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Research Article

**AN EMPIRICAL STUDY TO EXAMINE THE 3<sup>RD</sup> GENERATION  
ENDURANCE OF CEPHALOSPORIN AMONG PATIENTS  
HAVING COMMUNAL EXISTENCE OF SPONTANEOUS  
BACTERIAL PERITONITIS [SBP]****Maida Ghaffar<sup>1</sup>, Ammara Ghaffar<sup>2</sup>, Muzzammil Ghaffar Qureshi<sup>3</sup>,  
Muddassar Ghaffar Qureshi<sup>3</sup>**<sup>1</sup>King Edward Medical University, Lahore; <sup>2</sup>Fatima Jinnah Medical University, Lahore; <sup>3</sup>Fatima Memorial College of Medicine and Dentistry, Lahore; <sup>4</sup>Ameer Ud Din Medical College, Lahore.**Article Received:** July 2019**Accepted:** August 2019**Published:** September 2019**Abstract:**

**Objective:** We aimed in this study to define the 3<sup>rd</sup> generation endurance of cephalosporin among patients having communal existence of spontaneous bacterial peritonitis (SBP) by the help of early response assessment.

**Study Design:** This was an empirical interventional type of study.

**Place and duration:** This analysis was conducted at Jinnah Hospital, Lahore with the duration of one year started from March 2018 to February 2019.

**Methodology:** This empirical interventional type of analysis was having the sample size of 31 patients of spontaneous bacterial peritonitis [SBP] and cirrhosis. For the treatment of spontaneous bacterial peritonitis (SBP) 3<sup>rd</sup> generation cephalosporins that is formulated as cefotaxime or ceftriaxone were processed. Result was examined after 48 hours and decline in ascitic liquid neutrophil with the value of less than 25% of baseline was written as resilient of cephalosporin. For the second line treatment we used carbapenem drugs. Discharge or mortality of patients and recovery were main end points.

**Results:** Number of Male and female patients having spontaneous bacterial peritonitis were 17 and 14 with the ratio of 1.2 and 1.0 respectively. Among 11 patients with the percentage of 37.9%, hepato-renal syndrome was discovered. Cefotaxime and ceftriaxone were processed for the patients with the number of 16 and 15 with the percentage of 51.6 % and 48.3 % respectively. Number of 26 patients with the percentage of 83.8 % were noticed to have early retort of Spontaneous bacterial peritonitis whereas number of 5 patients with the percentage of 16.2 % were found to have no reaction with cephalosporins. All Spontaneous bacterial peritonitis patients which have no reactions were treated through intravenous carbapenem. Death ratio in hospital was of percentage 12.9 % and had no relevance to the confrontation of cephalosporin. P Value of High bilirubin test was 0.04, P value Disturbance of INR test was 0.008, P value of low albumin was 0.04, P Value of high Child Pugh [CTP] was 0.03 and P value of MELD scores was 0.009 were relevant to in-hospital death rate.

**Conclusion:** It was concluded through our study that the analyzed patients with the percentage of 16.2 % with communal existence of Spontaneous bacterial peritonitis [SBP] have cephalosporin confrontation. Deteriorating stage of liver disease was related to the death rate of patients with Spontaneous bacterial peritonitis.

**Keywords:** Spontaneous bacterial peritonitis, Death rate of in-hospital patients, Resistance, Cephalosporins.

**Corresponding author:****Maida Ghaffar,**

King Edward Medical University, Lahore.

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**INTRODUCTION:**

A fearful complexity among the patients of decompensated cirrhosis is Spontaneous bacterial peritonitis [SBP]. A potential analysis resulted that patients of cirrhosis with the percentage of 47% where been admitted in hospital having existence of bacterial influences and out of these patients, a percentage of 31% have Spontaneous bacterial peritonitis [1]. Regardless of optimal diagnosis with 1-year death ratio with the percentage of 60.0 % and 1-month death rate with the percentage of 32% was estimated [2]. It is the result of raised growth of intestinal bacterial infection, easy translocation through intestine directed to reduced host immune reaction in a patient having liver cirrhosis [3]. Each patient that was been admitted in hospital with ascites should be treated through diagnostic paracentesis to treat SBP. Death rate of patients that were processed through paracentesis during admission was less than patients which did not have ascitic liquid analysis with the comparison of percentage 6.3 % against 8.9 % sorting out the probability if missing treatment of Spontaneous bacterial peritonitis [4]. An else analysis found out that every hour postponement in paracentesis of admitted cases of cirrhosis with the reference of ascites raises death rate with the percentage of 3.3 % [5]. Treatment of SBP based on absolute neutrophil value in ascitic fluid and value more than 250 per mm<sup>3</sup> is supposed to diagnostic for spontaneous bacterial peritonitis. Cultures are positive in just 40.0 % of cases that can be raised to a percentage of 80.0 % with bedside inoculation of fluid in culture bottle [6]. Pre-empirical diagnosis through antibiotics is endorsed because of low yield of fluid culture and maximum death rate. Each hour postponement in processing of antibiotics raises the death rate with 1.86 times noticed by a study of Karvellas et al [7]. Suggestion of antibiotics is based on the type of microbes accountable for the disease. The most usual pathogens accountable for SBP were supposed to be the Gram-negative bacteria. That is the cause of 3<sup>rd</sup> generation cephalosporins are accountable medicines of choice for the diagnosis of SBP

empirically [8]. Since previous two eras, it is most likely because of deviating bacterial pathogens of SBP as now Multi Drug Resistance Organisms [MDRO] as and gram-positive bacteria are raising being secluded in SBP [9]. It is the influence of excessive, over the pledge wrong processing of cephalosporins in community and continuous revelation of cirrhosis cases with these medicines while persistent hospital admissions. The cause is this developing tendency of confrontation most international suggestions are indorsing selectivity of medicines considering regional frequency of micro-organisms accountable for the antibiotic confrontation methods and SBP. So, because of decreased ascitic fluid culture yield diagnosis might be directed by first refusal in PMN value after commencing antibiotic treatment. Current EASL directions have almost accounted the processing of early reaction valuation that is refusal of neutrophil value in ascitic fluid of equal or more than a percentage of 25.0 % of baseline value after 48 hours of antibiotic treatment for direction related to the diagnosis reaction [10].

This is rareness of information for the prevention of micro-organisms persistent for SBP in cirrhosis patients in our country there is no communal directed information on antibiotic confrontation to direct our running conclusions. Unjustified processing of antibiotic medicines is most maximum dominant in our community versus western nations [11]. So, we are more likely to conduct MDROs in our SBP patients. We require to acknowledge medicine confrontation methods specially for cephalosporins that are still first line suggested medicines for Spontaneous bacterial peritonitis. Because of very least yield of ascitic fluid culture, early retort analyzation in SBP patients can be a better implement to direct our diagnostic schedule. We prearranged an analysis to sort out the 3<sup>rd</sup> generation cephalosporin confrontation in our cases of SBP through processing early retort analyzation to direct diagnostic result.

**METHODOLOGY:**

This prospective quasi-experimental analysis was conducted at Jinnah Hospital, Lahore with the duration of one year started from March 2018 to February 2019. Liver cirrhosis patients that were admitted with ascites were sorted in this analysis. Liver cirrhosis was diagnosed in accordance with the coarse and nodular consistency of liver by ultrasound test. Patient that declined to ascitic fluid paracentesis, those with ascites subordinate to affects else than cirrhosis such as kidney disease, Congestive cardiac failure, malignancy, tuberculosis etc were not included in our research study. Patients who progressed Spontaneous bacterial peritonitis [SBP] more than 48 hours after admission as established by negative first ascitic fluid report were also not included. Ascites was identified as insignificant, just noticeable through ultrasound test restrained with reasonable symmetrical stomach disorder and tension, if abdomen is exceptionally inflated.

More than 48 hours after admission as confirmed by negative initial ascitic fluid report were also excluded. Ascites was graded as mild, only detectable on ultrasound examination, moderate, with moderate symmetrical abdominal distension and tense, if abdomen is completely inflated. European Association for Study of Liver has indorsed in its directions of the year 2018 to suggest the ailment harshness and regional confrontation method during the selection of antibiotics. Piperacillin or Tazobactam is supposed to be first line medicine for both communal existed and nosocomial infections ever for areas with minimum occurrence of MRDO. Paracentesis of ascitic fluid was processed through ultrasound test by drawing minimum 50ml of fluid by use of standard aseptic methods for various values, culture, cytology and biochemistry.

identification of SBP was verified if exact neutrophil value in ascitic fluid was value of  $>250/mm$ . Just cases verified to have Spontaneous bacterial peritonitis [SBP] on ascitic fluid examination at admission that were enrolled. Lab assessments consisting of renal activity examination, serum electrolytes, liver function analyzations, complete blood count and coagulation profile were carried out on admission. Model for End Stage Liver Disease [MELD] and Child Pugh Turcotte [CTP] were processed to classify liver disease. Sequential Organ Failure Assessment [SOFA] were carried out to analyze seriousness of disease. All cases were classified casually though online random table generator Stat Trek® such as Group A and Group B. Patients of Group A were treated with cephalosporin 3<sup>rd</sup> generation intravenously, cefotaxime with the

value of 8 grams per day in 4 merged medications while patients of Group B were treated through ceftriaxone with the value of 2 grams per day. All patients were treated through 20 grams albumin per day for the duration of 5 days. Patients of hepato-renal syndrome Type-1 were almost injected Terlipressin with the quantity of 4mg per day by regular medicine increase, if no retort, equal to maximum quantity of 12 mg per day. Hepatic encephalopathy, variceal bleeding, electrolyte disorders were coped if existed in accordance with standard protocol.

Patients were examined daily for renal activities, growth of hepatic encephalopathy or GI bleed, vital signs, symptoms, serum electrolytes and fluid intake or output if existed. Continuous paracentesis was processed after 48 hours of treatment and fluid was examined for actual value of neutrophil. Decrease in value of neutrophil more than or equal to a percentage of 25% of base line value was thought to be positive early response of spontaneous bacterial patriotic diagnosis and same method was processed for duration of 5 days. Patients out of those absolute neutrophil count failed to reject by percentage of 25% or above were written as cephalosporin reactant and their treatment was reformed according to ascitic fluid culture and sensitivity report. Intravenous carbapenem group of medicines by changing of dose for creatinine consent less than quantity of 50ml/min were given among patients of negative fluid culture report. Recheck paracentesis was performed again in all patients with medication variation to confirm reaction to treatment. Primary result evaluation was existence or non-existence of early reaction to cephalosporins while discharge from hospital or mortality at the time of enrollment in hospital were secondary result evaluations.

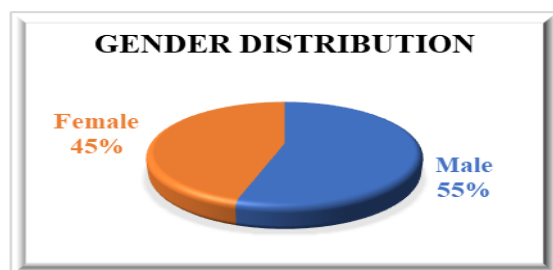
Information was studied through SPSS 21. Numerical changes as MELD score, CTP score, age etc were presented as Mean±Standard Deviation [SD] and categorial changes as grades of ascites etc were written in percentage for usually merged differences while median and Interquartile range [IQR] for variables not usually divided. Shapiro-wilk examination was carried out to examine if variables were normally divided or not. Unpaired student's examination was performed to evaluate numerical variables whereas  $\chi^2$  examination was processed to evaluate categorial differences. Mann-Whitney U test was carried out for variables not usually dispersed. Value of P less or equal to 0.05 was suggested to be definite or significant.

**RESULTS:**

Total number of 31 patients were sorted in this analysis. Number of male patients and female patients was 17 and 14 with the ratio of 1.2 and 1.0 respectively. Number of 19 patients with the percentage of 61.3 % were showing Fever, number of 28 patients with the percentage of 90.3 % were suffering from worsening ascites, 13 patients with percentage of 41.9 % were having hepatic encephalopathy at time of enrollment and 3 patients with the percentage of 9.7 % were undergoing variceal bleeding. Ascites was least in number of 2 patients with the percentage of 6.5 %, maximum in 21 patients with the percentage of 67.7 % and anxious in 8 patients with the percentage of 25.8 %.

**Table No 01: Gender distribution**

Gender	Quantity	Percentage
Male	17	54.84%
Female	14	45.16%



Pleural effusion was existed in number of 6 patients with the percentage of 19.4 %. Hepato-renal syndrome [HRS] was treated in 11 patients with the percentage of 35.5 %, number of 5 patients with the percentage of 16.1 % had HRS Type-1 and HRS Type-2 was found in 6 patients with the percentage of 19.4 %. Liver cirrhosis was CTP class B in number of 10 patients with the percentage of 32.3 % while left 21 patients with the percentage of 67.7 % were in CTP class C. MELD Score was value of 20 or above than it among 20 patients with the percentage of 64.5 % while SOFA score more than 9 was observed in 3 patients with the percentage of 9.6 %. Hepatocellular carcinoma was existed in 7 patients with the percentage of 22.5 %. Ascitic fluid culture was positive in just 1 patient for E. Coli.

Cefotaxime therapy was processed in Group A patients with the number of 16 with the percentage of 51.6% while number of 15 patients with the percentage of 48.4% were treated through ceftriaxone in Group B. Every patient was injected intravenously

albumin and 5 patients with the percentage of 16.1 % got terlipressin for HRS Type-1. Number of 26 patients with the percentage of 83.8 % got rejection of more than or equal to a percentage of 25.0 % in absolute in ascitic fluid within 48 hours while 5 patients with the percentage of 16.2 % were unable to get prior reaction to therapy, 2 patients with the percentage of 12.5 % among Group A and 3 patients with the percentage of 20.0 % among Group B and variables were indefinite or insignificant where the value of p was 0.57 and were represented as Cephalosporin resilient patients. Antibiotic was converted to Meropenem in 4 patients with the percentage of 12.9 % while 01 patient was treated with Tienam or cilastatin sodium and imipenem for the treatment of cephalosporin SBP resilient.

All 5 patients had determination of disease by new antibiotics as verified on continuous paracentesis. Out of 5 patients with HRS Type-1, 4 patients with the percentage of 80.0 % reacted to therapy whereas 1 patient gone died despite hemodialysis. Number of 4 patients with the percentage of 12.9 % died during stay in Hospital, 2 patients with the percentage of 6.4 % got death because of worsening encephalopathy, 1 patient with the percentage of 3.4 due to HRS and 1 patient with the percentage of 3.2 % died due to chronic liver failure and no one because of non-determination of SBP out of all enrolled patients.

Death rate was written in Group A having 01 patient with the percentage of 6.2 % and in Group B consisting 3 patients with the percentage of 20.0% and the variables were again indefinite or insignificant where the value of p was 0.25. We matched patients with and without cephalosporin confrontation. Patients were same according to the severity of liver ailment in every group considering that reaction to treatment is not an outcome of stage of liver disease but most usually is influence of type of organisms accountable for SBP. We almost performed virtual analysis of patients which died and those who got well of severe disease. In hospital mortality of patients with SBP was expressively related to deranged INR where the value of P was 0.008, increased bilirubin where the P value was 0.04, less albumin where the value of P was 0.04, high CTP score where the value of p was 0.03, worst MELD score where the p value was 0.009 and SOFA score more than 9 where the p value was less than 0.00. Death rate in patients with Spontaneous bacterial peritonitis was relevant to severity of existing liver cirrhosis but not a basic influence of cephalosporin. Details are given in following tabular forms.

**Table No 02: Patients comparison with and without cephalosporin resistance**

Variables	Cephalosporin sensitive patients (n=24)	Cephalosporin resistant patients (n=5)	P-value
	Mean±SD values	Mean±SD values	
Age in years	56.2±10.6	52.4±9.6	0.45
TLC (x 10 <sup>3</sup> /μL)	11.2±4.9	13.9±4.2	0.24
Platelet (x 10 <sup>9</sup> /L)	140.5±94.8	145.6±61.7	0.91*
PT (sec)	21.4±8.6	18.6±3.7	0.49
Bilirubin (mg/dl)	4.6±4.92	6.7±8.6	0.80*
Albumin (g/dl)	2.4±0.46	2.2±0.16	0.36
Creatinine (mg/dl)	1.52±0.9	2.26±2.14	0.20
CTP score	10.7±2.05	11.2±1.9	0.61
MELD score	23.4±8.3	24.8±9.5	0.73
SOFA score	4.85±3.3	6.6±3.9	0.30

\*Mann Whitney U test.

**Table No 03: Patient's variables associated with in-hospital mortality**

Variables	Patients who died (n=4)	Patients who recovered (n=25)	P-value
	Mean±SD values	Mean±SD values	
Age in years	53.5±14.8	55.9±10.0	0.66
TLC (x 10 <sup>3</sup> /μL)	15.8±2.7	11±4.7	0.06
Platelet (x 10 <sup>9</sup> /L)	109.5±73.7	146.1±91.7	0.45
INR	2.68±1.3	1.59±0.58	0.008
Bilirubin (mg/dl)	10.3±8.6	4.13±4.6	0.04*
Albumin (g/dl)	1.97±0.09	2.44±0.43	0.04
Creatinine (mg/dl)	2.7±2.3	1.48±0.88	0.04
CTP score	12.75±0.95	10.5±1.9	0.03
MELD score	33.5±2.3	22.1±7.9	0.009
SOFA score	11.25±2.9	4.22±2.4	0.00

\*Mann Whitney U test.

**DISCUSSION:**

The developing problem that is being confronted in each field of drugs is Antibiotic confrontation. It is the result of maximum processing of antibiotics since last few eras. Illogical processing of antibiotics and self-remedy are main consequents of increase of medicine confrontations. Now we have expressions as Multi-Drug Resistance [MDR], super Bugs, Extensive drug resistance [XDR], each presenting the extent of matter [12]. Administration of hypothetically fatal complexity of SBP in patients at last stage of liver disease is being opposingly influenced by raising medicine confrontation. Above than a percentage of 16 % of patients with communal attained SBP were confrontational to initial line diagnosis in this analysis, 3<sup>rd</sup> generation of cephalosporins with no variance in efficiency of ceftriaxone and cefotaxime. Total frequency of cephalosporin confrontation was 19.0 %, percentage for nosocomial attainment was 41.0 % and percentage for communal attainment was 8.0 %

through an analysis of 192 SBP patients [13]. Alexopoulou A, et al studied number of 47 SBP patients, a percentage of 60.0 % of these patients were relevant to healthcare diseases. Cephalosporin confrontation percentage was 49.0 % and quinolone confrontational percentage was 47.0 % whereas multi-drug resistance was observed in 19.0 % of isolated bacteria [14]. The raising confrontation with cephalosporins is most probably because of modifying microbiological flora accountable for SBP. Gram negative bacteria were usually observed as major etiology for SBP though it is being interrogated now. Gram positive cocci were accountable for a percentage of 45.9 % out of number of 140 patients of SBP surveyed by Enterobacteriaceae in patients with percentage of 31.7 % through an analysis by Novovic S et al [15]. Cephalosporin treatment for Spontaneous bacterial peritonitis flora was just of a percentage of 57.0 % in this analysis. Occurrence of gram-positive bacteria in culture positive SBP raised from a



percentage of 26.0 % to a percentage of 46.0 % through a 10 years continuous analysis of Oey RC et al [16]. Just single patient of SBP was culture positive by our analysis. Maximum of these cases are already on antibiotics either suggested by a general physician or because of self-remedy follow-on to negative culture outcomes. Through an else local analysis by Sajjad M et al, just a percentage of 25.0 % cases of SBP were cultural positive [17]. We haven't observed any relativity among stage of liver ailment and cephalosporin confrontation through our analysis. Preceding usage of cephalosporins, upper GI bleeding, nosocomial attainment and diabetes mellitus to be dangerous consequences for confrontation but irrelevant to degree of liver disorder by medicine confrontation that were acknowledged by Ariza X, et al. They distinguished raised death ratio of patients with cephalosporin confrontation [18]. Dangerous consequences for 1-month all-cause death presented maximum CTP score, confrontation to 3<sup>rd</sup> generation cephalosporins and severe kidney grievance were observed in a Korean analysis of number of 188 communally attained SBP patients [19]. Occurrence of hepatocellular carcinoma and hepatic encephalopathy were individual determinants for 30 days mortality in patients of SBP found through an analysis of number of 1176 SBP cases in Taiwan [20]. Relativity of death rate and antibiotic confrontation is usually observed on nosocomial diseases and minimum such in communally attained SBP [21]. Symptoms of deteriorating liver ailment such as MELD scores, high CTP, low albumin, deranged INR and high bilirubin were related by in-hospital death through our analysis but irrelevant to cephalosporin confrontation was observed by death rate. By this latest method of modifying SBP flora and manipulation of medicine confrontation the matching of antibiotics despite of 1 representative are being promoted for diagnosing SBP [22].

As we are highly facing confrontation to diagnosis of SBP so we require to change diagnostic methods. We require more information for prevention of microbial flora, confrontation methods and effectivity of different attained medicines. Our analysis outcomes will provide directions to these ideas in future. Our information is partial by mostly negative culture outcomes of ascitic liquid, a real-life condition where main choice of medicines is experimental. We have processed initial reactive analyzation at 48 hours of diagnosis to direct durable variations in therapy. It is an operative device for directing diagnosis decisions mainly in SBP patients with negative culture outcomes. Its processing would be empowered in administration of partial possessions for affluent

culture analyses and deprived adjustment of these examinations in the existence of maximum dangerous consequences of confrontation.

### CONCLUSION:

It was concluded through our analyses that the 3<sup>rd</sup> generation Cephalosporin confrontation is existed in patients with the percentage of 16.2 % with communal existence of Spontaneous bacterial peritonitis (SBP) have cephalosporin confrontation. deteriorating stage of liver disease was related to the death rate of patients with Spontaneous bacterial peritonitis but not with cephalosporin confrontation.

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