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Research Article

Study of Etiological Profile and Resistance Pattern of Spontaneous Bacterial Peritonitis in Chronic Liver Disease - ②

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Abstract

Introduction: Landscape of etiological profile and microbiological resistance of Spontaneous Bacterial Peritonitis (SBP) in Chronic Liver Disease (CLD) is continuously changing. Early antibiotic treatment of SBP is crucial but spread of Multidrug Resistant (MDR) organism makes its current management challenging. Our study provides fresh insight into its etiology and resistance profile to design better empiric regimen.

Objective: Study etiological profile and resistance pattern of SBP in CLD

Methods: This prospective observational study was conducted at Government Medical College, Srinagar from April 2018 to March 2019.

Results: Prevalence of SBP at our center was 38.09%. Eighty two patients were included in study. Mean age of cases was 59.09 \pm 12.90 years. Culture Positive SBP (CP-SBP) were 45 (54.87%), only 1 (2.22%) was fungal. Gram Negative Bacteria (GNB) were in 68.19% of bacterial cultures. Escheria coli was cultured in 25 (55.55%) bacterial cultures of which 12 (48%) were MDR and 1 Extended Drug Resistance (XDR); Staphylococcus aureus in 13 (28.88%) of which 3 (23%) were MDR. Among CP-SBP, Community Acquired-SBP (CA-SBP) were 26 (57.8%). Drug resistance in CA-SBP was high 34% and in hospital acquired SBP was 88%. Resistance to Quinolones and third generation Cephalosporins was also high ranging from 60% to 70%.

Conclusion: In our study prevalence of SBP was 38.09%. Infections caused by GNB were 67% and antibiotic resistance approaching 60%. Resistance was highest to current first line therapy. We suggest upgrade in empirical therapy for SBP according to evolving profile of organism and keeping in view risk factors for MDR and patient condition for better outcome.

Keywords: Spontaneous bacterial peritonitis; Community acquired; Hospital acquired; Hospital care associated; Multi drug resistant; Culture

INTRODUCTION

Spontaneous Bacterial Peritonitis (SBP) is an infection of the previously sterile Ascitic Fluid (AF), without any apparent intra-abdominal source of infection in patients of Chronic Liver Disease (CLD) [1]. It was first described by Conn and Fessel in patients with hepatic cirrhosis in 1906-1907 [2]. The prevalence of SBP varies from 1.5-3.5% in out-patients and 10-30% in hospitalized patients [3,4]. Factors associated with SBP include age, history of SBP [4], gastrointestinal bleeding [4,5]. Severity of liver dysfunction scores including the Child Turcotte Pugh (CTP) score or Model for End-Stage Liver Disease (MELD) score, neutrophil count, low protein concentration (< 1.5 g/dL) in the ascitic fluid, and long term Proton Pump Inhibitors (PPIs) use has been reported as a predictive factor [6-11] for SBP. In hospital mortality for first episode of SBP is 10-50% depending on various risk factors [12,13]. Recurrence rates are high, more than 70% within one year [14,15].

In cirrhosis disturbance in microcirculation of intestinal mucosa, results in a reduction of mucosal blood flow, intestinal bacterial overgrowth, impaired mucosal integrity [16-18] and deficiencies in local host immune defences are possible mechanisms for bacterial translocation [19,20]. Catheters and other equipment used during invasive procedures represent other possible sources of infection.

The gold standard for diagnosis of SBP consists of count ≥ 250 cells/ mm^3 and/or a positive AF culture without any evidence of intra-abdominal infectious source. Culture negative SBP (CN-SBP) is defined as negative ascitic fluid culture with neutrophil count of ≥ 250 cells/ mm^3 in ascitic fluid [21]. Culture positive SBP (CP-SBP) is seen in 35%-65% of SBP patients [22-26]. Enteric bacteria are the most common etiological agent [17]. Frequency of Multi Drug Resistance (MDR) bacteria in Hospital Acquired SBP (HA-SBP) is 20%-35% [11,27] and 4%-16% in Community-Acquired SBP (CA-SBP) [28]. Third-generation cephalosporins have been the most frequently used antibiotics in the treatment of SBP since 1985 [29]. They were effective for CA-SBP in CLD, with resolution rates of around 80% in past [30], but the development of resistance to third-generation cephalosporins is of great concern. Resistance can

result in failure to respond to initial empirical therapy with a third-generation cephalosporin in 33%-75% of cases [19,25]. Recent studies indicate that third-generation cephalosporins are not appropriate for the treatment of hospital acquired infections in patients with CLD [31] because of effectiveness as low as 40% related to an increase in the prevalence of MDR bacteria in nosocomial infections [9,26], that is why SBP treatment recommendations distinguish between CA-SBP and HA-SBP [9,32]. Moreover resistance to third-generation cephalosporins occurred in 7.1% of CA-SBP, 21.1% of health care associated SBP (HCA-SBP) and 40.9% of Hospital Acquired SBP (HA-SBP) in recent past [33]. Some studies recommend combination regimen of meropenem and daptomycin for the management of HA-SBP [25,26], and some recommend cefoperazone/sulbactam or piperacillin/tazobactam for the empirical treatment of SBP [34].

Overall paradigm of SBP is constantly changing with easy access to hospitals and ever increasing use of antibiotics. Early antibiotic treatment of SBP is crucial. With spread of MDR organisms its current management is still challenging. There is a constant need to evaluate this infection, by observing its behaviour, new strategies aiming towards diagnostic improvement and management can be sought. Our study provides fresh insight into its etiology and resistance profile to design better empiric regimen.

OBJECTIVE

Study etiological profile and resistance pattern of SBP in CLD.

MATERIALS AND METHODS

This prospective observational study was conducted in department of gastroenterology and hepatology, superspeciality hospital, Shreenbagh, Srinagar. It is a twenty seven bedded department with round the clock gastroenterology services.

All patients of cirrhosis and ascites with possibility of SBP more than 10 years of age were recruited from out-patient Department of Gastroenterology and Hepatology, and medical emergency of government medical college; Srinagar over one year period. A predesigned structured proforma was used to record patient's demographics, clinical presentation and laboratory results.

Exclusions

Etiology of ascitis other than liver disease, recent antibiotics use (within two weeks), suspected or conformed intra-abdominal source of infection like surgery or trauma, children under 10 years of age and those who did not consented to participate.

Paracentesis (only diagnostic tap) was performed bedside with under mentioned protocol:

1. Performed using standard aseptic precaution for all study participants.
2. Twenty milliliter syringes with 20 G (gauge) needle used for ascitic fluid (AF) tap in left iliac fossa or midline below umbilicus at bedside.
3. Total 20 milliliters AF was collected from each patient.
4. Ten ml for AF detailed biochemical and cytological report.
5. Ten ml of AF inoculated in blood culture bottles at the bedside using aseptic technique and send for microbiology (for aerobic and anaerobic culture).
6. Blood sample (10 ml) was collected at same time to perform serum/plasma based blood work up as deemed necessary.

Severity of liver disease was assessed by:

Child Turcotte Pugh (CTP) score: Depending of sum of these five variables patients are divided into three classes; A (score of 5-6), B (score of 7-9) and C (score of 10-15). Class A has 1 year survival of 100% and 2 year survival of 90%. Class B has 1 year survival of 81% and 2 year survival of 57%. Class C has 1 year survival of 45 % and 2 year survival of 35%.

Parameter	1	2	3
Encephalopathy	None	Stage 1-2	Stage 3-4
Ascitis	None	controlled	Poor control
Serum Bilirubin (mg/dl)	< 2	2-3	≥ 3
Serum Albumin (gm/dl)	> 3.5	3-3.5	< 3
Prothrombin time/ INR	0-4 / < 1.7	5-6 / 1.7-2.3	> 6 / > 2.3

Model of End-Stage Liver Disease (MELD) scores: Is calculated by using formula:

$$\text{MELD} = 9.57 \times \text{LOG}_e(\text{creatinine}) + 3.78 \times \text{LOG}_e(\text{total bilirubin}) + 11.2 \times \text{LOG}_e(\text{INR}) + 6.43$$

Originally was designed for post Transjugular intrahepatic portosystemic shunt survival. It also predicts severity of liver disease and cirrhosis related mortality (3 months). Mortality by MELD score 8% with score of 10-19, 24% with score of 20-29, 60% with score of 30-39, 81% with score of 40 and above. It is also used in allocation of organs for transplant.

Infections diagnosed on admission or within 2 days after admission were classified as Hospital Care Associated (HCA) in patients with a prior contact with the healthcare environment (hospitalization or short-term-admission for at least 2 days in the previous 90 days, residence in a nursing home or a long-term care facility or chronic hemodialysis). The infection was considered CA when present at time of admission or developed within the first 2 days after hospitalization with no history as mentioned above in HCA and HA when the diagnosis was made thereafter [32,35].

MDR was defined as non-susceptibility to at least one agent in 3 or more antimicrobial categories. Extended Drug Resistant (XDR) was defined as non-susceptibility to at least one agent in all but 2 or fewer antimicrobial categories and Pan Drug-Resistant (PDR) as non-susceptibility to all currently available agents [36].

Data analysis

Statistical analysis was conducted using SPSS ver. 16.0 for Windows (SPSS, Chicago, IL). Categorical variables were compared using the chi-square or Fisher's exact test where appropriate. Continuous data were compared using the t-test or the Mann-Whitney test, the Kruskal-Wallis test was used for multiple comparisons, when appropriate. Quantitative variables with a normal distribution were expressed as mean values \pm standard deviation and those with a non-normal distribution as median values (range). Significance level was two-sided and set to less than 0.05.

Informed consent was obtained from all participants or their attendants.

This study was cleared by institution's review board.

RESULTS

Prevalence of SBP in CLD presenting at our center was 38.09% (112/294). Eighty two patients were included in study. Mean age of patients was 59.09 ± 12.90 years with minimum of 20 and maximum of 89. Male were 47 (57.3%) and females were 35 (42.7%). Most common clinical presentations were ascitis 100% and hepatic encephalopathy 89%.

Majority of patients were CTP-C class i.e 73.2%. Other 15.9% and 11% were CTP-B class and CTP-A class respectively in our study.

Laboratory parameters are given in table 1. Ascitic fluid analysis is given in table 2. Mean leukocytes and neutrophils in ascitic fluid were 673 ± 340.11 and 517.95 ± 300.21 respectively. Mean SAAG was 1.30 ± 0.27 .

Table 1: Laboratory parameters (blood) of patients with SBP on admission.

S.No.	Parameter	n = 82
1	Haemoglobin g/ dl	8.43 \pm 2.42
2	Leukocyte count	14124.40 \pm 3953.82
3	Platelets	118759.96 \pm 65428.32
4	INR	1.86 \pm 0.73
5	S. Bilirubin total	2.70 \pm 2.53
6	S. Albumin	2.72 \pm 0.62
7	S. Total Protiens	5.91 \pm 0.79
8	S. Creatinine	1.34 \pm 0.58
9	S. Glucose	135.30 \pm 50.30
10	S. LDH	148.80 \pm 32.31
11	S. Aspartate transaminase	85.37 \pm 28.80
12	S. Alanine transaminase	73.39 \pm 29.28
13	S. Alkaline phosphatase	119.86 \pm 30.88
14	S. Sodium	132.70 \pm 7.72
15	S. Potassium	3.52 \pm 0.83
16	S. ESR	43.89 \pm 18.99
17	S. CRP	13.11 \pm 5.56



In our study CA-SBP was present in 55 (67%), HCA-SBP in 29.3% and HA-SBP in 3.7% respectively. We found CP-SBP in 54.87% and CN-SBP in 45.13% cases. On comparing culture positivity with SBP profile, 58% of CA-SBP, 67% of HCA-SBP and 100% of HA-SBP were CP (*p*-value = 0.044).

We compared SBP profile with resistance pattern of pathogens. In CA-SBP, Drug Sensitive (DS) were 18(69%), MDR were 7(27%) and XDR were 1(4%). In HCA-SBP, DS were 4(25%), MDR were 8 (50%) and XDR were 4(25%). In HA-SBP, DS were 1(33%) and MDR were 2(67%) as in table 3 & 4. (*p* -value = 0.03). Twelve cases have previous history of SBP, and all were culture positive. Out of which 7(58%) were MDR, 4 (33%) were XDR and 1 (8.3%) was drug sensitive as in table 5 (*p*-value =0.00).

Among cases with CP-SBP; 44 (97.78%) were caused by bacteria and 1 (2.22%) was fungal. In bacterial CP-SBP, GNB were 68.19% and Gram Positive Bacteria (GPB) were 31.81%. We compared pathogen profile with resistance pattern and found significant difference among pathogens regarding resistance to antibiotics (*p*-value =0.00). *Escheria coli* (*E. coli*) was cultured in 25 (55.55%) of which 12 were DS, 12 were MDR and 1 XDR; *Staphylococcus aureus* in 13 (28.88%) of which 10 were DS and 3 were MDR; *Klebsiella pneumoniae* in 2 (4.44%), both were MDR; *Pseudomonas aeruginosa* in 2 (4.44%) both were XDR; *Acinetobacter baumannii* 1 (2.22%) was XDR;

Table 2: Laboratory parameters (ascitic fluid) of patients with SBP.

S. No.	Parameter	n = 82
1	Leukocytes	673 ± 340.11
2	Neutrophils	517.95 ± 300.21
3	Proteins	3.13 ± 0.76
4	Albumin	1.44 ± 0.50
5	Saag	1.30 ± 0.27
6	Glucose	107.98 ± 44.23
7	Lactate Dehydrogenase	62.36 ± 14.81

Table 3: SBP profile compared with ascitic fluid culture.

SBP Profile	CA-SBP	Ascitic Fluid Culture		Total
		Negative	Positive	
SBP Profile	CA-SBP	29	26	55
		78.4%	57.8%	67.07%
	HA-SBP	0	3	3
		0.0%	6.7%	3.65%
SBP Profile	HCA-SBP	8	16	24
		21.6%	35.6%	29.26%
Total		37	45	82
		100.0%	100.0%	100%

p-value = 0.044

Table 4: SBP profile comparison with resistance profile

SBP	HCA	Resistance Profile			Total
		DS	MDR	XDR	
SBP	HCA	4	8	4	16
		25.0%	50.0%	25.0%	100.0%
	CA	18	7	1	26
		69.2%	26.9%	3.8%	100.0%
SBP	HA	1	2	0	3
		33.3%	66.7%	0.0%	100.0%
Total		23	17	5	45

p-value = 0.03

Table 5: Pathogen compared with resistance profile

Pathogen		Resistance Profile			Total
		DS	MDR	XDR	
Pathogen	<i>Acinetobacter Baumannii</i>	0	0	1	1
		0.0%	0.0%	100.0%	100.0%
	<i>Candida Albicans</i>	1	0	0	1
		100.0%	0.0%	0.0%	100.0%
	<i>Escheria Coli</i>	12	12	1	25
		48.0%	48.0%	4.0%	100.0%
	<i>Klebsiella Pneumonia</i>	0	2	0	2
		0.0%	100.0%	0.0%	100.0%
	<i>Micrococcus Luteus</i>	0	0	1	1
		0.0%	0.0%	100.0%	100.0%
	<i>Pseudomonas Aeruginosa</i>	0	0	2	2
		0.0%	0.0%	100.0%	100.0%
<i>Staphylococcus Aureus</i>	10	3	0	13	
	76.9%	23.1%	0.0%	100.0%	
Total		23	17	5	45
		51.1%	37.8%	11.1%	100.0%

p-value = 0.003

Micrococcus luteus in 1 (2.22%) was XDR and *Candida albicans* in 1 (2.22%) was DS as in table 6 and figure 1. Highest antibiotic resistance was seen with levofloxacin 71%, followed by ciprofloxacin 67.45%, cotrimoxazole 66% and ceftriaxone 64.52%. Reasonably good sensitivity in range of 70% to 90% was found in Ceftaroline, Piperacillin-tazobactam, Meropenem and Imipenem. Sensitivity was highest with Colistin, Tigecycline Daptomycin, and Ceftaroline approaching 100% as in figure 2.

Sixty six (80.49%) patient were treated successfully and discharged. Sixteen cases of SBP died during hospital stay giving mortality rate of 19.51%. Death rates as per CTP class were; 23.3% in CTP-C and 15.4% in CTP-B. There were no deaths in CTP-A.

Out of 16 deaths, 14 (71.42%) were CTP- C class. 100% deaths were recorded in patients with SBP because *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Micrococcus lutes*.

DISCUSSION

SBP is one of the infections in CLD with dynamic etiologic profile demanding meticulous observation and updated management strategy in view of ever changing antibiotic sensitivity profile to improve outcome. We provide fresh insight into etiologic profile and resistance pattern in this infection.

Prevalence of SBP in CLD with ascitis presenting at our center was 38.09%. Mean age of cases was 59.09 ± 12.90 years. Most common clinical presentations were ascitis 100% and hepatic encephalopathy 89%.

Harchand P et al. [37] studied 58 cases with SBP and found prevalence of 51.3% (58/ 113). Mean age of cases was 49.72 ±10.3 years with males 86.7% and females 13.3%. Li YT et al. [27] studied 288 cases with SBP with mean age of 55 ± 12.6 years, males were 198 and females were 90. Friedrich K et al. [19] studied 311 cases of 1st time SBP with mean age of 57.8 ± 23.7 years, males were 70% males and females were 30%. Li YT et al. [27] reported 68.9% in child C, 8.6% in child B, and 2.5% in child A class respectively in their study. Similarly studies by Kawale JB in 2017 and Harchand P in 2017 reported 56% and 87% majority of patients in CTP-C class respectively [37,38].



In our study CP-SBP was 54.87% and CN-SBP was 45.13%. Payal H Purohit et al. [39], Harchand P et al. [37] and Ivan Gunjace et al. [40] reported culture positivity of 43.6%, 38% and 15% respectively. Friedrich K. [19] reported culture positive in 138 /311 (44.37). These differences could be attributed to the evolution of pathogens, different culture techniques and variable antibiotic use. Etiological profile of SBP in CLD is changing world over. Among cases with CP-SBP; 44 (97.78%) were caused by bacteria and 1 (2.22%) was fungal (Table 6) (figure 1). Among bacterial CP-SBP, GNB were 68.19% and GPB were 31.81%. Fiore M et al. [41] reported 0%-7.2% CP for fungus and the most frequent isolate was *Candida albicans*. Harchand P et al. [37] reported GNB isolates in 77.3% and GPB isolates in 22.7% of cases. Ivan Gunjace et al. [40] reported GPB pathogens in 40% of patients. Payal H Purohit et al. [39] studied 31 (43.6%) cases of CP-SBP, most of them were GNB, mainly *E. coli* in 22 (70.9%) and GPB in 6 (19.3%) cases. Friedrich K et al. [19] reported GPB in 47.8%, GNB in 44.9% and fungal in 7.2% cultures. Li YT et al. [27] reported GPB in 27.8%, GNB in 58.2% and fungal in 2.9% cultures. Most of studies report predominance of gram negative organisms in ascitic fluid cultures, however there studies showing trend towards increasing percentage of infections caused by gram positive bacteria. Our study follows same changing trend of increasing gram positive infections world over with GPB cultures in 32% of cases.

Profile of organisms causing SBP in our study is shown in table 6 and figure 1 and their resistance profile in table 6 and figure 2. In our study, *E. coli* was most common organism causing SBP i.e 25/45 (55.55%) of which 12 were DS, 12 were MDR and 1 XDR. 52% of *E. coli* in our study was either MDR or XDR; Harchand P et al. [37] reported *E. coli* in 68.1% of cultures. Of 15 *E. coli* isolates, 13 (86.6%)

Table 6: Previous SBP compared with resistance profile

		Profile Resistance				Total
		DS	MDR	CN	XDR	
Previous SBP	NO	22	10	37	1	70
		95.7%	58.8%	100.0%	20.0%	85.4%
Previous SBP	YES	1	7	0	4	12
		4.3%	41.2%	0.0%	80.0%	14.6%
Total		23	17	37	5	82
		100.0%	100.0%	100.0%	100.0%	100.0%

p-value = 0.00

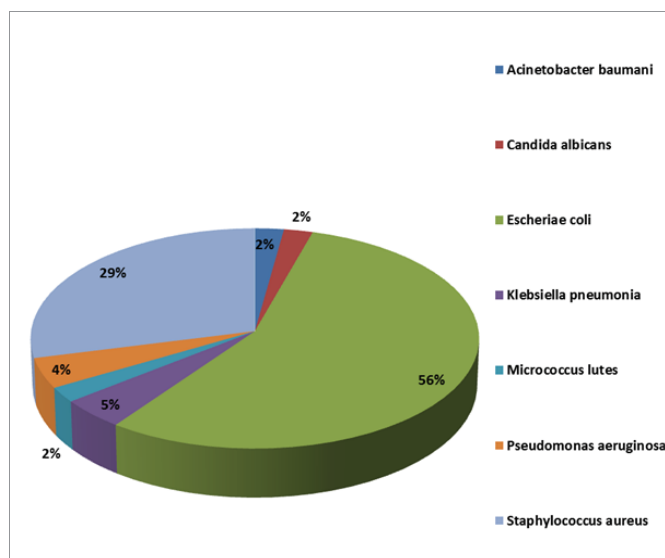


Figure 1: Etiological profile of SBP (n = 45).

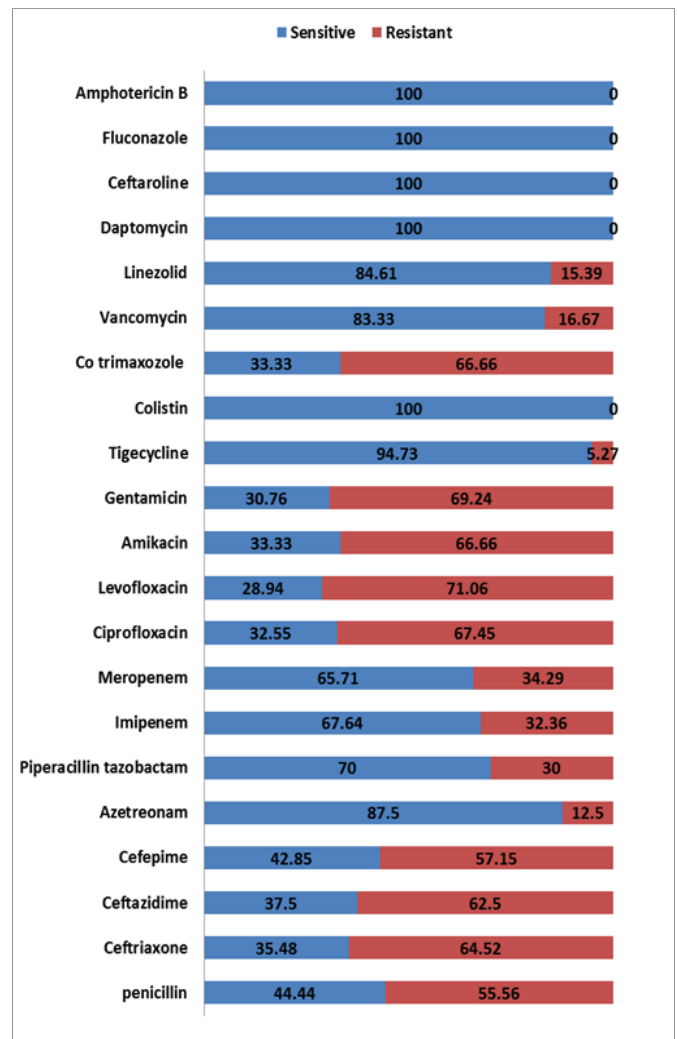


Figure 2: Antibiotic sensitivity profile % (n = 45)

were MDR and 3 (20%) were XDR. Friedrich K et al. [19] reported *Enterobacter sp.* in 41%. Li YT et al. [27] reported *E. coli* in 24.2% cases and drug resistance around 40%. Payal H Purohit et al. [39] in study of 31 culture-positive cases, *E. coli* was isolated from 17 (54.9%) cases. Ivan Gunjace et al 2010 [40] found *Escherichia coli* in 13 (43.6%) of cases and Li Sun et al. [42] in 53.1% (1st period part of study)/39.8% (2nd period of study) of ascitic fluid cultures respectively.

We found *Staphylococcus aureus* in 13 (28.88%) of which 10 were DS and 3 were MDR. Friedrich K et al. [19] reported *staphylococcus sp.* in 13.8%. Li YT et al. [27] reported *Staphylococcus aureus* in 7.5% cases. Ivan Gunjace et al. [40] cultured *staphylococcus* species in 4(24.9%) of cases. Li Sun et al. [42] reported *staphylococcus aureus* in 4.7%/ 7.2% in 1st/ 2nd period of his study. Over all there has been increasing frequency of gram positive infection as especially *staphylococcus sp.* as evident above. Our study shows similar trend.

We found *Klebsiella pneumoniae* in 2 (4.44%) and both were MDR, Harchand P et al. [357 in 4.05%, Friedrich K et al. [19] in 7.2%, Li YT et al. [247 in 18.9%. Payal H Purohit et al. [39] isolated *Klebsiella* species from 5 (16.2%) cases. Li Sun et al. [42] reported *Klebsiella* species in 10.9%/ 10.8% in 1st/ 2nd period of his study. We found *Pseudomonas aeruginosa* in 2 (4.44%) cases, both were XDR, Friedrich K et al. [19] in 0.7%, Li YT et al [27] in 2.9%. We found *Acinetobacter baumannii* in 1 (2.22%) case, it was XDR, Li YT et al.

[27] in 3.3%, Ivan Gunjace et al. [40] in 2 (12.5%). our study also have more of these bacteria in HCA-SBP and HA-SBP (p value = 0.003). We found *Micrococcus luteus* in 1 (2.22%) was XDR and *Candida albicans* in 1 (2.22%) was DS. Li Sun et al. [42] found *micrococcus lutes* in 1.2% of case.

Results of our study are in line with current trends world over with gram negative enteric organisms most frequent isolates. *Escheriae coli* being most common isolate from ascitic fluid cultures in SBP patients in most of these studies. However regarding other pathogens literature is heterogeneous regarding frequency and resistance pattern.

In our study overall 71.42%, 21.42% and 7.1% isolates of gram positive bacteria were DS, MDR and XDR respectively whereas 40%, 46.6% and 13.40% isolates of gram negative bacteria were DS, MDR and XDR respectively (Table 4 & 6) (Figure2). Highest antibiotic resistance was seen with levofloxacin 71% followed by ciprofloxacin 67.45%, co-trimoxazole 66% and ceftriaxone 64.52% (Figure 2). Sensitivity was highest with Colistin, Daptomycin, and Ceftaroline approaching 100% (figure 6). Friedrich K et al. [19] found highest resistance to erythromycin 87%, ampicillin i.e 40% followed by quinolones 58%, ceftriaxone 39%, vancomycin in 49% and sensitivity was highest in Tigecycline i.e 95% followed by piperacillin/tazobactam 89.9%, gentamicin 84.3% and meropenem 73.2%. He concluded third generation cephalosporins have poor antibiotic coverage of 60% and recommends against current guidelines of third generation as first line empiric therapy. Harchand P et al. [37] found Gram-negative isolates have high susceptibility to Colistin, Tigecycline, amikacin, and Carbapenems, while low susceptibility was seen toward Cephalosporins and Ampicillin. All the Gram-positive isolates susceptible to Penicillin, Teicoplanin, Vancomycin, Linezolid whereas showed less susceptibility to Aminoglycosides (40%) and to Fluoroquinolones, Macrolides, and Tetracycline's (20% each). Among the culture-positive isolates, MDR and XDR were seen more in *E. coli* isolates. Of 15 *E. coli* isolates, 13 (86.6%) were MDR and 3 (20%) were XDR. Payal H Purohit et al. [39] reported staphylococcus aureus resistance profile as; 20% in amoxicillin, 32% in erythromycin and 60% in penicillin's: *E. coli* resistance profile as; 30% in ciprofloxacin, 20% in tetracycline and 10 in Ofloxacin %. *Klebsiella* species resistance profile reported as; 20% in ciprofloxacin, 30% in tetracycline: *Pseudomonas* species resistance profile as; 22% in ampicillin, 33% in ciprofloxacin, 50% in tetracycline and 20% in ofloxacin. In our study highest antibiotic resistance was seen with levofloxacin 71% followed by ciprofloxacin 67.45%, co-trimoxazole 66% and ceftriaxone 64.52% because most of these antibiotic are available in government hospital supply free of cost so are more often used. Our study shows increasing trend of GP infections and increasing MDR in gram GN infections, similarly world literature is reporting increasing incidence infections by GPB and MDR bacteria [30,34,43].

Sixty six (80.49%) patient were treated successfully and discharged. Sixteen cases of SBP died during hospital stay giving mortality rate of 19.51%. Mortality was highest in CTP-C, out of 16 cases; 14 (87.5%) belonged to CTP-C. There were no deaths in CTP-A. 100% deaths were recorded in patients with SBP because *Acinetobacter baumani*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa* and *Micrococcus lutes*. Mortality in patients with SBP reported in other studies was 44% and 26.60% by Juhi B. Kawale et al. [36] and Ivan Gunjace et al. [40] respectively. Recent data reported that SBP mortality was 24.2% at 1 month and 66.5% at 3 year [16].

CONCLUSION

SBP in CLD with ascitis presenting at our center was 38.09%. Etiological profile of SBP in CLD is changing world over. In our study most of infections were caused by GNB (67%) and prevalence of antibiotic resistance is high approaching 60% (increasing trend). *E. coli* was cultured in 25 (55.55%) of which 52% were MDR's and XDR's; *Klebsiella pneumoniae* in 2 (4.44%), both were MDR; *Pseudomonas aeruginosa* in 2 (4.44%) both were XDR; *Acinetobacter baumannii* in 1 (2.22%) was XDR. High antibiotic resistance was seen to commonly used antibiotic in SBP like quinolones, aminoglycosides and third generation cephalosporins, approaching 60% to 70%. GPB were present in 31.81% of cases (increasing trend), and resistance was found in only 28.58% isolates. 50% of HCA- SBP was caused by MDR's and 25% by XDR's respectively i.e total of 75% (increasing trend).

We recommend all ascitic fluid culture to be screened for presence of MDR, XDR and PDR strains to improve outcome. We also suggest extended spectrum penicillin's or Carbapenems plus vancomycin or daptomycin therapy as Ist line for suspected cases of SBP keeping in view increasing MDR pathogen infection, rising cases of community acquired MDR SBP in our community with caveat that local resistance pattern be taken into account.

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