antibiotics higher resistance rate was found with cephalosporins (71.4%) and most sensitive antibiotics found to be carbapenems, linezolid, vancomycin (85%), then amino glycosides and tetracycline (71%)

Keywords: SAI, Ascitic fluid culture, Antibiotic sensitivity

I. INTRODUCTION

Spontaneous ascitic fluid infection (SAI) is common in cirrhotic patients leading to significant mortality and morbidity. Spontaneous ascitic fluid infection (SAI) has three subtypes ;SBP (spontaneous bacterial peritonitis) is established by an elevated ascitic fluid polymorphonuclear leukocyte (PMNL) count >250 cells/mm3 and a positive ascitic fluid bacterial culture ;Culture-negative neutrocytic ascites (CNNA), which is considered to be a variant of SBP, is diagnosed by elevated ascitic fluid PMNL count >250 cells/mm3 with a negative ascitic fluid culture; diagnosis of mono microbial non-neutrocytic bacterascites (MNB) include a positive ascitic fluid culture for a single organism and ascitic fluid PMNL count <250 cells/mm3.[1]

Spontaneous bacterial peritonitis (SBP) is a frequent and severe complication in cirrhotic patients with ascites and its prevalence ranges from 10% to 25% in hospitalized cirrhotic patients .SBP is the most frequent bacterial infection in cirrhotic patients, followed by urinary tract infection, pneumonia, skin and soft tissue infections,

and spontaneous bacteremia.[2] Diagnosis is based on a polymorphonuclear cell count greater than or equal to 250 cells mm^3 in ascitic fluid in the absence of an intra-abdominal source of infection. Bacterial cultures of the ascitic fluid are negative in approximately 50% of cases.[3-5]

Third generation cephalosporins are considered the drug of choice for empirical treatment of SBP according to most international guidelines.[3] These recommendations, however, are mainly based on studies conducted several years ago under the hypothesis that Gram-negative bacilli, such as Escherichia coli and Klebsiella species, are the most common cause of SBP.[5] The microbiological characteristics of spontaneous bacterial peritonitis (SBP) are changing worldwide with a shift in patterns of SBP and increasing prevalence of antibiotic-resistant bacteria. Major changes in this pattern occurred over the last few years with a rising prevalence of gram-positive organisms like Streptococcus species, Enterococcus species, and Staphylococcus species.[6] Therefore it is essential to study the bacterial profile and their antimicrobial susceptibility pattern at our hospital for initiation of appropriate therapy for patients admitted in our hospital.

II. MATERIALS AND METHODS

Study Area and Design: This study was done at Sri Manakula Vinayagar Medical College and Hospital Puducherry for a period of 6 months. The study design employed was an analytical cross sectional study.

Study participants: The study was conducted on randomly selected patients who get admitted in General Medicine department of Sri Manakula Vinayagar Medical College And Hospital and diagnosed with decompensated cirrhotic liver disease, satisfying inclusion and exclusion criteria and consenting to be a part of the study

Inclusion criteria

All patients diagnosed with decompensated cirrhotic liver disease will be included in the study after getting a informed consent

Definition: Decompensated liver disease is defined as an acute deterioration in liver function in a patient with cirrhosis and is characterized by jaundice, ascites, hepatic encephalopathy, variceal hemorrhage.[7]

Exclusion criteria

1. Patients with secondary bacterial peritonitis
2. Patients received antibiotics in last one month

III Sample size: Sample size for this study was calculated by using the software open EPI version 3 by considering the proportion of mono bacterial growth in cirrhotic ascites as 95.1% from a study done on change in pattern and microbiology of SBP by Al-Ghmadl H et al published on June 2019 [8] and considering maximum allowable error of 6.57% is 43. By adding the 10% non responsive rate of 4 which is fixed as 45.

IV METHODOLOGY

Decompensated cirrhotic liver disease patients were interviewed and questionnaire was used to collect the details. Physical examination was done. Blood sample was collected for complete blood count, renal profile, liver function test , INR, USG Abdomen done to confirm the diagnosis and presence of ascites Screened the patients according to inclusion and exclusion criteria .After getting an Informed written consent, after explaining about the study and the intervention patient has to undergo, diagnostic paracentesis done . The fluid sent for biochemical, pathological analysis including culture and sensitivity testing.

III. Statistical method

Data will be entered using the software EpiInfo version 7.2.2.6 and analysis will be done using the software

SPSS version 24.0. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. MS Excel and MS word was used to obtain various types of graphs such as bar diagram, pie diagram.

IV. RESULTS

A total of 45 patients were enrolled in this study. All underwent ascitic fluid analysis. The base line demographic and risk characteristics of the patients are shown in table 1.The median age of these patients are 54.33± 12.14. Male patients are more than female (figure 1) .Alcoholic liver disease was found to be the leading cause of cirrhosis among the patients (figure 2). In this study out of 45 patients 27 (60%) had SAI, in that SBP – 5 (19%) , MNB -3 (11%), CNNA- 19 (70%).(figure 3). The basic clinical and laboratory characteristics of the patients are shown in Table 3.

A total of 45 patients included in the study 9 had hepatic encephalopathy. Out of that 4 patients had SAI.(Table 2) And severity of cirrhotic liver disease are assessed using Child Pugh and MELD score. CNNA type of SAI is common in all classes of child Pugh classes and median meld score was-13 (Table 2, figure 4,5)

Table 1 : Baseline demographic and risk characteristics of patients with spontaneous ascitic fluid sinfection (n=45)

		Total (n=45)	CNNA (n=19)	SBP (n=5)	MNB (n=3)	p value#
Age (years), mean (±SD)		54.33(±12.14)	55.21(±13.05)	55.00(±10.70)	61.33(±8.96)	0.721*
Gender, n (%)	Male	35	13(37.1)	2(5.7)	2(5.7)	0.499
	Female	10	6(60)	3(30)	1(10)	
Alcohol consumption, n (%)	Yes	34	12(35.3)	2(5.9)	2(5.9)	0.620
	No	11	7(63.6)	3(27.3)	1(9.1)	
Risk, n (%)	Yes	12	6(50.0)	2(16.7)	2(16.7)	0.499
	No	33	13(39.4)	3(9.1)	1(3.)	
Anaemia, n (%)	Yes	30	12(40.0)	4(13.3)	3(10.0)	0.375
	No	15	7(46.7)	1(6.7)	0	
Etiology, n (%)	Alcoholic Liver Disease	31	11(35.5)	1(3.2)	1(3.2)	0.363
	Viral	10	6(60)	2(20)	2(20)	
	others	4	2(50)	2(50)	0	

*#- p value by chi-square test; *- p value by one-way ANOVA*

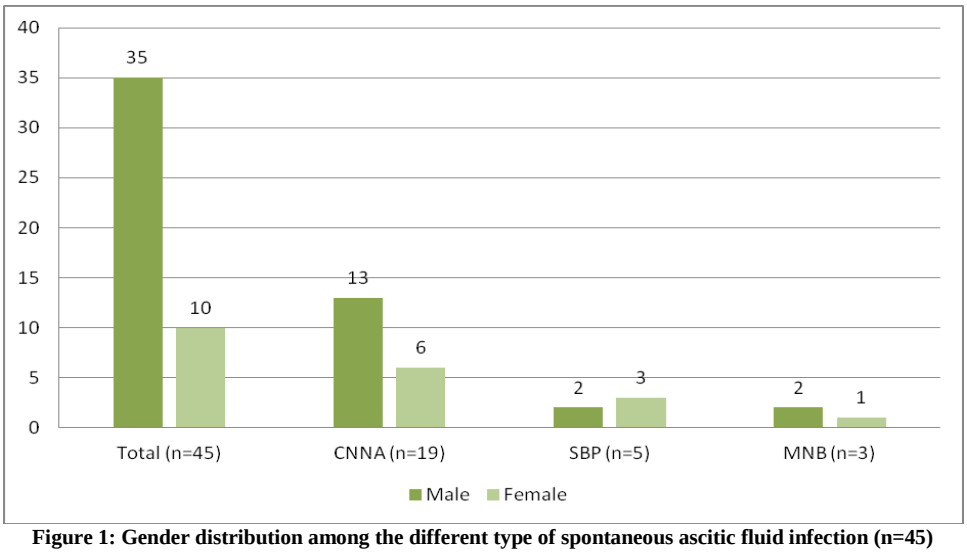

Figure 1: Gender distribution among the different type of spontaneous ascitic fluid infection (n=45)

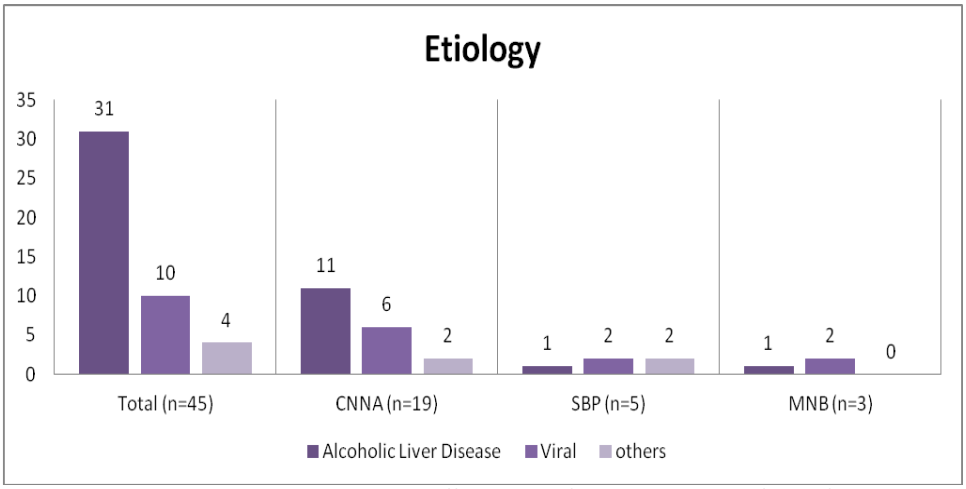

Figure 2 : Etiological distribution among the different type of spontaneous ascitic fluid infection (n=45)

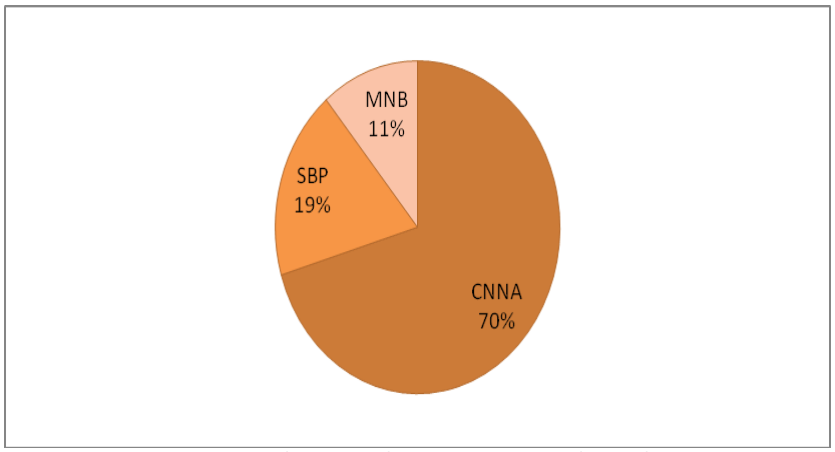

Figure 3: Distribution of the type of spontaneous ascitic fluid infection (n=27)

Table 2 : Baseline clinical characteristics of patients with spontaneous ascitic fluid infection (n=45)

		Total (n=45)	CNNA (n=19)	SBP (n=5)	MNB (n=3)	p value[#]
Hepatic Encephalopathy, n(%)	Present	9	2(22.2)	1(11.1)	2(22.2)	0.067
	Absent	36	17(47.2)	4(11.1)	1(2.8)	
Child–Pugh class, n(%)	A	5	4(80.0)	0	0	0.402
	B	23	11(47.8)	2(8.7)	2(8.7)	
	C	17	4(23.5)	3(17.6)	1(5.9)	
MELD score, median (range)		13 (4-33)	11 (4-32)	17 (7-33)	13 (9-16)	0.413*

*#- p value by chi-square test; *- p value by one-way ANOVA*

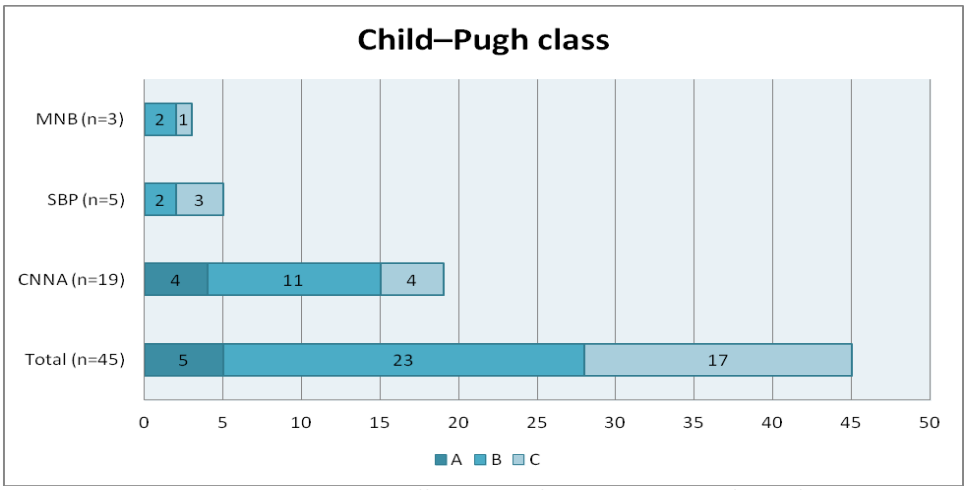

Figure 4 : Child-Pugh class among the different type of spontaneous ascitic fluid infection (n=45)

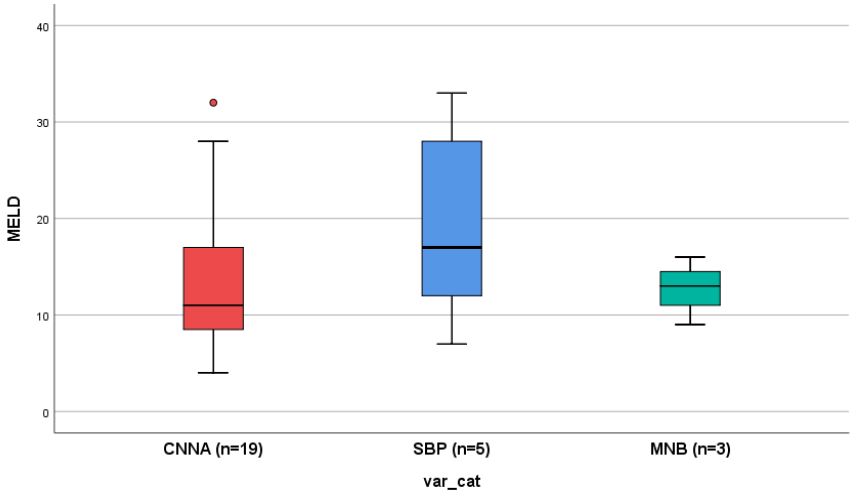

Figure 5: MELD score among the different type of spontaneous ascitic fluid infection (n=45)

Table 3: Baseline laboratory characteristics of patients with spontaneous ascitic fluid infection (n=45)

	Total (n=45)	**CNNA (n=19)**	**SBP (n=5)**	**MNB (n=3)**	**p value***
Total Leucocyte Count	11246.67 (±5891.58)	10526.32 (±5508.26)	17760 (±8928.21)	7233.33 (±3265.48)	0.042
Polymorphs	77.42 (±10.09)	76.62 (±11.81)	83.56 (±6.32)	75.67 (±9.29)	0.432
INR	1.63 (±.54)	1.53 (±.58)	2.22 (±.59)	1.53 (±.76)	0.087
Liver profile					
TB	4.17 (±6.19)	3.21 (±6.36)	5.64 (±8.66)	5.03 (±5.98)	0.740
DB	2.18 (±3.30)	1.61 (±3.20)	2.30 (±2.99)	3.13 (±4.05)	0.720
SGOT	75.53 (±60.57)	56.89 (±44.30)	42.20 (±32.35)	78.33 (±34.82)	0.505
SGPT	34.78 (±28.83)	34.47 (±33.08)	21.40 (±4.98)	41.33 (±22.81)	0.595
ALP	185.71 (±126.29)	187.63 (±159.61)	147.20 (±43.84)	254.67 (±132.88)	0.602
GGT	138.13 (±252.53)	118.58 (±206.15)	43.40 (±42.16)	316.67 (±442.25)	0.246
TP	6.38 (±.92)	6.29 (±.84)	6.18 (±1.16)	6.70 (±.75)	0.715
ALB	2.86 (±.37)	2.97 (±.33)	2.72 (±.54)	2.90 (±.46)	0.449
AST/ALT	2.48 (±1.24)	1.98 (±.67)	2.03 (±.95)	2.50 (±2.26)	0.686
Ascitic fluid					
SAAG	1.75 (±.60)	1.65 (±.65)	1.44 (±.57)	2.00 (±.00)	0.464
WBC	296.38 (±270.13)	473.05 (±275.68)	472.80 (±223.40)	83.33 (±25.01)	0.064

**p value by one-way ANOVA*

Microbiological findings

A total of 45 patients 27 patients had SAI. 7 (16%) showed growth and 38 (84%) showed no growth (figure 6). Common organisms isolated are gram positive cocci – streptococci and coagulase negative staphylococci (50%). Others are gram negative bacilli E. coli and klebsiella (37%) and Candida (13%),(figure 7).

Details of the organism and their susceptibility pattern are depicted in table 4. Other than E.coli all other organism are resistant to commonly using third generation cephalosporins (71.4%). Most of the organisms are sensitive to carbapenams, vancomycin, linezolid (85.7%) and aminoglycosides and tetracyclines (71.4%). Table 5, figure 8

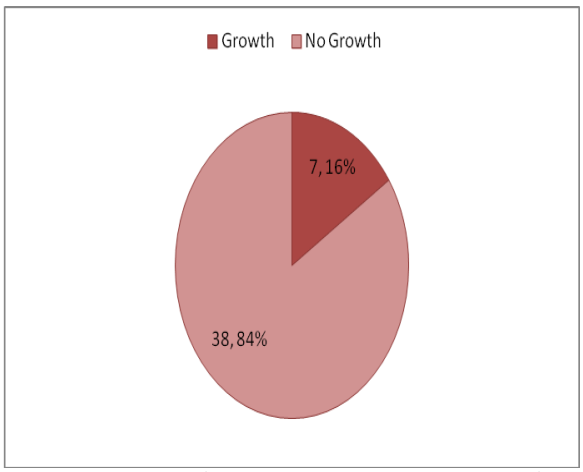

Figure: Percentage of patients with spontaneous ascitic fluid infection showing growth on bacteria media (n=45)

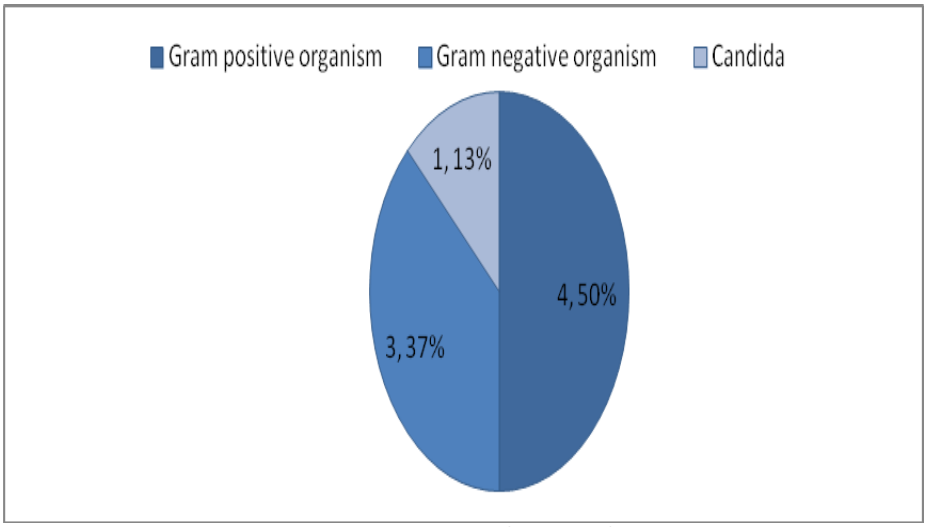

Figure7 : Graphical representation of the type of organism (n=8)

Table 4: Susceptibility patterns of bacterial isolates causing ascitic fluid infections (n=7)

Organism	CEPHALOSPORINS	PENCIILLIN GROUP	CARBAPENEMS	AMINOGLYCOSIDES	FLUOROQUINOLONES	MACROLIDES	TETRACYCLIN	VANCOMYCIN	CO-TRIIMOXAZOLE	LINEZOLID
Streptococcus Pneumoniae	R	S	S	0	R	S	R	S	R	S
Escherchia Coli	S	S	S	S	S	S	S	S	S	S
Coagulase negative staphylococci	R	R	S	S	S	R	S	S	R	S
Klebsiella pneumoniae	R	R	S	R	R	R	R	R	R	R
Coagulase negative staphylococci	R	R	S	S	S	R	S	S	R	S
Escherchia Coli	S	R	S	S	R	S	S	S	S	S
Streptococcus Pneumoniae	R	S	R	0	S	S	S	S	S	S

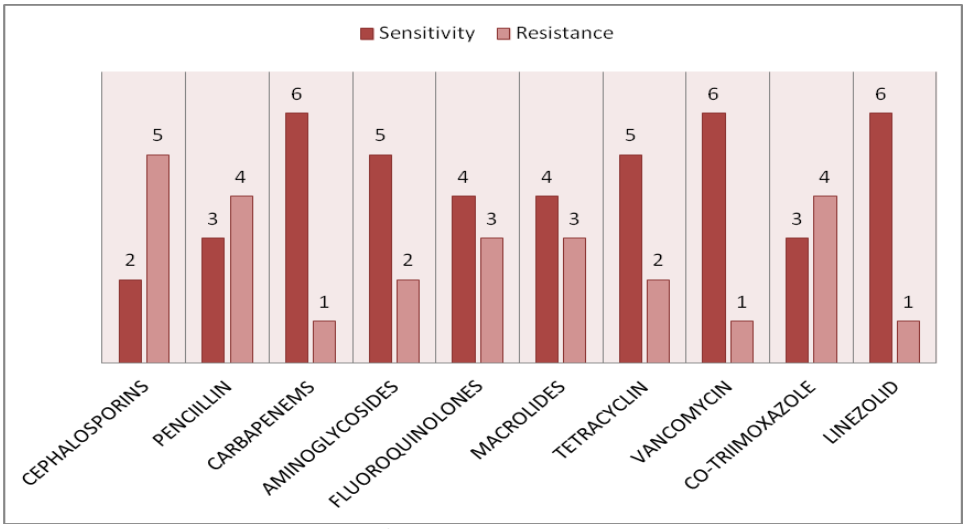

Figure 8: Graphical representation of the Antibiotic wise sensitive and resistance patterns (n=7)

Table 5: Antibiotic wise sensitive and resistance patterns (n=7)

Antibiotics	Sensitive		Resistance	
	Number	Percentage	Number	Percentage
CEPHALOSPORINS	2	28.6	5	71.4
PENCIILLIN	3	42.9	4	57.1
CARBAPENEMS	6	85.7	1	14.3
AMINOGLYCOSIDES	5	71.4	2	28.6
FLUOROQUINOLONES	4	57.1	3	42.9
MACROLIDES	4	57.1	3	42.9
TETRACYCLIN	5	71.4	2	28.6
VANCOMYCIN	6	85.7	1	14.3
CO-TRIIMOXAZOLE	3	42.9	4	57.1
LINEZOLID	6	85.7	1	14.3

V .DISCUSSION

We conducted this study to find out recent change in the bacteriological spectrum and their antibiotic sensitivity pattern in SAI that will help clinicians make decisions regarding choice of most suitable antibiotics, since most international guidelines recommend the use of third generation cephalosporins for empirical treatment of SBP**.** In this study out of 45 patients 27 (60%) had SAI. SBP – 5(19%), MNB -3(11%), CNNA- 19(70%). Patients with SBP and CNNA did not differ in terms of clinical characteristics .Male patients are more than female and most common etiology found to be alcoholism. out of 27 patients with SAI , 16% showed growth .Common organism isolated are gram positive cocci – streptococci and coagulase negative staphylococci (CoNS) (50%), others are E. coli and klebsiella (37%), Candida (13%). These major gram positive organisms were found to be resistant to commonly using empirical antibiotics like cephalosporins (71.4%). Among culture positive patients, most sensitive antibiotics found to be carbapenems, linezolid, vancomycin (85%), then aminoglycosides and tetracyclines (71%).

Study comparison	Findings
Kilian Friedrich et all[6]	Gram-positive bacteria (47.8%) were more frequently found than Gram-negatives (44.9%), fungi in 7.2%. Enterobacter spp. (40.6%), Enterococcus spp. (26.1%), and Staphylococcus spp. (13.8%) were the most frequently isolated agents. Third-generation cephalosporins have poor microbial coverage for treatment of SBP.
Sardan Novovic et all[9]	Gram-positive cocci (45.9%); Enterobacteriaceae (31.7%), with Escherichia coli identified in 31 cases; anaerobes (7.5%); yeast (6.4%); and cutaneous flora (8.0%).
Present study	Common organism isolated are gram positive cocci – streptococci and coagulase negative staphylococci (CoNS) (50%), others are E. coli and klebsiella (37%) , Candida (13%). These major gram positive organisms were found to be resistant to commonly using empirical antibiotics like cephalosporins (71.4%).

VI. CONCLUSION

The microbiological characteristics of spontaneous bacterial peritonitis (SBP) are changing worldwide. The findings of the study will help to characterize the current patterns and antimicrobial susceptibility pattern of SBP in our region helps to choose suitable antimicrobial agents in cirrhotic decompensated liver disease patients, both for empirical and therapeutic use. Third generation cephalosporins have poor microbial coverage for treatment of SBP. Current guidelines need to adapt for the emerging number of gram positive infectious agents in SBP patients

VII. Limitations

Small sample size and small number of culture positive patients and we also could not do the response rate of SAI to different sensitive antibiotic

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