ORIGINAL ARTICLE

BROAD-SPECTRUM CEPHALOSPORIN CEFTAROLINE: A NEW OPTION AGAINST METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS*

FARHAN RASHEED[1], SADAF MUNIR[2], IQRA JAMIL[3], SABA TARIQ[4], SANA ALLAH DITTA[5], MUHAMMAD BILAL[6]

[1]Professor of Pathology, Ameer ud Din Medical College/Post Graduate Medical Institute, Lahore.[2] Assistant Professor Pathology, Rahbar Medical & Dental college, Lahore.[3] Lecturer, Department of Microbiology, University of Central Punjab, Lahore.[4] Clinical Microbiologist, The Fleming Fund Country Grant Pakistan, DAI, Islamabad.[5] Senior Medical Technologist, Hameed Latif Hospital Laboratories.[6] Assistant Professor of Pathology, Nawaz Sharif Medical College, Gujrat

ABSTRACT

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) can cause variety of hospital-acquired and community-associated infections with limited treatment options. Ceftaroline belong to cephalosporin class showed effective bactericidal activity against MRSA and several other ESBL producing gram-negative rods. So, the current study was designed to check the activity of ceftaroline against MRSA.

Objectives: To check the sensitivity pattern and minimum inhibitory concentration of ceftaroline against methicillin resistant *Staphylococcus aureus.*

Methods: This was a cross-sectional study design and was done in Pathology department of AIMC over the period of two years. MRSA isolated from different clinical samples was confirmed phenotypically and sensitivity testing for different antimicrobials was done on Mueller-Hinton agar. MIC determination of MRSA was done by E-strip method.

Results: Total 282 MRSA isolates was collected among which maximum number was isolated from pus samples (49.2%), followed by wound swabs (18.7%). MRSA isolates showed 100% sensitivity against ceftaroline and vancomycin. MIC range was 0.25 to 4 µg/mL against MRSA isolates. While maximum number of isolates of MRSA showed inhibition at 1 µg/mL.

Conclusion: Ceftaroline showed excellent bactericidal activity against MRSA and can be used effectively to treat (cSSTI). It is considered safe to use because it is well-tolerated with minimum adverse reactions.

Key Words: Methicillin-resistant *Staphylococcus aureus,* Extended-spectrum ß-lactamases, Minimum inhibitory concentration, complicated skin and soft tissue infections.

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Correspondence to: *Farhan Rasheed*
Professor of Pathology, Ameer ud Din Medical College/ Post Graduate Medical Institute, Lahore

Email: *dr.farhanrasheed@gmail.com*

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INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a grave public health issue which roots a variety of infections in community as well as in hospital settings.[1] It can result in serious infections such as endocarditis, bacteremia, pneumonia, infections of skin and soft tissues and wound infections. Currently, Vancomycin is prescribed as choice of drug for treating MRSA infections.[2] But, due to gradual increase in resistance and reduced susceptibility against vancomycin along with necessity for additional safety precautions, use of newer drugs for MRSA treatment are increasing rapidly.[3,4] Among recent advancements, ceftaroline fosamil, a β-lactam antibiotic, which is the 5th generation cephalosporin showed effective in vitro bustle against several Gram-positive along with Gram-negative organisms which include MRSA and MDR-*S. penumoniae*

along with Non-Extended Spectrum Beta-Lactamases (ESBLs) producing organisms except *P.aeruginosa.*[5] Clinical and Laboratory Standards Institute placed ceftaroline in a separate and anonymous subclass of parenteral class of cephem.[6] Ceftaroline found to has a strong affinity for PBP2a, a protein that binds penicillin, which is the major cause of resistance against methicillin in MRSA strains.[7] Ceftaroline fosamil was firstly permitted in the European Union and the United States (US) for treating infections resulted from Methicillin-susceptible *S. aureus.* Initially, it was used to treat acute bacterial skin and skin structure infection (ABSSSI) and complicated skin and soft tissue infection (cSSTI) as well as to treat community-acquired pneumonia (CAP) and community-acquired bacterial pneumonia (CABP) in adults.[8,9] Since its approval, Ceftaroline has been frequently used in both adults and pediatric population off-label due to its effectiveness against MRSA in adult and pediatric patients since its approval because of its activity on MRSA, broader efficacy range against both gram positive as well as gram-negative organisms including β-lactam producers and good profiling of pharmacokinetics. Therefore, the current study was designed to square the efficacy of ceftaroline against methicillin-resistant *staphylococcus aureus.*

METHODS

The present study was done with the approval of Ethical Review Board of Allama Iqbal Medical College/Jinnah Hospital, Lahore, with the reference number: 142/8/18-04-2023/S1ERB. This was a cross-sectional study design and was performed at the pathology department of tertiary care hospital in Lahore over the period of 2 years from 1st April 2023 to 31st march 2024. Sample size (n) of 609 was calculated with 95% confidence interval (zα) .0127 margin of error € assuming 2.6% (p) MRSA clinical isolates resistant to ceftaroline using formula $\mathbf{n=p*\cdot q*(z\alpha/2E)^2}$.[17]Through a non-probability/consecutive sampling technique only confirmed isolates of MRSA were included. Inclusion criteria: Only confirmed isolates of MRSA were included. Exclusion criteria: All other bacterial isolates other than MRSA were not included. Repetitive clinical samples from the same patient were also excluded. Different types of microbiological samples including blood, pus, urine, tips and different types of fluids were received in microbiology lab. Samples were processed according to standard microbiological procedures. Following bacterial growth, gram staining was done and different biochemical tests including catalase, coagulase and DNase were used to identify *S. aureus.* After confirmation of bacterial isolate, antimicrobial sensitivity was done on Mueller-Hinton agar by modified Kirby-Bauer disc diffusion method. After this interpretation was done according to CLSI guidelines 2022.[10] Cefoxitin disc (30µg) was also placed with routine antibiotics for identification of MRSA. After isolation of MRSA, Minimum Inhibitory Concentration of ceftaroline against MRSA was done by E-strip placed on the agar's surface which was inoculated with adjusted bacterial suspension. Figure 1: After overnight incubation, MIC value in µg/mL was interpret from the scale where the edge of ellipse intersects the strip.

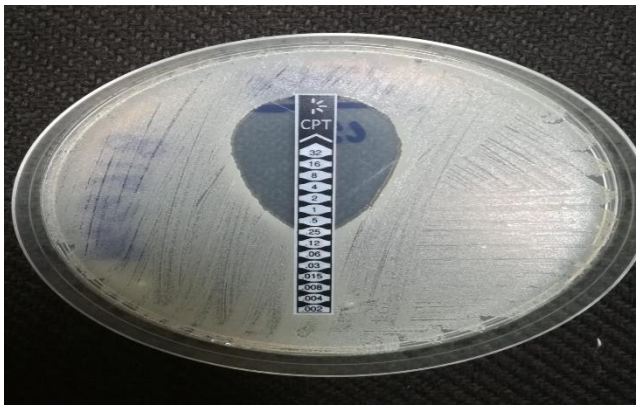

Figure 1: Ellipse edge intersects the strip at the value 0.25 which means MIC of Ceftaroline against MRSA is 0.25 µg/mL.

Data was analyzed by using Microsoft Excel 2010 and were presented in the form of frequencies and percentages. Graphical representation showed in the form of pie charts and bar charts.

RESULTS

Total 609 *S.aureus* were isolated from different clinical samples received in microbiology lab in study duration. Among 609 isolates, 282 were found to be Methicillin-Resistant *S.aureus* while 327 were Methicillin-Sensitive *S.aureus.* Maximum number of MRSA were isolated from Pus samples (49.2%), followed by wound swabs (18.7%), blood (17%) and urine (7.4%). Figure 2.

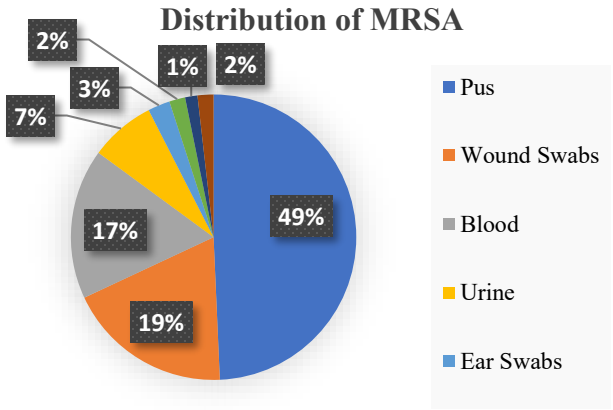

Figure 2: Distribution of MRSA in different clinical samples, which showed maximum numbers of MRSA were isolated from Pus (49%), followed by wound swabs (19%).

Antimicrobial sensitivity pattern of MRSA showed 100% sensitivity against Vancomycin and Teicoplanin. While

maximum resistance was observed against Tobramycin 100%, followed by Amoxicillin/Clavulanic acid (95.7%) and Fluoroquinolones 85.8%. Table 1

Minimum Inhibitory Concentration of Ceftaroline against MRSA was performed by E-Strip. 100% isolates were sensitive to Ceftaroline but their MIC values were variable

Table 1: Antibiotic Sensitivity Pattern of MRSA against commonly used antibiotics

Antibiotic class	Antibiotic	Sensitive		Resistant	
		Number	Percentage	Number	Percentage
Aminoglycosides	Amikacin	243	86.2%	39	13.8%
	Gentamycin	170	60.2%	112	39.8%
Ti-Folate	Co-trimoxazole	92	32.6%	190	67.4%
Cephalosporins	Ceftaroline	282	100%	00	0%
Fluoroquinolones	Ciprofloxacin	40	14.2%	242	85.8%
	Levofloxacin	40	14.2%	242	85.8%
Glycopeptides	Teicoplanin	282	100%	00	0%
	Vancomycin	282	100%	00	0%
Macrolides	Erythromycin	43	15.3%	239	84.7%
Pristinamycin	Chloramphenicol	247	87.5%	35	12.5%
	Clindamycin	164	58.2%	118	41.8%
Tetracycline	Doxycycline	179	63.5%	103	36.5%
Miscellaneous agents	Fusidic acid	155	55%	127	45%
	Linezolid	279	98.9%	3	1.1%

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Table 2: MIC Ranges of Ceftaroline in µg/mL in different clinical samples

Clinical Samples	Sensitive		Resistant		CPT MIC Range µg/mL
	Number	Percentage	Number	Percentage	
Pus	139	100%	00	0%	0.25-4
Blood	48	100%	00	0%	0.25-4
Wound swabs	53	100%	00	0%	0.25-4
Urine	21	100%	00	0%	0.25-1
Ear swabs	7	100%	00	0%	0.25-0.5
Tracheal secretions	5	100%	00	0%	0.25-1
Others	9	100%	00	0%	0.25-4

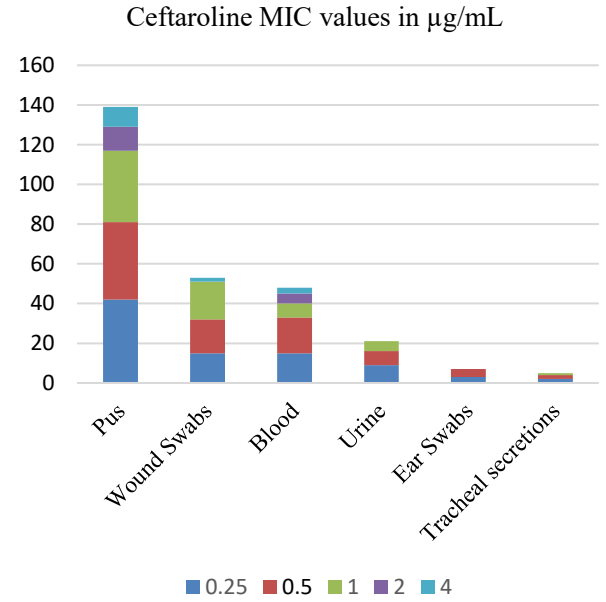

Figure 3: Distribution of Different clinical samples in MIC ranges from 0.25 µg/mL to 4 µg/mL.

Maximum number of isolates from variable clinical samples were inhibited at MIC of 0.25 µg/mL. Maximum number of MRSA isolated from blood samples showed MIC of 0.5 and 1 µg/mL.

DISCUSSION

Methicillin-Resistant *S.aureus* is a solemn public health issue causing range of community-associated and nosocomial infections.[11] Because of increasing resistance, drugs of choice become limited with linezolid and vancomycin being the preferred antibiotics to treat such infections. The most recent addition to cephalosporin antibiotics class, Ceftaroline fosamil exhibit effective bactericidal activity against MRSA, along with those isolates which showed resistance against vancomycin.[12,13] In our study, we estimated the in vitro efficacy of ceftaroline fosamil against MRSA isolated from different clinical samples.

In the present study, all isolates of MRSA show 100% sensitivity against ceftaroline. Castanheira*et al* evaluated Antimicrobial Resistance Evaluation program from 2008 to

2010 in the United States to check the susceptibility pattern of ceftaroline and the results showed 98% sensitivity against MRSA.[14] This was in accordance with our results.

MIC ranges of ceftaroline against MRSA isolated from pus and wound swabs were found to be 0.25-4 µg/mL. Similar results were reported by ATLAS Surveillance Database in 2018, which reported the MIC range of 0.12-8 µg/mL against MRSA isolates, 100% isolates were sensitive to ceftaroline at MIC value of 8 µg/mL.[15]Another study by Jones *et al* also reported the MIC range of 0.25-2 µg/mL of ceftaroline against MRSA causing skin and soft tissue infections.[16] Maximum number of isolates were inhibited at the MIC value of 0.5 µg/mL which was also in accordance with our results. Ceftaroline showed effective bactericidal activity against skin and soft tissue infections causative agents and thus becomes the preferred antibiotic for treatment of cSSTIs.

ATLAS in Taiwan determine the in vitro Ceftaroline susceptibility against MRSA in 2020 and reported about one-third of MRSA isolates among total numbershowed MIC of 1 mg/L against Ceftaroline fosamil.[17] Similar results were reported in our study in which about one-third of MRSA isolates collected from variable clinical samples had an MIC of 1 µg/mL.

According to EUCAST and CLSI, currentlythe ceftaroline-susceptible breakpoints are set at ≤1 mg/L for *S. aureus*. However, the resistance defining breakpoints are different (≥1 mg/L for EUCAST and for CLSI, it is ≥4 mg/L).[18,19] After a new antimicrobial drug is introduced into clinical usage, there is always concern about the quick emergence of resistance, which could be in the form of cross-resistance, or co-resistance to other antimicrobial agents and classes. However, there is no reported case of in vitro mutational resistance and cross-resistance to other medications in MRSA strains multi-drug resistant *S. pneumoniae* isolates even after 50 consecutive days of passages. From this, it can be concluded that there is less possibility of in vivo mutational resistance development of ceftaroline in these strains.[20] In developed countries, β-lactam drugs are considered as drugs of choice to treat intricate skin and soft tissue infections if the causative organism is found to be susceptible to these antibiotics. This emphasizes to promote the pathogen-directed therapy instead of empirical therapy.[21,22]

CONCLUSION

Ceftaroline showed broad-spectrum bactericidal activity against a range of gram-positive as well as gram-negative microorganism and can be used excellently to treat MRSA infections both community-associated and hospital acquired. In order to treat cSSTIs, ceftaroline provides much better bactericidal activity than several other drugs of first choice including linezolid and vancomycin. Ceftaroline is generally safe to use as compare to other drugs used for the treatment of MRSA because it is well-tolerated, easy to administer, less toxicity and has fewer side effects along with no drug interactions have been reported uptill now.

ETHICAL APPROVAL

Ethical approval of article was granted by the Ethical Review Board of Allama Iqbal Medical College vide reference No. ERB 142/8/18-04-2023/S1ERB dated 18 April, 2023.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTIONS

FR: Conceived idea, review of manuscript, supervision
SM: Data collection, lab work
IJ: Manuscript writing, data analysis
ST, SAD: lab work
MB: Data collection, review of manuscript
All Authors: Approval of the final version of the manuscript to be published

REFERENCES

1. Jamil I, Rasheed F. Association of PVL Gene with SCCmec Typing in MRSA (both community associated and hospital-acquired) from a Tertiary Care Hospital, Lahore. JIMDC. 2023 Oct 16;12(3):158-163.
2. Bhargava D, Deshpande A, Sreekumar K, Koneru G, Rastogi S. Guidelines of the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections: as applied to oral and maxillofacial clinical practice. J. Oral Maxillofac. Surg. 2013;12:354-358.
3. Hahn A, Frenck Jr RW, Allen-Staat M, Zou Y, Vinks AA. Evaluation of target attainment of vancomycin area under the curve in children with methicillin resistant *Staphylococcus aureus* bacteremia. Ther Drug Monit. 2015;37(5):619-625.
4. Sharma R, Hammerschlag MR. Treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in children: a reappraisal of vancomycin. Curr. Infect. Dis. Rep. 2019;21:1-8.
5. Pfaller MA, Mendes RE, Flamm RK, Jones RN, Sader HS. Ceftaroline activity against multidrug-resistant *Streptococcus pneumoniae* from US medical centers (2014) and molecular characterization of a single ceftaroline nonsusceptible isolate. Microb. Drug Resist. 2017;23(5):571-579.
6. Poon H, Chang MH, Fung HB. Ceftaroline fosamil: a cephalosporin with activity against methicillin-resistant *Staphylococcus aureus.* Clin. Ther. 2012;34(4):743-765.

7. Maselli DJ, Fernandez JF, Whong CY, Echevarria K, Nambiar AM, Anzueto A*et al*. Clinical evaluation of the role of ceftaroline in the management of community acquired bacterial pneumonia. Infect. Drug Resist. 2012 Feb 1:43-51.
8. Pfaller MA, Flamm RK, Sader HS, Jones RN. Ceftaroline activity against bacterial organisms isolated from acute bacterial skin and skin structure infections in United States medical centers (2009–2011). Diagn. Microbiol. Infect. Dis. 2014;78(4):422-428
9. Rasheed F, Jamil I, Tehseen T, Sikandar A, Anwar S, Rafique S. Bacterial profile and their antimicrobial susceptibility pattern in pediatric septicemia from tertiary care hospital.2023 JAIMC; 21(2): 86-91.
10. Mohakud NK, Mishra JP, Nayak MK, Mishra J, Pradhan L, Panda SS, *et al*. Bacteriological Profile and Outcome of Culture-Positive Neonatal Sepsis in a Special Newborn Care Unit Setting, Odisha. Cureus. 2022;14(5)
11. Yar A, Rasheed F, Ejaz A, Jamil I, Yasin B, Bilal M. Current Trends of Resistance Among Gram Negative and Gram-Positive Bacteria Isolated from Tertiary Care Hospital.JAIMC 2023; 21(04): 246-250
12. MacGowan AP, Noel AR, Tomaselli S, Bowker KE. Pharmacodynamics of ceftaroline against *Staphylococcus aureus* studied in an in vitro pharmacokinetic model of infection. Antimicrob. Agents Chemother. 2013;57(6):2451-2456.
13. Castanheira M, Sader HS, Farrell DJ, Mendes RE, Jones RN. Activity of ceftaroline-avibactam tested against Gram-negative organism populations, including strains expressing one or more β-lactamases and methicillin-resistant *Staphylococcus aureus* carrying various staphylococcal cassette chromosome mec types. Antimicrob. Agents Chemother. 2012;56(9):4779-4785.
14. Rossolini GM, Bochenska M, Fumagalli L, Dowzicky M. Trends of major antimicrobial resistance phenotypes in enterobacterales and gram-negative non-fermenters from ATLAS and EARS-net surveillance systems: Italian vs. European and global data, 2008-2018. *DiagnMicrobiol Infect Dis*. 2021;101(4):115512.
15. Esposito S, Carrothers TJ, Riccobene T, Stone GG, Kantecki M. Ceftaroline fosamil for treatment of pediatric complicated skin and soft tissue infections and community-acquired pneumonia. *Paediatr. Drugs*. 2021;23:549-563.
16. Jean SS, Lee WS, Ko WC, Hsueh PR. In vitro susceptibility of ceftaroline against clinically important Gram-positive cocci, *Haemophilus* species and *Klebsiella pneumoniae* in Taiwan: results from the Antimicrobial Testing Leadership and Surveillance (ATLAS) in 2012–2018. JMII. 2021;54(4):627-631.
17. Weinstein MP, Lewis JS. The clinical and laboratory standards institute subcommittee on antimicrobial susceptibility testing: background, organization, functions, and processes. J. Clin. Microbiol.. 2020;58(3):e01864-19.
18. Vanstokstraeten R, Belasri N, Demuyser T, Crombé F, Barbé K, Piérard D. A comparison of *E. coli* susceptibility for amoxicillin/clavulanic acid according to EUCAST and CLSI guidelines. *Eur. J. Clin. Microbiol. Infect*. Dis. 2021;40(11):2371-2377.
19. Steed ME, Vidaillac C, Winterfield P, Biek D, Rybak MJ. Evaluation of ceftaroline activity versus ceftriaxone against clinical isolates of *Streptococcus pneumoniae* with various susceptibilities to cephalosporins in an in vitro pharmacokinetic/pharmacodynamic model. Antimicrob. Agents Chemother. 2012;56(5):2691-2695.
20. Jamil I, Rehman AU, Rehman FU, Rasheed F. Emerging Antimicrobial Resistance in Typhoid Fever: Challenges in Diagnosis and Treatment. J. Med. Health Sci. Rev. 2025 Jun 18;2(2).
21. Rasheed F, Jamil I, Tehseen T, Yar A, Ali F, Ashraf A. Trend of antimicrobial resistance among Salmonella typhi isolated from the pediatric population presenting at a tertiary care hospital in Lahore. Biomedica. 2023 Apr 6;39(2):61-66.