


Assessment of the Appropriateness of Cefazidime Use in a Tertiary Teaching Hospital, Northern Ethiopia

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Background: Cefazidime is nowadays one of the most commonly used antibiotics due to its high antibacterial potency, wide spectrum of activity, and low potential for toxicity. However, the global trend shows huge misuse of cefazidime.

Objective: This study was conducted to assess the appropriateness of cefazidime use and to identify areas of intervention to prevent inappropriate use in different wards of Ayder Compressive Specialized Hospital, a tertiary teaching Hospital, Mekelle-Ethiopia.

Methods: A facility-based prospective cross-sectional study design was steered on 327 patients who received cefazidime during their hospitalization in the selected wards from February 1 to April 30, 2019.

Results: In the assessment of the appropriateness of cefazidime use, 2,084 (70.8%) were appropriate. Appropriateness of indication was 295 (90.2%), the effectiveness of cefazidime use was 221 (67.6%), correct dose of cefazidime use was 264 (80.4%), and the correct frequency of cefazidime use was 230 (70.3%). Its use was empiric in 275 participants (84.1%) and specific in 52 (15.9%) participants. The most common indication for cefazidime use was uncomplicated pneumonia, at 112 (34.3%). One hundred and seventy-one (52.3%) participants had intervention to prevent inappropriate use of cefazidime. Changing the drug combination (96, 29.4%), increasing the dose (13, 4%), decreasing the dose (21, 6.4%), holding the (21, 6.4%), and discontinuation of cefazidime (20, 6.1%) were among the interventions.

Conclusion: This study revealed that more than one-fourth of the cefazidime use was inappropriate. This may lead to the emergence of resistant pathogens which in turn lead to treatment failure and increased the cost of therapy. Therefore, adherence to current evidence-based guidelines and initiating antimicrobial stewardship are recommended.

Keywords: cefazidime, drug use evaluation, appropriateness, resistance

Background

Antibiotics are used to save the lives of millions of people and are among the most common medications prescribed in healthcare settings.^{1,3} Cephalosporin's are a commonly used class of antibiotics worldwide and the use of a newer generation of cephalosporin's have increased in the developing countries. The availability of various generations of cephalosporin like cefazidime (3rd generation), cefalexin (1st generation), cefotaxime (3rd generation), ceftriaxone (3rd generation), cefixime (4th generation), and formulations as well as their expanded indications have an impact on prescribing and drug use practice. The spectrum of activities had been

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broadening in the third generation to include gram negatives like *Enterobacter* species, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*.^{4,5}

Third generation cephalosporins are the most commonly prescribed broad-spectrum antibiotic even before culture sensitivity test results arrive. Ceftazidime, which is a semi-synthetic, broad-spectrum, beta-lactam antibacterial drug used for complicated and uncomplicated urinary infection, bone and joint infection, very severe life-threatening infection in immune compromised patients, peritonitis, sepsis and serious genealogical and intra-abdominal infections, lower respiratory tract infections, skin and skin-structure infections, bacterial septicemia, central nervous system infections in different doses (250 mg, 500 mg, 1 gm, 2 gm) intravenous or intramuscular route of administration on BID (twice per day) and TID (three times per day) frequency.¹

According to the World Health Organization (WHO), drug use evaluation (DUE) is a systematic, criteria-based drug evaluation that ensures the appropriateness of drugs. It is a method of obtaining information to identify problems related to drug use and means to correct the problem, thereby ensuring rational drug therapy.^{6,7} DUE of commonly used antibiotics will result in improved treatment efficacy, conserve costs, and prevent unwanted adverse effects.^{8,9} Irrational use of antibiotics can be associated with drug resistance,⁵ drug-induced diseases like adverse drug reactions,⁸ medicine stock outs,¹⁰ longer hospital stays,⁵ ineffective and unsafe treatment, prolongation of illness, distress, and higher costs.¹¹

Developing resistance has been troublesome early after antibiotics became available for widespread use depending upon early reports of resistance in the literature or reports of healthcare transmission or outbreaks.¹² The overuse of antibiotics had resulted in the advent of drug-resistant strains which are very difficult to treat, representing a major public health problem.^{13,14} Emergence of antibiotic resistant strains causes a considerable impact on patient treatment and outcomes, adding to the increased length of stay in the hospital, additional co-morbid conditions, and increased treatment cost.⁵ Many studies had been done on ceftriaxone use, but studies were lacking on the appropriateness of ceftazidime use.^{15,16} Since the status of ceftazidime use was not known in Ethiopia, this study was intended to assess ceftazidime use and to identify areas of intervention to prevent inappropriate use, which can be used as preliminary data for further research on drug resistance and sensitivity tests.

Methods

Study Area

This study was conducted in Ayder Comprehensive Specialized Hospital (ACSH), a tertiary and teaching hospital in Mekelle-Tigray, Northern Ethiopia, which is around 783 km from the capital city, Addis-Ababa. It started as a referral and specialized hospital in 2008 to a population of 8 million in the catchment areas of Tigray, Afar, and the South-eastern part of the Amhara regional states. It provides a broad range of medical services to both in-patient and out-patients. It also serves as a teaching hospital to several medical, dental, nursing, midwifery, public health, pharmacy, anesthesia, and medical laboratory students in both undergraduate and post-graduate programs. It is the second largest hospital in the nation, with more than 500 beds in the medical, pediatric, surgery, gynecology and obstetrics, adult and pediatric intensive care units. It has more than 100 specialists in various areas of medical specialization and more than 3,000 other health professionals.

Study Design and Study Period

A prospective cross-sectional study design was conducted from February 1 to April 30, 2019.

Source and Study Population

All patients admitted to the inpatient wards of ACSH for their medical care formed the study population. All patients admitted to medical, pediatric, intensive care unit (ICU), neonatal intensive care unit (NICU) and surgical wards of ACSH who took ceftazidime for their medical care during the study period were the study subjects.

Eligible Criteria

All patients admitted to inpatient wards of ACSH, who took ceftazidime within the study periods, were included in this study and outpatients were excluded from the study.

Sample Size Determination and Sampling Technique

The sample size was determined by using the single population proportion, assuming the prevalence rate of the good utilization of ceftazidime as 50%, the desired degree of precision was 5%, 95% confidence interval.

$$n = Z^2 \alpha / 2p(1 - p) / d^2$$

where n=Required sample size;

z =The standard score corresponding 95% confidence level=1.96;

P =Prevalence rate of good ceftazidime utilization=50%; d =Margin of sampling error=5%; and

$$n = (1.96)^2 \times 0.5 \times 0.5 / (0.05)^2 = 384.16, \sim 384.$$

As the study population was less than 10,000, around 15 participants were expected to take ceftazidime daily. Then $15 \times 3 \times 30 = 1,300$ finite population correction formulas were applied:

where nf =Desired sample size;

n =The calculated sample size;

N =Total population; and

$$nf = \frac{384}{1 + \left(\frac{n}{N}\right)} \quad nf = \frac{384}{1 + \left(\frac{384}{1300}\right)}$$

$nf=300$, with 10% non-response rate=330.

By adding a 10% (30) allowance to compensate for non-respondents and incompleteness, a total of 327 study subjects were recruited in this study. The study participants were selected by non-probability convenience or availability method where an attempt was done to include all participants who took ceftazidime during the study period without any probability sampling method until the required sample size for the study was obtained.

Data Collection Instrument and Data Collection Procedure

A data abstraction tool was prepared from different guidelines and research articles to include information about socio-demographic characteristics (sex, age, and residence), clinical characteristics (admitted ward, comorbidities, and combination of disease presentation), common

indications of ceftazidime, type of treatment ceftazidime use (empirical or specific), dose and frequency of ceftazidime use, concomitant drugs used with ceftazidime, and appropriateness of ceftazidime use (disease-ceftazidime interaction (Yes/No), any drug interaction with ceftazidime (Yes/No), appropriateness of indication (Yes/No), effectiveness of ceftazidime use (Yes/No), correctness of ceftazidime dose and its frequency (Yes/No), least expensive alternativeness of ceftazidime use for the indication (Yes/No), presence of unnecessary duplication therapy with other drugs (Yes/No), and acceptability of the duration of ceftazidime use (Yes/No).¹⁷ The Appropriateness of Ceftazidime use was calculated from the variables indicated in Table 1.

Appropriate use of ceftazidime was defined as using ceftazidime for the intended indication, when the recommended dose and frequency of ceftazidime was administered, the optimal duration of treatment was given, disease presentation and co-administered drug had no interaction with ceftazidime, effectiveness for the prescribed illness, its least expensiveness as compared with other drugs used for the same indication as well as non-duplication therapy with other drugs.^{18,19}

Empirical treatment of ceftazidime was also defined as when ceftazidime was prescribed initially before or without identification of ceftazidime culture-sensitive bacterial pathogens, whereas specific treatment was defined as when ceftazidime was prescribed after identification of ceftazidime culture sensitive bacterial pathogens.¹⁹

In this study assessment of the common intervention provided by the attending physician and clinical pharmacist working in the selected wards was described as changing the drug combination with ceftazidime, increasing or

Table 1 Appropriateness of Ceftazidime Use in the In-Patient Wards of Ayder Comprehensive Specialized Hospital (N=327)

Variables	Appropriate (No Problem)	Inappropriate (There Is a Problem)
Disease drug interaction with ceftazidime	295 (90.2%)	32 (9.8%)
Any drug interaction with ceftazidime	249 (76.1%)	78 (23.9%)
Appropriateness of indication of ceftazidime	295 (90.2%)	32 (9.8%)
Effectiveness of ceftazidime use for the indication	221 (67.6%)	106 (32.4%)
Correctness of the dose of ceftazidime use	263 (80.4%)	64 (19.6%)
Correctness of the frequency of ceftazidime use	230 (70.3%)	97 (29.7%)
Least expensive alternativeness of ceftazidime use compared to others of equal utility	75 (22.9%)	252 (77.1%)
Unnecessary duplication therapy with other drugs	234 (71.6%)	93 (28.4%)
Acceptance of the duration of ceftazidime therapy	222 (67.9%)	105 (32.1%)
Total	2,084 (70.8%)	859 (29.2%)

decreasing the dose of ceftazidime administered, holding or discontinuation of the dose of ceftazidime.

Data was collected from patient medication record chart scrutinized in order to pursue all ceftazidime use in the selected wards and data was collected by trained data collectors under the supervision of the investigator.

Data Quality Assurance and Analysis Procedure

Training of data collectors was given to acquire the basic skills necessary for data collection during the follow-up periods. Every activity was strictly followed by the principal investigator for the completeness of collected data. The data abstraction format was commented on by independent specialists in the respective areas of the study settings. Terms used were made clear and pre-tests were done in Mekelle General Hospital before starting the main study and then correction was made according to the review of the pre-tested data. The data abstraction format was prepared in the English language since the data collectors were professionals. All completed data abstraction format was examined for completeness and consistency during data management, analysis by the principal investigator, so that data was intensively cleaned before analysis and then coded, entered by using EpiData version 3.1, and analyzed using SPSS version 21. Simple descriptive statistical analysis, including percentage and frequency distribution, was used to describe ceftazidime use in inpatient wards.

Results

Socio-Demographic and Clinical Characteristics of Study Participants

A total of 327 participants were included in the present study. The gender distribution of participants was nearly similar, with 166 (50.8%) males. Two hundred and thirty-eight (72.8%) were from rural areas. Most participants were from medical wards (177, 54.1%), followed by 96 (29.4%) participants from the pediatric ward, 21 (6.4%) from the ICU, 17 (5.2%) from the surgical ward, and 16 (4.9%) from the NICU. From this study, 98 (30%) of the participants had more than four comorbidities. Congested heart failure (82, 25.1%), surgical site infection (74, 22.6%), and diabetic mellitus (36, 11.0%) were the most common comorbidities. More than half of the participants (180, 55%) had one indication, and 112 (34.3%) of them had two infectious disease presentations (Table 2).

Table 2 Socio-Demographic and Clinical Characteristics of Participants Taking Ceftazidime in In-Patient Wards of Ayder Comprehensive Specialized Hospital (N=327)

Variables	Categories	Frequency (N)	Percent (%)
Sex	Male	166	50.8
	Female	161	49.2
Age	<5	86	26.3
	6–15	47	14.4
	16–30	65	19.9
	31–59	71	21.7
	>60	58	17.7
Admission ward	Medical wards	177	54.1
	Pediatric wards	96	29.4
	Intensive care unit	21	6.4
	Neonatal intensive care unit (NICU)	16	4.9
	Surgical ward	17	5.2
Resident	Rural	238	72.8
	Urban	89	27.2
Number of comorbidities	0	0	0
	1	86	26.3
	2	6	1.8
	3	70	21.4
	4	67	20.5
	>4	98	30.0
Types of comorbidities	Congested heart failure	82	25.1
	Surgical site infection	74	22.6
	Diabetic Mellitus	36	11.0
	Retrovirus infection	33	10.1
	Chronic kidney disease	32	9.8
	Hypertension	20	6.1
	Cancer	13	4.0
	Others*	37	11.3
Combination of infectious disease presentations	1	180	55.0
	2	112	34.3
	3	14	4.3
	4	7	2.1
	>4	14	4.3

Notes: *Co-morbidities: Tuberculosis (n=15), Stroke (n=10), Pancytopenia (n=4), Seizure (n=4), Asthma (n=2), Hypothyroidism (n=2).

Indications and Prescribing Pattern of Ceftazidime

From this study the top three indications for ceftazidime use were hospital-acquired pneumonia (112, 34.3%), Peritonitis and Sepsis (60, 18.3%), and meningitis (44, 13.5%) (Table 3). Descriptive analysis of ceftazidime use indicated that most prescriptions were issued for empirical therapy (275, 84.0%). It was also found that only 52 (16%)

Table 3 Indications of Ceftazidime Use in the In-Patient Wards of Ayder Comprehensive Specialized Hospital (N=327)

Indication of Ceftazidime	Frequency (N)	Percent (%)
Uncomplicated pneumonia	112	34.3
Peritonitis and Sepsis	60	18.3
Meningitis	44	13.5
Intra-abdominal infections	25	7.6
Very severe life threatening infection in immunocompromised patient	23	7
Lung infection or cystic fibrosis	22	6.7
Complicated urinary tract infection	21	6.4
Bone and joints infections	7	2.2
Neutropenic Fever	7	2.2
Uncomplicated urinary tract infection	6	1.8

participants received ceftazidime for the specific therapy (Figure 1).

Type of treatment of ceftazidime use

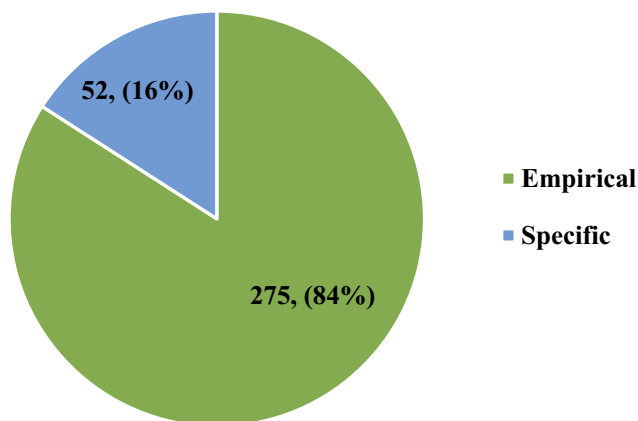


Figure 1 Type of treatment of ceftazidime use in the inpatient wards of Ayder Comprehensive Specialized Hospital (N=327).

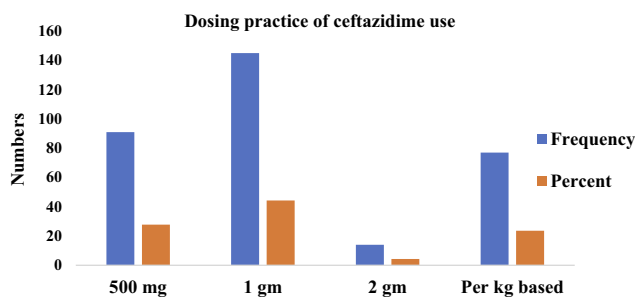


Figure 2 Dose of ceftazidime use in the inpatient wards of Ayder Comprehensive Specialized Hospital (N=327) per kilogram based on (30–50) mg/kg per dose in <12 years.

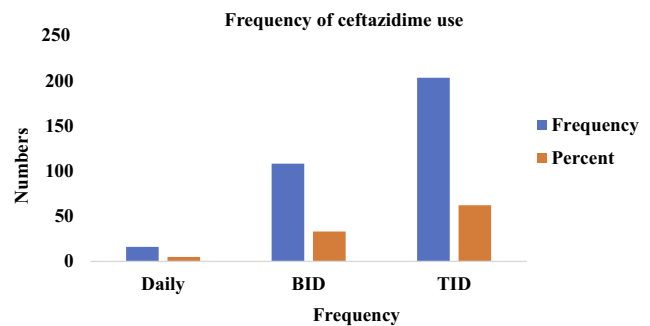


Figure 3 Frequency of ceftazidime use in the inpatient wards of Ayder Comprehensive Specialized Hospital (N=327), BID, Twice per day; TID, Three times per day.

Dosage and Frequency of Ceftazidime

The most commonly prescribed amount of ceftazidime per dose was found to be 1 gm (145, 44.3%) of participants. This was followed by the 500 mg dose (91, 27.8%) of participants. The most common frequency of ceftazidime administration was found to be the TID (203, 62.1%) of participants. The details of dosage and frequency of administration ceftazidime are shown in Figures 2 and 3.

Concomitant Drugs Administrated with Ceftazidime

Among the antibiotic drugs co-administered with ceftazidime, vancomycin (208, 63.6%) took the first place. This was followed by metronidazole (67, 20.5%). On the other hand, furosemide was the most common concomitant non-antibiotic drug used with ceftazidime (Tables 4 and 5).

Appropriateness of Ceftazidime Use

In this study, 2,084 (70.8%) ceftazidime use was appropriate in the study participants. In the assessment of the appropriateness of ceftazidime use, 295 (90.2%) of the participants

Table 4 Concomitant Antibiotic Drugs Administrated with Ceftazidime in the In-Patient Wards of Ayder Comprehensive Specialized Hospital (N= 327)

Concomitant Antibiotic Drugs	Frequency (N)	Percent (%)
Vancomycin	208	63.6
Metronidazole	67	20.5
Meropenem	13	4.0
Azithromycin	13	4.0
Ampicillin	7	2.2
Clindamycin	7	2.1
Ceftriaxone	6	1.8
Gentamycin	6	1.8

Table 5 Non-Antibiotics Concomitant Drugs Administered with Ceftazidime in the In-Patient Wards of Ayder Comprehensive Specialized Hospital (N=327)

Concomitant Non-Antibiotic Drugs	Frequency (N)	Percent (%)
Furosemide	71	21.7
Enalapril	65	19.9
Diclofenac	41	12.5
Tramadol	32	9.8
Insulin	32	9.8
3TC+TDF+EFV	30	9.2
Dexamethasone	20	6.1
Others*	36	11.0

Notes: * Morphine (n=12), Aspirin 81 mg (n=10), Phenobarbitone (n=5), Warfarin (n=4), Heparin (n=3), L-thyroxine (n=2), 3TC = lamivudine.

Abbreviations: TDF, tenofovir disoproxil; EFV, Efavirenz.

had no disease that could interact with ceftazidime, there was no drug–drug interaction in 249 (76.1%) participants, 295 (90.2%) had appropriate indications, ceftazidime use was effective in 221 (67.6%) participants, the correct dose of ceftazidime was used in 264 (80.4%) participants, the correct frequency of ceftazidime was used in 230 (70.3%) participants, and ceftazidime use was the least expensive alternative in 75 (22.9%) participants. No unnecessary duplication of therapy with other drugs was seen in 234 (71.6%) participants and the duration of therapy with ceftazidime was accepted in 222 (67.9%) participants (Table 1).

Intervention Done in the Ceftazidime Use

From this study 156 (47.7%) participants were not given any intervention. But, 171 (52.3%) of the participants had intervention on ceftazidime use. As shown in Figure 4, changing the drug combination (96, 29.4%), increasing the

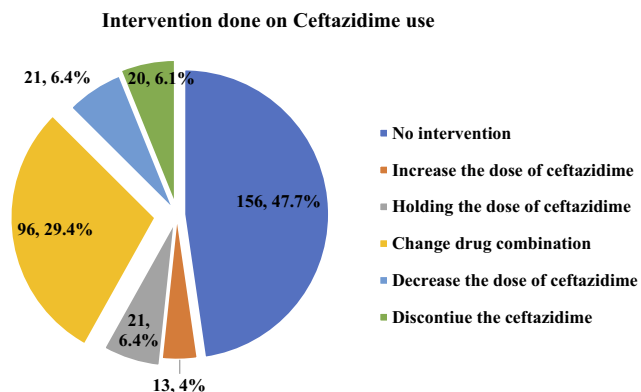


Figure 4 Intervention done on ceftazidime use in the inpatient wards of Ayder Comprehensive Specialized Hospital (N=327).

dose of ceftazidime (13, 4%), decreasing the dose of ceftazidime (21, 6.4%), holding the dose of ceftazidime (21, 6.4%), and discontinuation of the ceftazidime used (20, 6.1%) interventional changes were identified.

Discussion

This study was mainly aimed at evaluating the appropriateness of ceftazidime utilization by using nine criteria besides identifying the potential interventions recommended to prevent inappropriate use. Unlike with other antibiotics like ceftriaxone, few studies have been done on the appropriateness of ceftazidime use.¹⁵ The most prevalent primary indication for ceftazidime use in the current study was hospital-acquired pneumonia, supported by the study done in Eastern Eran.²⁰ Vancomycin was the most common drug combination administered with ceftazidime (63.6%) (from Table 4). This might be for better coverage in considering methicillin resistant staphylococcal infections.

In this study, 84.1% ceftazidime use was for empirical treatment purposes, which shows a huge percentage of ceftazidime use was not based on the culture sensitivity test and there might be giant irrational prescribing practice. Prescribing empirically could be a risk for the development of resistance, increase costs, and compromise patient safety. Antimicrobial resistance is a serious growing public health problem and it is widely accepted that the major cause for the emergence and spread of antimicrobial resistance is misconsumption of antimicrobial drugs. Antibiotic prescribing guidelines should be considered before prescribing antibiotics like ceftazidime.^{18,19} Similarly, delayed ceftazidime prescribing strategies should also be introduced to reduce the misuse of ceftazidime.

In the assessment of the appropriateness of ceftazidime use from Table 1, being ineffective (32.4%), the incorrect frequency (29.7%), not the least expensive alternative drugs (77.1%), having unnecessary duplication therapy (28.4%), and non-optimal duration of therapy (32.1%) of ceftazidime were factors that might be responsible in the development of antimicrobial resistance, and treatment failure to ceftazidime. This might be related with the more empiric use of ceftazidime in the study setting in contrast to undertaking culture and sensitivity tests. This was supported by a study done on the relationship between exposure to antibiotics and increased risk of infection with resistant pathogens at a population level¹⁴ with more pronounced to most antipseudomonal drugs like ceftazidime.^{21,22} In a study from the Slovak republic, 1.2% of *Pseudomonas aeruginosa* were resistant to meropenem, 4.1–7.7% to ceftazidime and cefepime, 12% to amikacin,

and greater than 30% to ciprofloxacin.^{23,24} Therefore, providing training on the use of ceftazidime, preparing institutional prescribing guidelines of ceftazidime, and active involvement of a clinical pharmacist in each ward besides research on the resistant pattern and responsible factors for the resistance of ceftazidime are recommended.

In this study, the inappropriate indication of ceftazidime use was 9.8%. This was comparably high as compared with the inappropriate indication of ceftriaxone use in Gonder (3.5%)²⁵ and very low as compared with that of ceftriaxone use in Tikur Anbessa specialized hospital (18.5%).²⁶ This might be due to duplicated therapy, or the presence of untreated indication. The presence of disease ceftazidime interaction might be attributed to the presence of chronic kidney diseases which need dose adjustment based on glomerular filtration rate. On the other hand, around one-quarter of the participants were on ceftazidime and furosemide, which might be a contributing factor for the drug–drug interactions identified in this study. Attention should be paid in prescribing furosemide or gentamycin with ceftazidime. Inappropriate dosing and the frequency of ceftazidime use might be related with poor professional communication and poor dose calculation based on the weight of the participants, especially in the pediatric wards and chronic kidney disease participants.²⁷ On the other hand, since ceftazidime is given over 8 hours for most indications this might confuse the professional in changing from ceftriaxone to ceftazidime for more coverage. Giving attention to the right dose and right frequency of ceftazidime will help to prevent other inappropriate use. Proper dose adjustment and using online dosing information might also be recommended.

In the case of effectiveness of ceftazidime use, 32.4% of the participants were on ceftazidime for the intended indication. This might be due to the wrong dose and frequency of ceftazidime use, and drug interaction and inappropriate duration of therapy. Prolonged hospitalization might also be a factor that affects the effectiveness of ceftazidime.

In the current study, ceftazidime use was not the least expensive alternative in more than three-quarters of the participant's indication. Lack of knowledge on the available alternative drugs might be the leading reason. This could have a significant effect on the development of ceftazidime resistance in the study setting. Preparing appropriate first- and second-line alternative drugs for the intended indication might be helpful. Clinical conditions of the participant, length of hospitalization and professional knowledge as well as practice might be responsible for the non-optimal

duration of ceftazidime use. Generally, in this study, the inappropriate use of ceftazidime was 29.2%, unlike a study done in the United States, where 87% of ceftazidime use was inappropriate.¹⁵ The significant different in appropriateness of ceftazidime use might be due to the information gap between the studies.

During the study period, more than half of the participants had interventional treatment modifications on ceftazidime use. As shown in Figure 4, changing the drug combination had the highest percentage (29.4%). This might be due to poor diagnosis and a lack of working guidelines on the specific use of ceftazidime in different indications. Among the other interventions holding the dose of ceftazidime and discontinuation of ceftazidime before the optimal duration was also high, which needs greater attention. This could be due to poor communication between professionals and weakness in regular follow-up of the clinical status of the participants. Therefore, improving knowledge and diagnostic confidence of health-care professionals will be recommended.

Limitations

In this study, factors associated with inappropriate use of ceftazidime were not studied. Unlike with ceftriaxone use, studies were lacking on ceftazidime use, so a parallel comparison was not done with other study settings.

Conclusions and Recommendations

This study revealed that more than one-quarter of ceftazidime use was not appropriate. The least expensive alternative of ceftazidime had the highest degree of inappropriateness, followed by less effectiveness of ceftazidime use, unacceptable duration of ceftazidime therapy, unnecessary duplication therapy, incorrect frequency use, having drug interactions, whereas the appropriateness of indication of ceftazidime use was comparably good. More than half of the participants had one or more intervention on ceftazidime use during the study, noticeable by changing the combination of drugs, holding the dose of ceftazidime, and increasing the dose of ceftazidime. Prescribers should limit the use of ceftazidime only for infections proven or strongly suspected to be caused by ceftazidime susceptible microorganisms. As part of this, prescribers should also straight therapy with culture and sensitivity test result whenever it is possible.

Institutional policies should be prepared to reduce the inappropriate use of ceftazidime. Some policies may focus

on improving the quality of the microbiology laboratory, establishing an antimicrobial stewardship program, consulting clinical pharmacists, and establishing institutional prescribing guidelines for antibiotics. Furthermore, research should be done to investigate factors attributable to high inappropriate use of ceftazidime and resistance pattern of ceftazidime in the study area.

Abbreviations

ACSH, Ayder Compressive Specialized Hospital; BID, Twice per day; ICU, Intensive care unit; NICU, Neonatal intensive care unit; TID, Three times per day.

Operational Definitions

Appropriate: The indication for use, dose, and frequency of administration, duration of treatment, culture and sensitivity test investigation, and drug–drug interaction with ceftazidime are according to the recommendations in the current treatment guidelines clinical and laboratory standards Institute.¹⁵

Inappropriate: The indication for use, dose, and frequency of administration, duration of treatment, and drug–drug interaction with ceftazidime was not according to the recommendations of the clinical and laboratory standards institute.¹⁵

Empirical treatment: Ceftazidime administration initiated before or without identification of ceftazidime-sensitive bacterial pathogens.¹⁵

Specific treatment: Ceftazidime administration initiated after identification of ceftazidime-sensitive bacterial pathogens.¹⁵

Ethical Statement

The institutional review board of the School of Pharmacy, College of Health Sciences, Mekelle University approved this study and the verbal informed consent. Verbal informed consent was obtained from each participant as well as parents or guardians for those children less than 18 years old. Confidentiality and privacy were maintained by using code during data collection. A letter of permission was also obtained from the chief clinical director of the ACSH. All the study participants were informed about the purpose of the study.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author Contributions

TGG and AG were involved in the conception, reviewing, analysis, study design, and wrote the manuscript. TGG, AG, and HHG participated in the study design, supervised the development of the manuscript, and were involved in manuscript writing and editing. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Disclosure

The authors report no competing interests.

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