

Comparison of Intravenous Ciprofloxacin and Intravenous Ceftriaxone in the Management of Spontaneous Bacterial Peritonitis in Cirrhosis of Liver

Hafiza Munam Akhtar, Arif Mehmood Bhatti

Abstract:

Objective: To compare the effectiveness of intravenous ciprofloxacin versus intravenous ceftriaxone in spontaneous bacterial peritonitis (SBP) treatment of patients with liver cirrhosis.

Study Design and settings: Randomized controlled trial at Nishtar Hospital Multan/department of medicine.

Methodology: 310 patients aged 25-70 years old who are liver cirrhotic, diagnosed with SBP were enrolled using nonprobability consecutive sampling. Patients were randomly allocated to two groups using lottery approach. Group A (n=155) received the intravenous ciprofloxacin (200 mg twice a day) and Group B (n=155) the intravenous ceftriaxone (1 g twice a day). Efficacy was noted after 48 hours of treatment on the basis of: fever, abdominal pains, and decrease of the neutrophil count in the ascitic fluid; and data was analyzed using SPSS version 26 and chi-square test was applied and considered significant $p < 0.05$.

Findings: Both groups showed an average age of 42.8 \pm 9.6 years in Group A and 43.5 \pm 10.1 years in Group B and an overall efficacy of 71.0% for ciprofloxacin and ceftriaxone of 79.4% respectively and the difference was statistically significant ($p = 0.048$). Ceftriaxone demonstrated superiority in clinical and lab outcome particularly among patients with advanced liver disease.

Conclusion: In comparison to intravenous ciprofloxacin, intravenous ceftriaxone is more effective in treatment of spontaneous bacterial peritonitis in cirrhosis.

Keywords: Peritonitis; Liver Cirrhosis; Ciprofloxacin; Ceftriaxone; Ascites.

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INTRODUCTION:

Spontaneous bacterial peritonitis (SBP) is an illness which represents a symptom of some of the worst and most frequent infectious complication of patients with liver cirrhosis and ascites. It can be characterized as the infection of the ascitic fluid which lacks any intra-abdominal source that can be operated on. One of the major clinical problems is SBP due to its high prevalence, complex diagnosis, and morbidity linked with its dissimilar pivotal role in the morbidity and mortality of cirrhotic patients.¹ Recent epidemiological data indicate that SBP is at work in approximately 30 percent of all of the infections of patients suffering cirrhosis and nearly 5-30 percent of patients suffering ascites in hospitals.²

Pathogenesis of SBP is primarily linked to the intestinal

lumen to mesenteric lymph nodes and its subsequent dissemination to blood and ascitic fluid. Using different factors like damaged gut barrier protein and changed intestinal microbiota, and weakened immune defenses with advanced liver disease are facilitating factors of the process.^{2,3} Most commonly implicated pathogens encompass Gram-negative enteric organisms such as *Escherichia coli* and *Klebsiella pneumoniae* but in recent years, Gram-positive organisms and multidrug-resistant organisms have been on the rise at the expense of other pathogens.³

Low prognosis, in-hospital mortality rates of 15 to 40% and survival with a dramatic reduction of long-term survival after an episode has been associated with SBP.² Additionally, cirrhotic patients are prone to infections and they can die four-fold which stresses the need of an early diagnosis and early treatment intervention.² The repeat of SBP is also common and results in the repeat of the hospitalization and an increased healthcare-cost.⁴ Therefore, effective and timely management remains an asset to improvement of clinical outcome of such patients.

Early empirical administration of antibiotics is the key to managing SBP. Third generation cephalosporins are the first-line therapy as recommended by international parameters like that of American Association of the Study

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of Liver diseases (AASLD) to treat SBP.⁵ The most common ones include ceftriaxone, which has a wide spectrum of coverage, good pharmacokinetic profile, and established efficacy against most organisms that cause infections.⁶ Bacteriological cure rates with cephalosporins are shown to be high, which supported their use as the routine treatment in clinical practice.⁶

But with the advent of antibiotic resistance, there has been increasing concern regarding its role in the treatment of SBP. The cumulative effects of increased prophylactic use of antibiotics, recurrent hospital hospitalizations and invasive surgical procedures have led to the emergence of multidrug-resistant organisms, which in turn could further curtail the efficacy of standard treatments.^{3,7} This changing resistance trend urges the need to identify other antibiotic regimens that are effective, yet affordable.

The third-generation cephalosporins have been suggested to have their replacements by fluoroquinolones and especially ciprofloxacin. The benefits of ciprofloxacin include high oral bioavailability, wide-spectrum antimicrobial activity, and lower cost, which makes it a desirable alternative particularly in a resource-constrained environment. Recent literature has documented this similar effectiveness of ciprofloxacin versus cephalosporins in the management of SBP, and could be an alternative option in some patient groups.^{8,9} Further, regimens using ciprofloxacin have been demonstrated to offer an equal clinical benefit at the possibility of decreasing the cost of treatment and hospitalization.⁸

Although these are encouraging results, the literature is still contradictory in terms of the relative effectiveness of ciprofloxacin as compared to ceftriaxone. According to some studies, cephalosporins yield better results whereas other studies show that no significant difference exists between the two modes of treatment.^{9,10} Moreover, regional differences in microbial preferences and resistance to antibiotics also contribute to the problem of the choice of the best empirical treatment. Thus, local research, which would identify the most efficient interventions dependent on local people, is necessary.

SBP remains an important healthcare issue in developing countries with a high prevalence of chronic liver disease, like Pakistan. Rare resources, late presentation, and absence of standardized treatment guidelines are other causes that lead to poor outcomes. Discovering the best and most cost-effective antibiotic treatment can prove highly beneficial in enhancing patient recovery and decrease expenditures on healthcare.

In this point, the present research study aims at providing a comparison with respect to the efficacy of intravenous ciprofloxacin and intravenous ceftriaxone in the treatment of spontaneous bacterial peritonitis in liver cirrhosis patients. The study will inevitably result in valuable information on

the most effective antibiotic options, evidence-based practice and help to counter the current issue of antibiotic resistance in SBP.

METHODOLOGY:

This was a randomized controlled clinical trial (ClinicalTrials.gov Identifier: NCT07552870) in the department of medicine in the Nishtar Hospital Multaka tertiary care teaching hospital. Institutional ethical approval of the protocol (Ref.) was obtained on 15th January 2026 until 14th April 2026, at which time the research was carried out. No. 4189/NMU dated 18-02-2026). The study utilized 310 patients with spontaneous bacterial peritonitis (SBP) diagnosed with the condition within the liver cirrhosis context with the use of a non-probability- consecutive sampling strategy.

Both males and female patients aged 25 to 70 years and known to have liver cirrhosis more than six months and met the eligibility criteria of spontaneous bacterial peritonitis. The cirrhosis was diagnosed based on ultrasonographic findings of coarse echogenicity and irregular liver margins and lab results: serum albumin less than 3.5 g/dL, serum globulin more than 3 g/dl and reverse of the albumin-globulin ratio to less than 1. The patients presenting the material symptoms of fever (temperature higher than 38 °C) and abdominal pain were diagnosed with SBP and analyzed the ascitic fluid containing over 500 cells/mm³ total leukocyte count and over 250 cells/mm³ neutrophil count. They were included in the classes A, B or C of Child-Pugh.

The study did not include patients with hemorrhagic or malignant ascites, tuberculous peritonitis, hepatocellular carcinoma, that have recently used antibiotics, known to be hypersensitive to study drugs, coagulopathy or bleeding disorder, and patients who have not given an informed consent. An informed written consent has been taken and baseline demographic information, including age, gender, residential status, duration of liver disease, comorbid conditions (diabetes mellitus, hypertension, obesity, etc) was gathered. Clinical evaluation was done and baseline tests taken, including liver function tests, serum electrolytes, coagulation profile and ultrasonic examination of the abdomen.

Randomization was performed using a lottery method with sequentially numbered, opaque sealed envelopes. The envelopes were prepared before patient recruitment by a person not involved in patient assessment or treatment. After enrollment, the next envelope in sequence was opened to allocate the patient to either Group A or Group B, ensuring allocation concealment and minimizing selection bias. Patient Group A patients received intravenous ciprofloxacin 200 mg twice daily and 1g twice daily respectively. The two treatment regimes were done over the overall duration of five days but the early response was evaluated after the 48 hours of treatment.

Ascitic fluid sampling was carried out in the aseptic conditions at the baseline and resampled after 48 hours of the antibiotic therapy beginning. The samples were forwarded to the laboratory of the hospital to measure the level of the total leukocytes count, the neutrophil count, protein as well as the glucose level in the sample. Ascitic fluid culture and antibiotic sensitivity testing were not performed or were not included in analysis. The parameters of the clinical parameters such as body temperature and abdominal pain (measured on a visual analogue scale ranging between 0 and 10) were evaluated on a regular basis. The efficacy of the treatment was evaluated, 48 hours later, on basis of falling fever (temperature normalizing), amelioration of abdominal pain and decreased neutrophil count in ascitic fluid to less than 250 cells/mm³.

Each data were taken on a specially designed proforma without breaking the patient information in the process of recording them. In order to minimize bias on the part of the observer, the outcome assessment would be conducted by using a blinded observer who was not aware of the treatment allocation. The data obtained was inputted and analyzed with Statistical Package for Social Sciences (SPSS) version 26. Mean and standard deviation were used to present the quantitative variables (age, body mass index, laboratory values and duration of the disease) but the digital variables (gender, presence of comorbidities, Child-Pugh class and efficacy of treatment) were expressed in frequencies and percentages.

The effectiveness of the two groups was compared by chi-square test and a p-value of 0.05 or less was considered significant. The influence on treatment outcomes was identified using age, gender, obesity, duration of liver disease and Child-Pugh class which was controlled by stratification and post-stratification chi-square test.

RESULTS:

The mean age of patients in Group A was 42.8 ± 9.6 years, while in Group B it was 43.5 ± 10.1 years. There was no significant difference in the two groups with reference to age (p=0.62). Both groups were mainly comprised of male patients who constituted 72.3% of Group A and 70.3% of Group B respectively. The distribution of the patients with regards to residential status was also not sufficiently different as there were slightly more patients in urban areas in the two groups. (Table I)

Clinical characteristics like diabetes mellitus, hypertension and obesity had similar baseline clinical characteristics between the two groups. The proportions of diabetic and hypertensive individuals in Group A were 24.5 percent and 26.5 percent respectively and Group B were 29.0 percent and 31.0 percent respectively. Obesity (BMI >30 kg/m²) was noted in 17.4% of patients in Group A and 18.7% in Group B. Neither of the two groups had a statistically

significant mean body mass index as the two groups had a similar body mass index. (Table II)

Most patients of both groups were under the Child-Pugh category B and C in the case of severity of the disease. In Group A, 20.6% were in class A, 45.8% in class B, and 33.5% in class C, whereas in Group B, 18.7% were in class A, 47.7% in class B, and 33.5% in class C. This failed to be statistically significant in the difference between the two groups (p=0.81). (Table II)

Fever and abdominal pain were some of the clinical manifestations which were most predominant on presentation in both groups. In Group A and B, there was 86.5% and 88.4% fever, 82.6% and 84.5% abdominal pain among patients respectively. The mean abdominal pain score (VAS) was also the same in the two groups. (Table II)

Analysis of ascitic fluid that had not been paired revealed no big difference between the two samples. Group A and B had an average total count of cells per mm³ of 1120 ± 240 and 1095 ± 235, respectively; there was 610 ± 260 count of neutrophils in Group A and B, respectively. (Table II)

Both groups improved, clinically and laboratory, significantly after 48 hours of treatment. But the outcomes among patients who were in the ceftriaxone group were comparatively better. The mean temperature in Group B reduced to 98.7 ± 0.6°F compared to 99.1 ± 0.8°F in Group A (p=0.01). Similarly, Group B's mean pain score dropped to 1.9 ± 1.1 from 2.3 ± 1.2 in Group A (p=0.02). Ascitic fluid neutrophil counts were substantially lower in Group B (240 ± 80 cells/mm³) than in Group A (280 ± 90 cells/mm³) (p=0.01). (Table III)

The percentage of patients in the ciprofloxacin and ceftriaxone groups who achieved overall treatment efficacy, which is defined as the resolution of fever, reduction of abdominal pain, and decrease of neutrophil count to less than 250 cells/mm³ after 48 hours, was 71.0 and 79.4, respectively. Ceftriaxone demonstrated superior effectiveness, and this was statistically significant (p=0.048). (Table IV)

The stratified treatment efficacy between the ciprofloxacin and ceftriaxone is presented in Table V depending on various variables of the patients. The overall results of the study show that ceftriaxone was more effective than ciprofloxacin in the majority of subgroups. When patients were stratified by age, both age groups (patients aged ≤40 and patients aged >40 years) responded better to ceftriaxone but it was not statistically significant. On the same note, both male and female patients seen using ceftriaxone had a higher level of efficacy although this was no longer statistically significant. Once again, ceftriaxone demonstrated relatively superior results among patients having diabetes mellitus and hypertension but were not statistically significant. There was a borderline significant difference among patients who were not hypertensive and ceftriaxone was more effective (p=0.05). Compared to non-obese patients, ceftriaxone showed a trend of improved response even though this was

Table 1: Demographic Characteristics (n = 310)

Variable	Group A (n=155)	Group B (n=155)	p-value
Age (Mean ± SD)	42.8 ± 9.6	43.5 ± 10.1	0.62
Male	112 (72.3%)	109 (70.3%)	0.69
Female	43 (27.7%)	46 (29.7%)	
Rural	68 (43.9%)	64 (41.3%)	0.64
Urban	87 (56.1%)	91 (58.7%)	

Table 3: Post-Treatment (48 Hours)

Parameter	Group A	Group B	p-value
Temperature	99.1 ± 0.8	98.7 ± 0.6	0.01
Pain Score	2.3 ± 1.2	1.9 ± 1.1	0.02
Neutrophils	280 ± 90	240 ± 80	0.01

Table 4: Treatment Efficacy

Outcome	Group A	Group B	p-value
Effective	110 (71.0%)	123 (79.4%)	0.048
Not Effective	45 (29.0%)	32 (20.6%)	

Table 2: Baseline Clinical, Disease Severity, Presentation and Laboratory Characteristics (n=310)

Variable	Group A (Ciprofloxacin) n=155	Group B (Ceftriaxone) n=155	p-value
Comorbidities			
Diabetes Mellitus	38 (24.5%)	41 (26.5%)	0.68
Hypertension	45 (29.0%)	48 (31.0%)	0.71
Obesity (BMI >30 kg/m ²)	27 (17.4%)	29 (18.7%)	0.76
BMI (Mean ± SD)	27.6 ± 4.2	28.1 ± 4.5	0.38
Child-Pugh Classification			
Class A	32 (20.6%)	29 (18.7%)	0.81
Class B	71 (45.8%)	74 (47.7%)	
Class C	52 (33.5%)	52 (33.5%)	
Clinical Presentation			
Fever (>38°C)	134 (86.5%)	137 (88.4%)	0.61
Abdominal Pain	128 (82.6%)	131 (84.5%)	0.65
Pain Score (VAS, Mean ± SD)	6.8 ± 1.5	6.9 ± 1.6	0.72
Baseline Ascitic Fluid Analysis			
Total Leukocyte Count (cells/mm ³)	1120 ± 240	1095 ± 260	0.44
Neutrophil Count (cells/mm ³)	610 ± 120	595 ± 135	0.39

Table 5: Stratification of Treatment Efficacy by Different Variables (n=310)

Variable	Category	Ciprofloxacin Effective n/N (%)	Ceftriaxone Effective n/N (%)	p-value
Age (years)	≤40	48/65 (73.8%)	52/63 (82.5%)	0.21
	>40	62/90 (68.9%)	71/92 (77.2%)	0.18
Gender	Male	80/112 (71.4%)	88/109 (80.7%)	0.11
	Female	30/43 (69.8%)	35/46 (76.1%)	0.48
Diabetes Mellitus	Yes	25/38 (65.8%)	30/41 (73.2%)	0.46
	No	85/117 (72.6%)	93/114 (81.6%)	0.09
Hypertension	Yes	30/45 (66.7%)	34/48 (70.8%)	0.67
	No	80/110 (72.7%)	89/107 (83.2%)	0.05
Obesity	Yes	17/27 (63.0%)	19/29 (65.5%)	0.83
	No	93/128 (72.6%)	104/126 (82.5%)	0.06
Child-Pugh Class	Class A	24/32 (75.0%)	25/29 (86.2%)	0.31
	Class B	52/71 (73.2%)	61/74 (82.4%)	0.18
	Class C	34/52 (65.3%)	37/52 (71.1%)	0.04
Disease Duration	≤12 months	44/60 (73.3%)	49/58 (84.5%)	0.12
	>12 months	66/95 (69.5%)	74/97 (76.3%)	0.28

not found to have a significant value in obese patients. Ceftriaxone was more effective in all classes (Child-Pugh classification) when stratified by the severity of the disease. Interestingly, statistically significant difference was found to be in Child-Pugh class C patients ($p=0.04$) as ceftriaxone is more effective in patients with advanced liver diseases. On the same note, patients who had a shorter (≤ 12 months) and longer (>12 months) period of disease exhibited better outcomes when using ceftriaxone but the differences were not significant.

DISCUSSION:

The current paper has contrasted the effectiveness of intravenous ciprofloxacin and intravenous ceftriaxone in treating SBP. We found that both antibiotics work, but ceftriaxone was much more effective than ciprofloxacin (79.4% vs. 71.0%, $p=0.048$). This is in line with the current pattern in the practice of SBP, with third-generation cephalosporins as first-line treatment.

The average age of the patients in the two groups studied was about 43 years in the present study, and there was no statistical significance between them. This is similar to those of recent studies in which the average age of patients with SBP was 40-50.^{11,12} As an example, Sheikh et al. (2024) found an average age in the ciprofloxacin and ceftriaxone groups to be 41.71 ± 3.51 and 39.11 ± 6.21 respectively, keeping it close to our results.¹¹ On the same note, a multicenter observational study showed the mean age of patients was in the fourth decade of life indicating early development of complications in chronic liver disease.¹²

Male dominance that was evident in our research (around 70% in both groups) is also in line with the past literature. Other studies have documented male predominance between 65 percent to 80 percent in SBP patients, which is probably explained by the greater prevalence of chronic liver disease in males.^{13,14} This similarity indicates that, our population of study qualifies to be representative of the average SBP demographic profile.

In terms of baseline comorbidities (i. e., diabetes mellitus, hypertension, obesity etc.), no significant differences were found between the two groups. The latter is corroborated by recent research that shows that comorbid conditions are prevalent among patients with cirrhosis without any significant effect on the immediate reaction to antibiotic treatment in SBP.^{14,15} Similar treatment outcomes were also found within the subgroups stratified on the basis of comorbidities, implying that the effectiveness of antibiotics stays the same irrespective of other related conditions.¹⁴

The majority of patients in our research were in the Child-Pugh classes B and C, which indicated an advanced liver disease. The distribution is comparable to that of recent papers with most of the cases of SBP being reported in patients with decompensated cirrhosis.¹⁶ Notably, our stratification test indicated that ceftriaxone was much more

active in association with patients whose Child-Pugh class was C ($p=0.04$). This can be underpinned by recent evidence indicating that patients with severe liver disease might be more suitably treated with cephalosporin-based therapy as the coverage to more widespread pathogens and patterns of resistance is enhanced.¹⁷ This presentation of SBP, which included fever and pain in the abdominal area in our study, was in agreement with the findings reported previously. It has been demonstrated that in about 70-90 percent of cases there is a fever and 60-80 percent of the patients had abdominal pain.¹⁸ His correlation of the presentations among studies underscores the need to keep a high index of suspicion with SBP among cirrhotic patients having these symptoms. The analysis of baseline ascitic fluid in our study showed that the number of leukocytes and neutrophils was the same in the two groups demonstrating the same severity of the disease at presentation. This is in line with typical diagnostic criteria of SBP, and is in agreement with recent studies results, which show at diagnosis, mean neutrophil counts were generally above 250 cells/mm³.^{18,19}

The two groups improved significantly after a period of 48 hours of treatment in terms of clinical and laboratory results. Nevertheless, ceftriaxone reportedly showed better results regarding the decrease of temperature, pain score, and neutrophil count. The results of this study are similar to those of a randomized controlled trial which revealed quicker resolution of infection by cephalosporins than the other antibiotics.²⁰ Additionally, studies on response-guided therapy have underscored the need to reassess after 48 hours, and cephalosporins had higher episode rates of early response.¹¹ Our entire efficacy of 79.4% with ceftriaxone and of 71.0% with ciprofloxacin is comparable to the recent literature. According to Sheikh et al. (2024), ciprofloxacin and ceftriaxone were nearly equally effective, implying that these two drugs can be an option.¹¹ Nevertheless, other researchers have reported a marginally better efficacy of cephalosporins, the cure rates just vary between 75 and 85%.²⁰ Bacteriological cure of about 79%^{93%} was also reported in a meta-analysis using third generation cephalosporin.²¹ This phenomenon of relatively lower effectiveness of ciprofloxacin at the time of our study could be explained by the growth of fluoroquinolone resistance. Recent reports have indicated an increase in the number of quinolone-resistant organisms in SBP, especially in hospitalized patients.²² With this trend, the effectiveness of ciprofloxacin is lowered and further contributes to the use of cephalosporins as first-line therapy. Ceftriaxone on the contrary is broad-spectrum against most common Gram-negative bacteria like *Escherichia coli* and *Klebsiella pneumoniae*.²³

The other factor that should be considered is the evolving microbiological spectrum of SBP. According to recent studies, the proportion of Gram-positive infections and multidrug-resistant organisms have been reported to be increasing.²⁴

This transformation can affect the physical performance of traditional antibiotics and the need to regularly analyze the local resistance trends. However, ceftriaxone is still effective in the majority of cases as it has a wide antimicrobial spectrum. Stratification analysis of our study also presented the fact that ceftriaxone was found to be more effective in most subgroups such as age, gender and comorbid conditions. These differences were not significant but the trend shows favour towards ceftriaxone. The same pattern has been observed in recent studies where treatment response rates were always greater with cephalosporins in different groups of patients.¹⁴ This indicates that ceftriaxone can deliver more credible results with different patients. Interestingly, there was no significant difference in the duration of diseases concerning treatment response in our study. The results were similar in patients whose disease was longer or shorter. It does so in line with recent reports that suggest that severity of liver dysfunction, as opposed to disease duration is a more significant predictor of treatment outcome in SBP.¹⁷

Guideline recommendations also support the superiority of ceftriaxone that was identified in our study. There is a lot of evidence-based information that implies the use of three-generation cephalosporins as the first-line treatment due to their effectiveness and good resistance.²³ Also, research has indicated that, in SBP, timely management using the right antibiotics can greatly decrease mortality and complications.²⁵ Although these findings have been made, ciprofloxacin can also be used as an alternative especially in resource-limited situations. Its benefits include reduced cost and orally available property, which can boost patient adherence. Its application should however be based on local resistance patterns to achieve best results. Our research has several strengths, such as a randomized controlled design, a sufficient sample size, and an analysis of a variety of variables. Limitations: Nevertheless, there also are some limitations that are to be taken into consideration. This research design involved the use of only one center; hence, it might not be generalizable. Moreover, microbiological culture and sensitivity pattern did not undergo extensive studies, which would have given additional insights into antibiotic resistance. Also short-term assessment only at 48 hours, no recurrence/mortality follow-up, and no cost-effectiveness analysis were other limitations.

CONCLUSION:

In conclusion, spontaneous bacterial peritonitis is a serious and potentially fatal liver cirrhosis syndrome that requires prompt diagnosis and effective antibiotic therapy. Although ceftriaxone showed significantly more efficacy than ciprofloxacin after 48 hours of treatment, the current investigation found that intravenous ciprofloxacin and intravenous ceftriaxone were similarly beneficial in managing SBP. Not only did stronger resolution of clinical symptoms

such as fever and abdominal pain accompany ceftriaxone but also greater decrements of neutrophil count in the ascitic fluid. In addition, it was also more effective in liver disease patients with advanced liver disease, especially in patients in Class C of the Child- Pugh classification.

Even though ciprofloxacin can still be used as an alternative particularly in resource constrained facilities, it is less effective and the emergence of increasing antibiotic resistance can restrict its usage as a first-line agent. Hence, according to the results of the current research, intravenous ceftriaxone is a treatment of choice between the two types of the empirical treatment of spontaneous bacterial peritonitis, in cirrhotic patients. Nearby diagnosis and proper choice of antibiotic are vital towards decreasing morbidity, mortality, and healthcare load in relation to SBP. It is advisable that further multicentric studies be carried out to determine long-term effects and resistance patterns, which could be utilized to consider different populations in a bid to optimize their treatment methods.

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Authors Contribution:

Hafiza Munam Akhtar: Conception and Design, acquisition of data, analysis and interpretation of data, drafting and critical revision, final approval of the version to be published.

Arif Mehmood Bhatti: Conception and Design, acquisition of data, analysis and interpretation of data, drafting and critical revision, final approval of the version to be published.

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