Asian Journal of Research in Infectious Diseases

Volume 15, Issue 6, Page 12-19, 2024; Article no.AJRID.116987
ISSN: 2582-3221

Assessment of Cefuroxime and Cefuroxime Clavulanic Acid Prescription Practices for Infection Management in Routine Indian Healthcare Settings: Expert Insights

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.9734/ajrid/2024/v15i6351

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/116987

Original Research Article

Received: 08/03/2024
Accepted: 10/05/2024
Published: 15/05/2024

ABSTRACT

Background: Cefuroxime axetil has shown effectiveness as part of intravenous/oral sequential therapy for community-acquired pneumonia (CAP) treatment, although some countries currently lack dosage recommendations for this regimen. In addition, the perspectives of clinicians were not studied. So, this study evaluated the prescription practice of cefuroxime, and cefuroxime+ clavulanic acid in the management of infections in routine Indian settings.
Methods: The cross-sectional survey, titled 'Cefuroxime & Cefuroxime+Clavulanic acid in Management of Infections: Expert Perspective (CARE) Study', utilized a 20-item, multiple-response questionnaire to gather expert opinion from specialists regarding the clinical use of cefuroxime and

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Cite as: *Manjula S, & Krishna Kumar M. (2024). Assessment of Cefuroxime and Cefuroxime Clavulanic Acid Prescription Practices for Infection Management in Routine Indian Healthcare Settings: Expert Insights. Asian Journal of Research in Infectious Diseases, 15(6), 12–19. https://doi.org/10.9734/ajrid/2024/v15i6351*

cefuroxime + clavulanic acid in managing infections. The survey encompassed questions about current prescription practices, clinical observations, preferences, and experiences related to the use of these antibiotics in routine settings.

Results: Among the 164 clinicians surveyed, 78% of the respondents indicated that cefuroxime was highly effective in managing lower respiratory tract infections. Additionally, 91% of the experts stated that the combination of cefuroxime and clavulanic acid was very effective in managing infections. The majority of clinicians recommended cefuroxime + clavulanic acid as the initial therapy for complicated urinary tract infections (88%), as well as first-line therapy for uncomplicated skin and soft tissue infections (45%) and community-acquired pneumonia (58%). According to 40% of the clinicians, cefuroxime + clavulanic acid was recommended as the initial therapy for 21-30% of patients suspected of methicillin-resistant *Staphylococcus aureus* infection. Most respondents (88%) preferred cefuroxime + clavulanic acid as the antibiotic for managing *Pseudomonas aeruginosa* infection.

Conclusion: The survey has emphasized the critical role of cefuroxime and cefuroxime + clavulanic acid as antibiotics in managing diverse infections. Clinicians' recognition of their efficacy and preference for combination therapy has underscored the importance of antibiotic stewardship in optimizing patient care.

Keywords: Cefuroxime; clavulanic acid; infection; respiratory tract infections; urinary tract infection.

1. INTRODUCTION

Common infections, encompassing respiratory tract infections (RTIs), urinary tract infections (UTIs), and sexually transmitted infections, as well as emerging infectious diseases and antimicrobial resistance, constitute a significant portion of the global disease burden. According to the 2016 global burden of disease estimate, RTIs alone contributed to approximately 336.5 million infections and 2.4 million deaths [1]. Additionally, data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 indicate that incident cases of upper respiratory tract infections (URTIs) reached around 17.2 billion, accounting for 42.83% of cases from all causes [2]. According to the National Health Portal of India in 2019, there were 41,996,260 reported cases and 3,740 fatalities due to respiratory infections in India in 2018 [3]. In the country, acute respiratory infections (ARIs) represent 30-50% of health facility visits and 20-40% of hospital admissions [4].

Women have a higher susceptibility to UTIs compared to men due to factors such as the shorter length of the urethra, lack of prostatic secretion, pregnancy, and the increased risk for tract contamination with fecal flora [5]. Approximately 40% of women and 12% of men experience at least one UTI infection in their lifetime [6]. The worldwide data revealed that UTIs accounted for an estimated 404.61 million cases, resulting in 236,790 deaths and 520,200 disability-adjusted life years (DALYs) in 2019. Over the period from 1990 to 2019, there was a notable 2.4-fold increase in deaths attributed to UTIs. In India, the prevalence of UTI was estimated to be around 37% [7].

Cefuroxime and cefuroxime-clavulanic acid combinations play a crucial role in managing bacterial infections by disrupting bacterial cell wall synthesis. The addition of clavulanic acid enhances the spectrum of activity, including those that produce beta-lactamase. The mechanism of action of cefuroxime involves binding to penicillin-binding proteins (PBPs), which ultimately leads to cell wall disruption and bacterial cell death. Cefuroxime exhibits broad-spectrum activity against both Gram-positive and Gram-negative bacteria [8].

There is substantial clinical evidence from randomized, controlled trials substantiating the effectiveness of oral cefuroxime axetil (250 or 500 mg twice daily) for 5 to 10 days in patients with URTIs and lower respiratory tract infections (LRTIs), as evaluated by clinical and bacteriological criteria. The drug has proven to be both effective and well-tolerated in treating various infections, including otitis media, pharyngitis, sinusitis, community-acquired pneumonia (CAP), and acute exacerbations of chronic bronchitis. Cefuroxime axetil has shown effectiveness as part of intravenous/oral sequential therapy for CAP treatment, although some countries currently lack dosage recommendations for this regimen [9]. Furthermore, the clinician's perspectives regarding the prescription were lacking. The

present study was aimed to evaluate the prescription practice of cefuroxime, and cefuroxime+ clavulanic acid in the management of infections in routine Indian settings.

2. MATERIALS AND METHODS

We carried out a cross sectional, multiple-response questionnairebased survey among clinicians specialized in managing infections in the major Indian cities from June 2023 to December 2023. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

2.1 Questionnaire

The questionnaire booklet titled CARE (**C**efuroxime & Cefuroxime+ Cl**a**vulanic acid in Management of Infections: Exper**t** Persp**e**ctive) study was sent to the physicians who were interested to participate. The CARE study questionnaire comprised 20 questions about current feedback, clinical observations, and clinical experience of specialists in managing infections with the use of cefuroxime and cefuroxime+ clavulanic acid in routine settings. Reliability as determined by a split-half test (coefficient alpha) was adequate but should be improved in future versions of the questionnaire. A study of criterion validity was undertaken to test the questionnaire and to develop methods of testing the validity of measures of Physicians Perspectives. However, the extraneous variable in this includes the clinicians experience, usage of the newer drugs etc. The two criteria used were the doctors' perspectives from the clinical practice and the assessment of an external assessor and statistician.

2.2 Participants

An invitation was sent to leading clinicians in managing infections in the month of March 2023 for participation in this Indian survey. About 164 clinical specialists from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provided necessary data. They were instructed to complete the survey alone without consulting their colleagues.

2.3 Statistical Methods

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to provide a clear insight into their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, graphs were created using Microsoft Excel 2013 (version 16.0.13901.20400).

3. RESULTS

Among the 164 clinicians surveyed, 28% reported prescribing cefuroxime for cases with LRTIs, followed by 20% for UTIs. According to 43% of the experts, pneumonia was the most common type of LRTI seen in routine practice, followed by acute bronchitis (32.93%). Around 37% of clinicians reported prescribing cefuroxime + clavulanic acid to 26-50% of patients in routine practice over cefuroxime alone, whereas 35% reported prescribing it to 51-75% of patients. Approximately 315 clinicians reported that the cefuroxime + clavulanic acid combination is commonly preferred for managing skin and soft tissue infections, while 29% reported prescribing it for LRTIs.

Majority (78%) of the respondents stated that cefuroxime is very effective in managing LRTIs (Fig. 1). According to 70% of the subjects, the average duration of prescribing cefuroxime for managing LRTIs is 6-10 days (Table 1). Nearly 41% reported the advantages of cefuroxime as broad spectrum, a favorable pharmacokinetic profile, and better tissue penetration. Most of the experts (91%) stated that the cefuroxime + clavulanic acid combination was very effective in managing infections (Table 2). Majority of the experts (75%) reported gastrointestinal disturbances (nausea, vomiting, diarrhea) as the most common side effects observed in patients prescribed with cefuroxime or cefuroxime + clavulanic acid. Around 46% reported lower recurrence rates of infections for patients treated with cefuroxime + clavulanic acid compared to cefuroxime alone.

Nearly half of the clinicians (47%) reported that the severity of the infection should be considered when deciding the prescription of cefuroxime or cefuroxime + clavulanic acid. According to 58% of the clinicians, cefuroxime + clavulanic acid was the preferred first-line therapy for patients with community-acquired pneumonia (Table 3). As per 88% of the clinicians, cefuroxime + clavulanic acid was recommended as the initial therapy for patients presenting with

complicated UTIs (Fig. 2). About 45% of the experts reported that cefuroxime + clavulanic acid was the first-line therapy for uncomplicated skin and soft tissue infections (SSTI) (Table 4).

Table 1. Distribution of response to average duration of cefuroxime prescribed for managing LRTIs

Average duration	Response rate (n = 164)
<5 days	24 (14.63%)
6-10 days	114 (69.51%)
10 days	23 (14.02%)
Post-operative wound care for 5 days	1 (0.61%)
8 to 10 days in surgical prophylaxis cases	1 (0.61%)
10 to 15 days and would continue with a review	1 (0.61%)

Table 2. Distribution of response to the effectiveness of cefuroxime + clavulanic acid in treating infections

Effectiveness of cefuroxime + clavulanic acid in treating infections	(n = 164)
Very effective	149(90.85%)
Moderately effective	14 (8.54%)
Not very effective	1 (0.61%)

According to 40% of the clinicians, 21-30% of the patients suspected of methicillin-resistant *Staphylococcus aureus* (MRSA) infection were recommended cefuroxime + clavulanic acid as the initial therapy (Fig. 3). Nearly 44% of the clinicians stated that 21-30% of the patients suspected of pseudomonal infection are prescribed cefuroxime + clavulanic acid as the initial therapy. Most respondents (88%) preferred cefuroxime + clavulanic acid as the antibiotic for managing *Pseudomonas aeruginosa* infection (Fig. 4).

Table 3. Distribution of response to antibiotic chosen as the first-line therapy for a patient with community-acquired pneumonia

Antibiotic	Response rate (n = 164)
Cefuroxime	62 (37.8%)
Cefuroxime + clavulanic acid	95 (57.93%)
Azithromycin	5 (3.05%)
Levofloxacin	2 (1.22%)

Table 4. Distribution of response to antibiotic chosen as the first-line therapy for uncomplicated skin and soft tissue infections

Antibiotic	(n = 164)
Cefuroxime	66 (40.24%)
Cefuroxime + clavulanic acid	74 (45.12%)
Amoxicillin-clavulanate	18 (10.98%)
Doxycycline	6 (3.66%)

Approximately 31% of the experts reported that cefuroxime + clavulanic acid was recommended as the initial therapy to 11-20% of the patients with penicillin allergy, while 29% of the clinicians reported it as 31-40%. Around 40% of the respondents stated that 21-30% was the proportion of patients with suspected hospital-acquired pneumonia recommended for cefuroxime + clavulanic acid as the initial therapy.

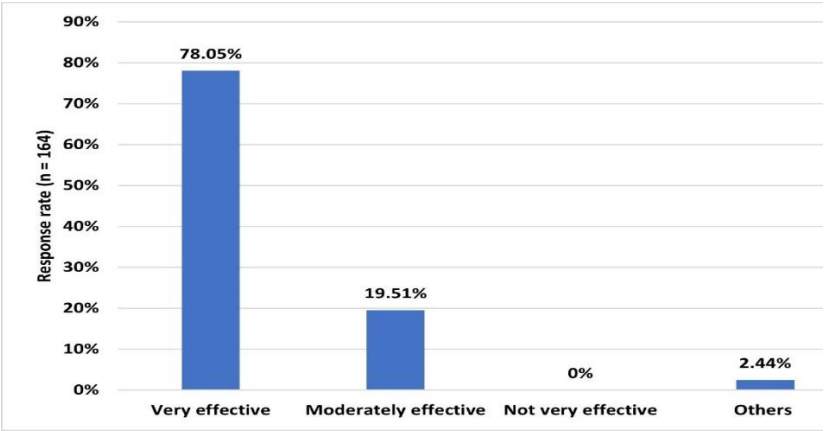

Fig. 1. Distribution of response to the effectiveness of cefuroxime in treating lower respiratory tract infections

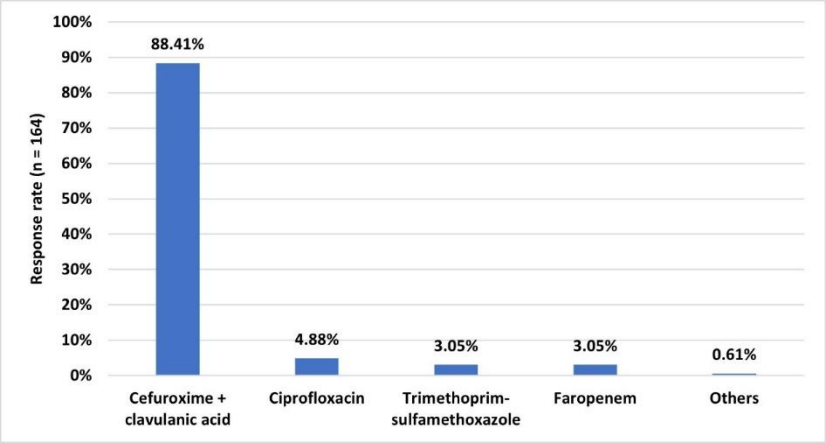

Fig. 2. Distribution of response to antibiotics prescribed as the initial therapy to patients presenting with a complicated urinary tract infection

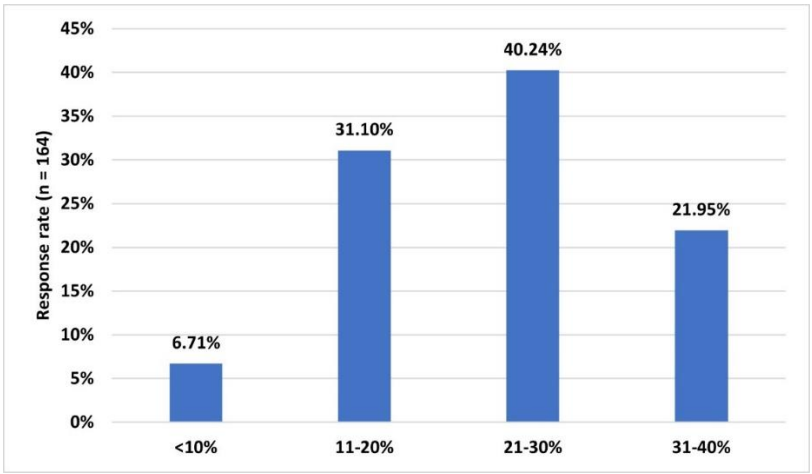

Fig. 3. Distribution of response to proportion of patients suspected with methicillin-resistant *Staphylococcus aureus* infection recommended with cefuroxime + clavulanic acid as the initial therapy

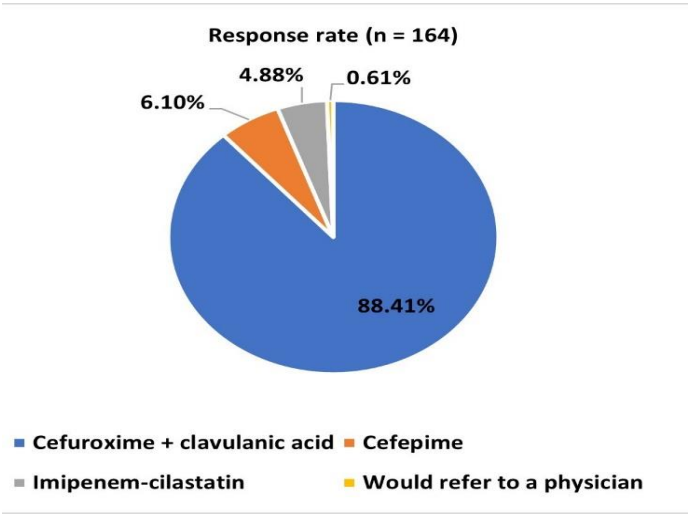

Fig. 4. Distribution of response to antibiotic preferred for *Pseudomonas aeruginosa* infection

4. DISCUSSION

The survey provides valuable insights into the antibiotic choices made by clinicians when treating infections. It highlighted the potential benefits of prescribing cefuroxime with clavulanic acid and cefuroxime monotherapy for effective infection management in the Indian population.

A significant proportion of current survey clinicians reported cefuroxime as highly effective in managing LRTIs, with the majority indicating an average prescription duration of 6-10 days. In a clinical trial conducted by Bax et al., 57 patients received 750 mg of cefuroxime for 7-10 days, while 54 patients were administered 500 mg of ampicillin. The study findings showed that the regimen of 750 mg of cefuroxime administered every 8 hours proved effective in treating LRTIs, and more effective compared to ampicillin [10]. Another clinical trial study involving 512 hospitalized patients with LRTIs, it was found that 87.1% and 72.8% of patients treated with cefuroxime achieved clinical improvement and bacterial clearance, respectively [11]. Henry et al. concluded that cefuroxime axetil was effective in treating secondary bacterial infections associated with acute bronchitis [12]. Samanta et al. conducted a clinical study on 23 in-patients and concluded that cefuroxime sodium was an effective and well-tolerated drug for treating severe LRTIs [13]. Adam et al. compared the efficacy of short-course (5-day) cefuroxime axetil with the standard 10-day oral penicillin V regimen for managing tonsillopharyngitis. The study results indicated that the short-course treatment with cefuroxime axetil was as effective as the standard 10-day oral penicillin V regimen [14].

In the current survey, most of the clinicians agreed on the efficacy of the cefuroxime + clavulanic acid combination in treating infections. They advocated for its use as the primary treatment option for patients with community-acquired pneumonia, UTIs, and uncomplicated SSTI. Jalil et al. assessed the restoration or augmentation of sensitivity in beta-lactamase-producing strains of *Staphylococcus aureus*. The results indicated that the use of cefuroxime in combination with clavulanic acid led to the development of larger zones of inhibition. This suggested a significant enhancement in the activity of cefuroxime against *Staphylococcus aureus* facilitated by clavulanic acid [15]. Sawant et al. tested the antimicrobial efficacy of five commercially available fixed-dose combination antibiotics in India, including cefuroxime combined with clavulanic acid (500:125 mg). The study results indicated that the minimum inhibitory concentration and minimum bactericidal concentration of the cefuroxime/clavulanate combination were higher compared to those of cefuroxime alone across all tested organisms, including *Staphylococcus aureus*, *Klebsiella pneumoniae, Hemophilus influenzae, Escherichia coli*, and *Streptococcus pneumoniae* [16].

Majority of the current survey respondents suggested the cefuroxime + clavulanic acid combination as the first choice for initial therapy in patients suspected of MRSA infection and for managing *Pseudomonas aeruginosa* infection. Bacterial resistance to cephalosporins predominantly occurs through the action of beta-lactamases found in both Gram-positive and Gram-negative bacteria. An innovative strategy to address this challenge involves administering a beta-lactam antibiotic alongside a beta-lactamase inhibitor [17]. Therefore, the combination of cefuroxime with clavulanic acid emerges as a promising and effective option. Over recent decades, the escalation of bacterial evolution alongside antibiotic misuse has led to a progressive rise in drug resistance among *S. aureus* strains [18]. De et al. recommended the use of the combination of cefuroxime and clavulanic acid for treating SSTIs caused by *Staphylococcus aureus*, as well as in infections where biofilm formation was implicated in increased drug resistance [17]. Zubair et al. reported promising outcomes in the treatment of biofilms associated with diabetic foot cases. The study found that the cephalosporin-clavulanic acid combination (with resistance rates of 12.2% for cefotaxime-clavulanic acid and 9.2% for ceftazidime-clavulanic acid) exhibited superior efficacy compared to cephalosporins used alone [19].

The current findings underscore the importance and potential of this combination therapy in managing a range of infections, offering valuable insights for clinical practice. The study results, derived from a meticulously designed and validated questionnaire-based survey, hold substantial relevance in guiding antibiotic prescribing decisions and enhancing patient care, as well as contributing to antibiotic stewardship efforts. However, it was crucial to acknowledge certain study limitations. The reliance on expert judgments may introduce bias, as individual viewpoints and preferences could influence the reported conclusions. Therefore, it

was imperative to interpret the results with these limitations in mind and advocate for further research to validate and build upon the findings.

4. CONCLUSION

The survey underscored the efficacy of cefuroxime in treating LRTIs and the preference among clinicians for the cefuroxime + clavulanic acid combination in managing infections caused by methicillin-resistant MRSA and *Pseudomonas aeruginosa*. Moreover, the clinicians recognized its effectiveness in treating community-acquired pneumonia, UTIs, and SSTIs.

CONSENT

Written informed consent was obtained from all the participants before the study began

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

ACKNOWLEDGEMENT

We would like to thank all the clinicians who were participated in this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Grech AK, Foo CT, Paul E, Aung AK, Yu C. Epidemiological trends of respiratory tract pathogens detected via mPCR in Australian adult patients before COVID-19. BMC Infectious Diseases. 2024;24 (1):38.
2. Jin X, Ren J, Li R, Gao Y, Zhang H, Li J, et al. Global burden of upper respiratory infections in 204 countries and territories, from 1990 to 2019. eClinical Medicine 2021;37.
   Accessed On:2024 Apr 5
   Available:https://www.thelancet.com/journals/eclinm/article/PIIS25895370(21)00266-2/fulltext
3. Waghmode R, Jadhav S, Nema V. The Burden of Respiratory Viruses and Their prevalence in different geographical Regions of India: 1970–2020. Front Microbiol 2021;12.
   Accessed On:2024 Apr 5
   Available:https://www.frontiersin.org/journals/microbiology/articles/10.3389/fmicb.2021.723850/full
4. Kumar SG, Majumdar A, Kumar V, Naik BN, Selvaraj K, Balajee K. Prevalence of acute respiratory infection among under-five children in urban and rural areas of puducherry, India. J Nat Sci Biol Med. 2015;6(1):3–6.
5. Almutawif YA, Eid HMA. Prevalence and antimicrobial susceptibility pattern of bacterial uropathogens among adult patients in Madinah, Saudi Arabia. BMC Infectious Diseases. 2023;23(1):582.
6. Christy VR, Athinarayanan G, Mariselvam R, Dhasarathan P, Singh R. Epidemiology of urinary tract infection in south India. Biomedical Research and Clinical Practice. 2019;4:1-5.
7. Yang X, Chen H, Zheng Y, Qu S, Wang H, Yi F. Disease burden and long-term trends of urinary tract infections: A worldwide report. Front Public Health. 2022;10:888205.
8. Omole AE, Awosika AO, Patel P. Cefuroxime. In: Stat Pearls. Treasure Island (FL): StatPearls Publishing; 2024 Accessed On:2024 Apr 5.
   Available:http://www.ncbi.nlm.nih.gov/books/NBK599503/
9. Scott L, Ormrod D, Goa K. Cefuroxime axetil: An updated review of its use in the management of bacterial infections. Drugs. 2001;61:1455–500.
10. Bax RP, Dawson AF, Mullinger BM, Dash CH. Cefuroxime in the treatment of lower respiratory tract infection. Curr Med Res Opin. 1979;5(10):772–8.
11. Brambilla C, Kastanakis S, Knight S, Cunningham K. Cefuroxime and cefuroxime axetil versus amoxicillin plus clavulanic acid in the treatment of lower respiratory tract infections. Eur J Clin Microbiol Infect Dis. 1992;11(2):118–24.
12. Henry D, Ruoff GE, Rhudy J, Puopolo A, Drehobl M, Schoenberger J, et al. Effectiveness of short-course therapy (5 days) with cefuroxime axetil in treatment of secondary bacterial infections of acute bronchitis. Antimicrob Agents Chemother. 1995;39(11):2528–34.
13. Samanta TC, Bax RP, Pearson RM, Havard CW, Brumfitt W, Hamilton-Miller JM. Clinical study of cefuroxime in the

treatment of lower respiratory tract infections. Curr Med Res Opin. 1980;6(7):466–71.
14. Adam D, Scholz H, Helmerking M. Comparison of short-course (5 day) cefuroxime axetil with a standard 10 day oral penicillin V regimen in the treatment of tonsillopharyngitis. J Antimicrob Chemother. 2000;45 Suppl:23–30.
15. Jalil A, Niazi ID, Khan SU. Evaluation of restoration of sensitivities of resistant Staphylococcus aureus isolates by using cefuroxime and clavulanic acid in combination. J Ayub Med Coll Abbottabad. 2008;20(2):28–30.
16. Sawant C. In-Vitro Study of Antimicrobial Activities of Five Different Commercial Fixed Dose Combination Drugs in Indian Market. Indian medical gazette. 2015;3:101–8.
17. De A, Tayal R, Baveja S. Comparison of sensitivity of cefuroxime-clavulanic acid combination v/s cefuroxime alone in biofilm and/or beta-lactamase-producing bacteria. European Journal of Biomedical and Pharmaceutical Sciences. 2016;3(1): 242-246.
18. Guo Y, Song G, Sun M, Wang J, Wang Y. Prevalence and Therapies of Antibiotic-Resistance in Staphylococcus aureus. Front Cell Infect Microbiol. 2020;10. Accessed On:2024 Apr 5 Available:https://www.frontiersin.org/articles/10.3389/fcimb.2020.00107
19. Zubair M, Malik A, Ahmad J, Rizvi M, Farooqui K, Rizvi M. A study of biofilm production by gram-negative organisms isolated from diabetic foot ulcer patients. Biology and Medicine. 2011; 3:147–57.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/116987