


# Antimicrobial Use-Related Problems Among Hospitalized Pediatric Patients: A Prospective Observational Study

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**Introduction:** Antimicrobials are among the most commonly misused medications, leading to antimicrobial resistance, and therefore demand more attention. There are limited studies documenting “antimicrobial use-related problems” in developing countries, especially in pediatric patients.

**Objectives:** This study aimed to evaluate the prevalence of antimicrobial use-related problems and risk factors among hospitalized pediatric patients.

**Materials and Methods:** A hospital-based prospective observational study was conducted in Ayder comprehensive specialized hospital (ACSH) in the Tigray region, Ethiopia. The participants of the study were pediatric patients aged  $\leq 15$  years who were admitted with a diagnosis of infectious disease between September 2019 and November 2019.

**Results:** A total of 232 pediatric patients were included in the study. Of these, 59.5% of the patients were male and the mean age (SD) of the patients was 5.8 (5.2) years. Of the 232 patients surveyed, a total of 177 antimicrobial use-related problems were identified. One or more antimicrobial use-related problems have occurred in more than half of the patients (53.9%). The commonest antimicrobial use problems were unnecessary antimicrobial therapy (22.8%) followed by need additional antimicrobial therapy (16.4%). In a multivariate logistic regression model, patients with comorbidities (Adjusted odds ratio (AOR): 1.84, 95% confidence interval (CI): 1.04–3.27) and hospital stays exceeding one week (AOR=1.88, 95% CI: 1.08–3.26) were predictors of antimicrobial use-related problems.

**Conclusion:** Antimicrobial use-related problems were found in a significant proportion of pediatric patients. Addressing these issues necessitates collaborative efforts, emphasizing targeted education, strengthened antimicrobial stewardship, ensuring responsible antimicrobial use and enhancing pediatric care.

**Keywords:** antimicrobial use-related problems, pediatric, Ethiopia

## Introduction

Antimicrobial drugs are the most prescribed and widely used drugs, responsible for some of the significant advances in the history of medical therapy.<sup>1</sup> Despite the substantial benefits of antimicrobials, these drugs are among the commonly misused drugs.<sup>2,3</sup> Studies have reported that majority of drug-related problems in hospitals are caused by antimicrobial drugs.<sup>4,5</sup> This is of particular concern in pediatric patients where high proportions of antimicrobials are prescribed inappropriately.<sup>6</sup>

The occurrence of any antimicrobial use-related problems can potentially lead to increased antimicrobial resistance, morbidity, prolonged hospital stays, and increased healthcare costs.<sup>7–9</sup> Common antimicrobial use-related problems include delayed initiation of effective therapies, unnecessary use of antimicrobials, prescribing broad-spectrum antibiotics unnecessarily, exceeding recommended treatment duration, and dosing errors.<sup>6,10</sup>

The World Health Organization has identified AMR as one of the ten greatest threats to global health. Its implications are dire, making currently treatable infections potentially untreatable and leading to increased morbidity and mortality.<sup>11</sup> Developing countries are particularly vulnerable due to limited resources and the potential for ineffective existing antibiotics further accelerating resistance patterns.<sup>12</sup>

Failing to address antimicrobial use-related problems, many antimicrobials will be out of use due to the increasing emergence of antimicrobial-resistance. This can lead to uncontrolled infections, especially in developing countries where access to alternative medicines is limited.<sup>13</sup> With the global increase in antimicrobial resistance, investigating antimicrobial use in hospitals is very important to understand the current situation and formulate policies to promote the appropriate and proper use of antibiotics.

Hospital antimicrobial stewardship programs are responsible for ensuring that all antimicrobials are utilized appropriately and safely to improve patient outcomes, prevent adverse drug reactions, and prevent antimicrobial resistance.<sup>14</sup> However, such program is not implemented in most developing countries including Ethiopia. There are limited studies documenting antimicrobial use-related problems in developing countries, especially in pediatric patients.

This study focuses on various antimicrobial use-related problems encompassing unnecessary use of antimicrobials, the need for additional antimicrobials, use of incorrect dosing, ineffective therapy, non-compliance, and adverse drug reactions related to antimicrobials. The primary objective of this study is to assess the prevalence of antimicrobial use-related problems in a pediatric ward of a tertiary hospital in Tigray, Ethiopia. As a secondary objective, we attempted to determine the predictors of antimicrobial use-related problems.

## Methods and Participants

### Study Setting and Period

The study was conducted at Ayder Comprehensive Specialized Hospital in Mekelle City, Tigray Region, Ethiopia. The hospital offers a wide range of services, including pediatrics, internal medicine, surgery, and maternity care, providing both inpatient services, including pediatric and adult intensive care units, and outpatient services. Ayder comprehensive specialized hospital, a 500-bed facility, is one of the tertiary hospitals in the nation and serves as a teaching hospital and a referral center for approximately 10 million people in northern Ethiopia.<sup>15</sup> The data were collected from September 01, 2019, to November 30, 2019.

### Study Design and Participants

A hospital-based prospective observational study design was conducted to assess antimicrobial use-related problems. All patients who were admitted to the pediatric wards of ACSH during the study period were included in the study, provided they were diagnosed with infectious disease. Criteria for selecting the subjects were as follows: patients admitted to the non-ICU unit of pediatric wards, patients with a length of hospital stay of more than 24 hours, and patients aged  $\leq 15$  years (ie this age group is a cutoff for pediatric patient at the hospital). Patients or caregivers who refused to participate and patients who were readmitted during the study period were excluded.

### Sample Size Determination and Sampling Technique

The sample size was calculated using a single proportion sample size estimating formula.

$$n = \frac{(z_{1-\alpha/2})^2 P(1-P)}{d^2} = \frac{(1.96)^2 0.5(1-0.5)}{0.05^2} = 384$$

Where,  $n$  = sample size,  $Z$  = confidence interval (1.96),  $p$  = the expected prevalence of antimicrobial use-related problems with a proportion of 50% ( $p=0.5$ ) was considered (due to the absence of similar study in the study area in this population group), and  $d$  = Margin of error to be tolerated (0.05).

Correction formula was used since the source population was  $<10,000$  (a total of 471 patients were expected to be admitted during the study period considering previous year data). Correction formulas were employed with the following formula:

$NF = n/(1 + n/N) = 384/(1 + 384/471) = 211$  where  $n$  = minimum sample size (384),  $N$  = total number of simple size (471),  $NF$  = minimum final sample size (211). By adding 10% ( $211 \times 0.1 = 21$ ) of the sample size to compensate non-respondents, the total sample size required was 232. Subjects were recruited using consecutive sampling technique.

## Data Collection Procedure and Instrument

We developed a data abstraction tool to collect all the necessary information. The data abstraction tool consists of three parts including i) socio-demographic characteristics (sex, age, weight, residence), ii) Patients' clinical information (relevant medical and medication histories, physical examination, laboratory results, diagnosis, co-morbidities, length of hospitalization), iii) Patients' medication information (history of antimicrobial use, current antimicrobial medications, other medications, number of current medications, patient adherence). These data were collected through a review of the patient medical chart and interview. Some supplementary information was obtained through discussion with the physician. All included patients were followed for the duration of hospital stay and the data were collected during this period.

Two trained pharmacists were involved in the data collection. A senior clinical pharmacist supervised the data collection. The data collection tools were pre-tested on 20 patients and little amendments were made. The data from the pretest, however, were not part of the study results.

## Outcome Measures and Identification of Antimicrobial Use-Related Problems

The primary outcome was to determine the prevalence of antimicrobial use-related problems occurring in pediatric patients with a diagnosis of infectious disease. The secondary outcomes were to identify the factors affecting antimicrobial use-related problems.

We evaluated the appropriateness of antimicrobial therapy using guidelines followed by a consensus review with a panel of experts including pediatricians and clinical pharmacy specialists. The guidelines used were the Infectious Diseases Society of America (IDSA) guidelines,<sup>16</sup> World health organization's (WHO) pediatric guideline,<sup>17</sup> and the Ethiopian standard treatment guideline.<sup>18</sup> In some scenarios, the appropriate antimicrobial regimens were prescribed based on the individual patient clinical assessment and evaluations of appropriateness of antimicrobial therapy were not applicable using the guidelines. In such cases, the decision was made based on the panel consensus.

## Definition of Terms and Variables

Antimicrobial use-related problem was defined as any undesirable event or circumstance involving antimicrobial therapy that actually or potentially interferes with the patient's optimum outcome of health care.<sup>19</sup> Different methods of classifying drug-related problems have been published.<sup>20</sup> In the present study, Cipolle's drug-related problems classification was used.<sup>19</sup> Cipolle's classification categorizes drug-related problems by seven main domains: needs for additional drug therapy, unnecessary drug therapy, dosage too low, ineffective drug, dosage too high, adverse drug reaction, and patient non-compliance.

The definition of drug-related problems was based on Cipolle's classification<sup>19</sup> as follows:

### Needs Additional Antimicrobial Therapy Was Considered if

- No antimicrobials were prescribed when there is a valid indication for therapy or
- Preventive antimicrobial is needed to reduce the risk of developing new infection or
- An infectious disease requires a combination of antimicrobials to achieve synergism or additional coverage.

### Unnecessary Drug Therapy Was Considered if

- There is no valid indication for antimicrobial therapy or
- More than one antimicrobial is used while one drug can cover the possible pathogen or
- The condition is better treated with nondrug or non-antimicrobial therapy.

## Dosage Too Low Was Considered if

- The antimicrobial dose is too low to produce the desired outcome or
- The dosage interval is too infrequent or
- A drug interaction reduces the amount of active drug available or
- The duration of antimicrobial therapy is too short.

## Ineffective Drug Therapy Was Considered if

- The antimicrobial is not the most effective one for the infection or
- The antimicrobial drug is not effective for the infectious disease or
- The infection is resistant to the drug product being used or
- The route of antimicrobial administration is inappropriate.

## Dosage Too High Was Considered if

- The antimicrobial dose is too high for the patient or
- The dosing frequency is too short or
- The duration of antimicrobial therapy is too long or
- Drug interaction causes a toxic reaction to the antimicrobial drug.

## ADR is Considered if

- The antimicrobial drug causes an undesirable reaction that is not dose-related or
- A safer antimicrobial is needed because of patient risk factors or
- Drug interaction causes an undesirable reaction that is not dose-related or
- The antimicrobial causes an allergic reaction or
- The antimicrobial drug is contraindicated because of patient risk factors.

## Noncompliance Was Considered if

- The patient/caregiver does not understand the instructions or
- The patient prefers not to take the medication or
- The patient/caregiver/nurse forgets to take/administer the medication or
- The antimicrobial is too expensive or not available.

## Hospital Stay

The time gap spent in the hospital from the time of admission until time of discharge.

## Comorbidity

It is the diagnosis of any medical condition other than infectious diseases.

## Data Analysis

The data were entered into Epi data management (version 4.2.0) and analysed using STATA version 14.1 (STATA Corp, TX, USA). Data were summarized as the mean  $\pm$  standard deviation and for continuous variables, and frequency (%) for categorical variables. Regression analysis was used to predict the factors associated with the occurrence of antimicrobial use-related problems. Values were considered significant at a p-value of  $<0.05$  ( $\alpha=0.05$ ).

## Results

### Socio-Demographic Characteristics

A total of 232 pediatric patients were included in this study. Of these, 59.5% of the patients were male and the mean age (SD) of the patients was 5.8 (5.2) years. The majority of the study participants (64.7%) had no history of previous admission to healthcare. More than half (57.8%) of the patient received health care for free [Table 1].

### Disease and Treatment-Related Characteristics of Pediatric Inpatients

The most frequently observed type of infection was pneumonia reported in 42.2% of the cases. More than one-third (39.2%) of the patients have one or more comorbidity. Nearly half (47.8%) of the patients had used antimicrobials during the previous three months. Most of the patients (90.9%) received  $\geq 2$  drugs. The most commonly prescribed antimicrobials were ceftriaxone 161(69.4%), ampicillin 71(30.6%), and metronidazole 57(24.6%), respectively [Table 2].

### Prevalence of Antimicrobial Use-Related Problems

Of the 232 patients surveyed, a total of 177 antimicrobial use-related problems were identified. One or more antimicrobial use-related problems have occurred in more than half of the patients (53.9%). The commonest antimicrobial use problems were unnecessary antimicrobial therapy (22.8%) followed by the need for additional antimicrobial therapy (16.4%) [Table 3]. Some examples of the types and description of antimicrobial use-related problems are provided in Table 4.

### Factors Associated with Antimicrobial Use-Related Problems

We conducted a univariate logistic regression analysis to determine the association of each independent variable with the outcome. Subsequently, variables with a P-value  $< 0.25$  were entered into the multivariate logistic regression analysis to assess the predictors of antimicrobial use-related problems. The full model containing all the covariates was statistically significant ( $\chi^2 = 17.23$ ,  $df = 5$ ,  $p\text{-value} = 0.004$ ). Multicollinearity test was conducted to determine any correlation between the independent variables and no collinearity (variance inflation factor  $< 3$  for all the variables) was observed among the variables.

**Table 1** Socio-Demographic Characteristics of Pediatric Inpatients in Ayder Comprehensive Specialized Hospital from September 2019 Up to November 2019

Socio-Demographic Data	Category	Frequency (%)
Gender	Male	138 (59.5)
	Female	94 (40.5)
Age	$\leq 5$ year	136 (58.6)
	6–10 year	39 (16.8)
	11–15 year	57 (24.6)
	Mean $\pm$ SD	5.8 $\pm$ 5.2
Residence	Rural	156 (67.2)
	Urban	76 (32.8)
Referral status	Referred	181 (78)
	New patient	51 (22)
Cost of health care covered	Self-payment	98 (42.2)
	Free	134 (57.8)

**Table 2** Disease and Treatment-Related Characteristics of Pediatric Inpatients in Ayder Comprehensive Specialized Hospital from September 2019 Up to November 2019

Variables	Categories	Frequency %
History of hospitalizations	No	148 (63.8)
	Yes	84 (36.2)
Type of infections	Pneumonia	98 (42.2)
	Sepsis	36 (15.5)
	Meningitis	22 (9.5)
	SAM	16 (6.9)
	Surgical site infections	9 (3.9)
	Skin/soft tissue infections	8 (3.4)
	Urinary tract infections	6 (2.6)
	Others	37 (15.9)
Comorbidities	Yes	91 (39.2)
	No	141 (60.8)
Antimicrobial use in the past 3 months	Yes	111 (47.8)
	No	90 (38.8)
	Unknown	31 (13.4)
Indications for antimicrobial therapy	Therapeutic	157 (67.7)
	Prophylactic	75 (32.3)
Number of antimicrobial drugs	<2	21 (9.1)
	≥2	211 (90.9)
Hospital stays in days	≤ 1 week	126 (54.3)
	> 1 week	106 (45.7)
Most frequently used antimicrobial drugs	Ceftriaxone	161 (69.4)
	Ampicillin	71 (30.6)
	Metronidazole	57 (24.6)
	Gentamicin	47 (20.3)
	Vancomycin	34 (14.7)
	Ceftazidime	20 (8.6)
	Amoxicillin	14 (6)
	Azithromycin	13 (5.6)
	Ciprofloxacin	10 (4.3)
	Anti-TB	6 (2.6)
	HAART	5(2.2)

(Continued)

**Table 2** (Continued).

Variables	Categories	Frequency %
	Meropenem	4(1.7)
	Cotrimoxazole	4(1.7)
	Others	7(3)

**Abbreviations:** Anti-TB, anti-tuberculosis; HAART, Highly active antiretroviral treatment.

**Table 3** Prevalence and Types of Antimicrobial Use Problems Identified in Ayder Comprehensive Specialized Hospital from September 2019 Up to November 2019

Variables	Frequency (%)
Presence of antimicrobial use-related problems	
Yes	125 (53.9)
No	107 (46.1)
Number of antimicrobial use-related problems	
One	79 (34.1)
Two	43 (18.5)
Three	4(1.7)
Total number of antimicrobial use-related problems (average per patient)	177 (0.76)
<b>Type of antimicrobial use-related problems</b>	
Unnecessary use of antimicrobials	53 (22.8)
Needs additional antimicrobials	38 (16.4)
Dosage too low	35 (15.1)
Dosage too high	24 (10.3)
Ineffective antimicrobial therapy	20 (8.6)
Non compliance	6(2.6)
Adverse drug reaction	1(0.4)

The multivariate logistic regression analysis revealed that patients with comorbidities were more likely to have antimicrobial use-related problems (Adjusted odds ratio (AOR): 1.84, 95% confidence interval (CI): 1.04–3.27). Similarly, patients with a length of stay >1 week were more likely to have antimicrobial use-related problems (AOR = 1.88, 95% CI: 1.08–3.26) [Table 5].

## Discussion

In resource-limited settings, antimicrobials are highly prescribed in children with evidence suggesting both overuse and underuse in different settings.<sup>21</sup> Studying antimicrobial drug-related problems in pediatric patients is essential for designing rational antimicrobial use programs. We found that at least one type of antimicrobial use-related problem in 54.3% of pediatric patients. In accordance with our study, comparable results were reported in different countries, including Turkey (46.7%)<sup>22</sup> and Spain (51.9%).<sup>23</sup> On the other hand, our result is higher than the results reported in China (21%)<sup>24</sup> and lower than those reported in Ghana (86.6%)<sup>25</sup> and Ethiopia (74.3%).<sup>26</sup> The difference in the

**Table 4** Examples of Antimicrobial Use-Related Problems Among Pediatric Patients Admitted in Ayder Comprehensive Specialized Hospital from September 2019 Up to November 2019

Antimicrobial Use Related Problems	Classification	Description
A patient in the age range of 3–5 years was admitted to pediatric ward with the diagnosis of bacterial meningitis and prescribed with ceftriaxone and vancomycin. However, vancomycin was not administered to the patient.	Non compliance	The medication was not available in this governmental hospital and the patient's caregiver could not afford to buy it from a private pharmacy.
A patient in the age range of 13–15 years was admitted to the pediatric ward with the diagnosis of diabetes mellitus type I and periodontal abscess. The patient was prescribed with Amoxicillin/clavulanic acid and metronidazole for the infection in addition to the insulin therapy.	Unnecessary use of antimicrobials	Betalactam-betalactamase inhibitors including amoxicillin/clavulanic acid have excellent anaerobic coverage when used alone for the oral flora's. Hence, metronidazole should not be added for the purpose of anaerobic coverage
A known patient with human immune deficiency virus in the age range of 6–9 years was admitted to the hospital with a diagnosis of bacterial meningitis. The patient was prescribed with vancomycin and ceftriaxone for empiric therapy of meningitis.	Needs additional antimicrobials	Management of meningitis in immune-compromised patients including HIV patients requires empiric coverage of listeria monocytogenes with ampicillin or other active agents.
A neonate in the age range of 8–28 days with a normal birth weight was admitted to the ward with the diagnosis of late onset sepsis and prescribed ampicillin 50 mg/kg BID (two times daily) and gentamicin 5mg/kg daily.	Dosage too low	The dosage interval for ampicillin is too infrequent. In neonates in this age range with normal body weight ampicillin is recommended in a dose of 50 mg/kg/dose IV QID. Its action is time dependent.
A child in the age range of 10–13 years was admitted with the diagnosis of acute appendicitis. The patient was started on ceftriaxone and metronidazole for surgical prophylaxis preoperatively. Appendectomy was performed for non-perforated appendicitis and the antimicrobials were continued for 5 days.	Dosage too high	In this patient the duration of antimicrobial prophylaxis is too long. Therapeutic antimicrobials should only be continued if there is perforated or gangrenous appendicitis.
A patient in the age range of 7–10 years was admitted with dog bite and a falling down accident (have fracture on the right hand). The patient was prescribed with cephalexin for the management of animal bite.	Ineffective antimicrobial therapy	In the empiric management of animal bite, first-generation cephalosporins should be avoided as these agents have poor activity against <i>Pasteurella multocida</i> (common pathogen in animal bite). The preferred drug is amoxicillin/clavulanate.
A patient in the age range of 2–4 years and a weight of 12.6 kg was admitted with a diagnosis of tuberculosis, severe pneumonia and severe acute malnutrition. The patient was prescribed with 2 tab RHZ (rifampicin, isoniazid, and pyrazinamide) + 2 tab E (ethambutol), Ceftriaxone 446 mg iv bid, and pyridoxine. After one month of follow-up the patient was evaluated to have drug induced hepatitis.	Adverse drug reaction	The antimicrobial drug causes an undesirable reaction that is not dose-related: The patient developed drug induced hepatitis due to the anti-tuberculosis medications. After discontinuation of the anti-tuberculosis medications the patients liver function test and symptoms were started to normalize.

prevalence of antimicrobial use-related problems observed in different countries may be due to variations in classifications of antimicrobial use-related problems, populations, level of healthcare facilities, study settings, and the availability of trained prescribers.

In the present study, we found that the most frequently identified antimicrobial use-related problems were unnecessary antimicrobial therapy (22.8%) and the need for additional antimicrobial (16.4%). Similar to our study, unnecessary drug treatment (32.8%) and the need for additional drug treatment (28.1%) were the most prevalent antimicrobial use-related problems in a study in south west Ethiopia.<sup>27</sup> Unnecessary antimicrobial was prescribed for 17% of patients in southwest Ethiopia, which is comparable with our finding.<sup>2</sup>



**Table 5** Multivariable Logistic Regression Analysis of Predictors of Antimicrobial Use-Related Problems at Ayder Comprehensive Specialized Hospital from September 2019–November 2019

Variables	Category	Antimicrobial Use-Related Problems		COR (95% CI)	P- value	AOR (95% CI)	P -value
		Yes, (%)	No, (%)				
Sex	Female	69 (55.2)	69 (64.5)	1	–	1	
	Male	56 (44.8)	38 (35.50)	1.47 (0.87–2.50)	0.152	1.39 (0.81–2.45)	0.233
Comorbidities	No	65 (52)	76 (71)	1		1	
	Yes	60 (48)	31 (29)	2.26 (1.31–3.91)	0.003	<b>1.84 (1.04–3.27)</b>	<b>0.036*</b>
No. of antimicrobials	<2	13 (61.9)	8 (38.1)	1		1	
	≥2	94 (44.5)	117 (55.5)	2.02 (0.81–5.08)	0.134	1.36 (0.52–3.53)	0.536
History of hospitalization	No	73 (49.3)	75 (50.7)	1		1	
	Yes	34 (40.5)	50 (59.5)	1.43 (0.83–2.46)	0.195	1.33 (0.75–2.34)	0.327
Hospital stays	≤ 1 week	68 (54)	58 (46)	1		1	
	> 1 week	39 (36.8)	67 (63.2)	2.17 (1.28–3.68)	0.004	<b>1.88 (1.08–3.26)</b>	<b>0.025*</b>

**Notes:** \*Statistical significance at p-value <0.05. The values in bold font represent variables that are significantly associated with the occurrence of antimicrobial use related problems.

**Abbreviations:** AOR, adjusted odds ratio; CI, confidence interval.

The other main aim of this study was to identify predictors of antimicrobial use-related problems. Multivariate analysis showed that patient length of hospital stay >1 week was significantly associated with the occurrence of antimicrobial use-related problems. Consistent with the present study, a longer hospital stay was associated with antimicrobial use-related problems in a study conducted in different settings.<sup>10,28,29</sup> This could be explained by the fact that the longer patients stay in the hospital, the more likely patients are to contract new infections, such as health care-associated infections. These infectious diseases require a new and complex antimicrobial therapy that further contributed to the occurrence of antimicrobial use-related problems. Thus, patients will be exposed to additional antimicrobial drugs and could increase the risk of drug interaction, adverse drug events, and non-compliance due to unaffordable drugs and an increased number of drugs.

Our study identified that comorbidity was significantly associated with the occurrence of antimicrobial use-related problems. This was also supported by the finding reported by Mechessa et al<sup>26</sup> and Zed et al.<sup>30</sup> The possible justification for this finding is that complex patients often require different antibiotics for treatment of infections than non-complex patients and only few guidelines are available for such patients. Patients with medical comorbidity often use multiple drugs causing interactions (drug–drug, disease–disease, and drug–disease) that predispose patients to one or more antimicrobial use-related problems.<sup>31</sup>

These findings have important implications. The high rate of antimicrobial use-related problems found in the current study underscores the importance of designing different strategies, including establishing an antimicrobial stewardship program. Studies have reported that a high rate of antimicrobial use-related problems can be prevented by implementing rational antimicrobial use programs and implementing disease-specific treatment guidelines.<sup>21</sup> While the positive impact of antimicrobial stewardship programs on reducing inappropriate prescribing, cost, and antimicrobial resistance is well-documented,<sup>1,32</sup> it is essential to acknowledge the challenges faced in their implementation. Similar to numerous low- and middle-income countries, the implementation of antimicrobial stewardship in Ethiopia encounters challenges like limited awareness among healthcare professionals and the public, absence of standardized guidelines, and insufficient resources; addressing these issues requires comprehensive strategies involving education, policy development, improved

access to diagnostic tools, and enhanced collaboration among stakeholders to ensure effective and sustainable antimicrobial use.<sup>33</sup>

Finally, our study was not without limitations. The hospital lacks its own antibiogram, and information on microbiology and antimicrobial susceptibility results were largely unavailable for most patients. This absence of data makes it challenging to assess the appropriateness of prescribing antimicrobials. Although identification of the predictors in the present study might provide important clue based on the included variables, there are other factors related to the healthcare system (eg healthcare providers characteristics) that are not considered. In addition, our study was conducted in a single center in an inpatient setting. Thus, our results may not be generalizable to other hospitals and outpatient settings.

We recommend a periodic multicenter study to assess the appropriateness of antimicrobial use, possibly including drug resistance. Furthermore, healthcare providers and policymakers should use the finding of this and other similar studies and implement strategies to improve the rational use of antimicrobial.

## Conclusion

Antimicrobial use-related problems were found in a significant proportion of hospitalized pediatric patients. The commonest antimicrobial use problems were unnecessary antimicrobial therapy followed by need additional antimicrobial therapy. Addressing these issues necessitates collaborative efforts, emphasizing targeted education, strengthened antimicrobial stewardship, ensuring responsible antimicrobial use and enhancing pediatric care.

## Data Sharing Statement

The dataset of this study is available from the corresponding author upon reasonable request.

## Ethics Statement

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.<sup>34</sup> The study was approved by the Ethics Review Committee of the School of Pharmacy, College of Health Sciences, Mekelle University. The medical director of the hospital was requested permission. Written informed consent was obtained from the study participants and/or caregivers. Name and other identifiers of the patients were not recorded to ensure confidentiality.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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The authors have declared that there is no conflict of interests with respect to the authorship and/or publication of this study.

## References

1. Donà D, Barbieri E, Daverio M, et al. Implementation and impact of pediatric antimicrobial stewardship programs: a systematic scoping review. *Antimicrob Resist Infect Control*. 2020;9(1):3. doi:10.1186/s13756-019-0659-3
2. Tefera GM, Feyisa BB, Kebede TM. Antimicrobial use-related problems and their costs in surgery ward of Jimma University Medical Center: prospective observational study. *PLoS One*. 2019;14(5):e0216770. doi:10.1371/journal.pone.0216770
3. Marcelo C, Tanise F, Marina B, Bruna EK. Antibiotic prescription in a teaching hospital: a brief assessment. *Rev Assoc Med Bras*. 2011;57:414–417. doi:10.1016/S0104-4230(11)70087-2
4. Bizuneh GK, Adamu BA, Bizuayehu GT, Adane SD. A prospective observational study of drug therapy problems in pediatric ward of a referral hospital, Northeastern Ethiopia. *Int J Pediatr*. 2020;2020:4323189. doi:10.1155/2020/4323189
5. Lim MK, Lai PSM, Ponnampalavanar SSSL, et al. Antibiotics in surgical wards: use or misuse? A newly industrialized country's perspective. *J Infect Dev Ctries*. 2015;9(11):1264–1271. doi:10.3855/jidc.6731
6. Miao R, Wan C, Wang Z, et al. Inappropriate antibiotic prescriptions among pediatric inpatients in different type hospitals. *Medicine*. 2020;99(2):e18714. doi:10.1097/MD.00000000000018714
7. Kranz J, Schmidt S, Lebert C, Schneidewind L, Schmiemann G, Wagenlehner F. Uncomplicated bacterial community-acquired urinary tract infection in adults. *Dtsch Arztebl Int*. 2017;114(50):866–873. doi:10.3238/arztebl.2017.0866
8. Chatterjee S, Hazra A, Chakraverty R, et al. A multicentric knowledge-attitude-practice survey in the community about antimicrobial use and resistance in India. *Trans R Soc Trop Med Hyg*. 2020;2020:1.
9. Nisabwe L, Brice H, Umuhire MC, et al. Knowledge and attitudes towards antibiotic use and resistance among undergraduate healthcare students at University of Rwanda. *J Pharm Policy Pract*. 2020;13:7. doi:10.1186/s40545-020-00207-5
10. Tribble AC, Lee BR, Flett KB, et al. Appropriateness of antibiotic prescribing in United States children's hospitals: a national point prevalence survey. *Clin Infect Dis*. 2020;71(8):e226–e234. doi:10.1093/cid/ciaa036
11. World Health Organization. 10 global health issues to track in 2021; 2020. Available from: <https://www.who.int/news-room/spotlight/10-global-health-issues-to-track-in-2021>. Accessed December 1, 2023.
12. Villanueva P, Coffin SE, Mekasha A, McMullan B, Cotton MF, Bryant PA. Comparison of antimicrobial stewardship and infection prevention and control activities and resources between low-/middle- and high-income countries. *Pediatr Infect Dis J*. 2022;41(3s):S3–S9. doi:10.1097/INF.00000000000003318
13. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. *Pathog Glob Health*. 2015;109(7):309–318. doi:10.1179/2047773215Y.0000000030
14. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the infectious diseases society of America and the society for healthcare epidemiology of America. *Clin Infect Dis*. 2016;62:e51. doi:10.1093/cid/ciw118
15. College of Health Sciences, Mekelle University; 2023. Available from: <https://ayder.info/index.php/about-us>. Accessed January 9, 2024.
16. IDSA Practice Guidelines; 2019. Available from: [https://www.idsociety.org/practice-guideline/practice-guidelines/#/+0/date\\_na\\_dt/desc/](https://www.idsociety.org/practice-guideline/practice-guidelines/#/+0/date_na_dt/desc/). Accessed January 9, 2024.
17. World Health Organization. *Pocket Book of Hospital Care for Children: Guidelines for the Management of Common Childhood Illnesses*. World Health Organization; 2013.
18. Food M, Administration H; Ethiopia CAo. Standard treatment guidelines for general hospitals; 2014.
19. Cipolle RJ, Strand LM, Morley PC. *Pharmaceutical Care Practice: The Patient-Centered Approach to Medication Management*. McGraw Hill Professional; 2012.
20. van Mil JW, Westerlund LO, Hersberger KE, Schaefer MA. Drug-related problem classification systems. *Anna Pharmacoth*. 2004;38(5):859–867. doi:10.1345/aph.1D182
21. Rogawski ET, Platts-Mills JA, Seidman JC, et al. Use of antibiotics in children younger than two years in eight countries: a prospective cohort study. *Bull World Health Organ*. 2017;95(1):49–61. doi:10.2471/BLT.16.176123
22. Ceyhan M, Yildirim I, Ecevit C, et al. Inappropriate antimicrobial use in Turkish pediatric hospitals: a multicenter point prevalence survey. *Internat J Infect Dis*. 2010;14(1):e55–e61. doi:10.1016/j.ijid.2009.03.013
23. Santander BC, Alonso EC, Carrión AS, et al. Appropriateness of antibiotic prescribing in paediatric patients in a hospital emergency department. *Anales de Pediatría*. 2018;88(5):259–265. doi:10.1016/j.anpedi.2017.06.001
24. Rashed AN, Wilton L, Lo CC, Kwong BY, Leung S, Wong IC. Epidemiology and potential risk factors of drug-related problems in Hong Kong paediatric wards. *Br J Clin Pharmacol*. 2014;77(5):873–879. doi:10.1111/bcp.12270
25. Afari-Asiedu S, Oppong FB, Tostmann A, et al. Determinants of inappropriate antibiotics use in rural central Ghana using a mixed methods approach. *Front Public Health*. 2020;8:90. doi:10.3389/fpubh.2020.00090
26. Feyissa Mechessa D, Dessalegn D, Melaku T. Drug-related problem and its predictors among pediatric patients with infectious diseases admitted to Jimma University Medical Center, Southwest Ethiopia: prospective observational study. *SAGE Open Med*. 2020;8:2050312120970734. doi:10.1177/2050312120970734
27. Adere A, Edao A, Tesfaye M, Petros Z. Antimicrobial use-related drug therapy problems and associated factors among patients in the medical ward of Wachemo University Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital, Southwest Ethiopia. *SAGE Open Med*. 2022;10:20503121221140228. doi:10.1177/20503121221140228
28. Yadessa TM, Gudina EK, Angamo MT. Antimicrobial use-related problems and predictors among hospitalized medical in-patients in Southwest Ethiopia: prospective observational study. *PLoS One*. 2015;10(12):e0138385. doi:10.1371/journal.pone.0138385
29. Dedefo MG, Mitike AH, Angamo MT. Incidence and determinants of medication errors and adverse drug events among hospitalized children in West Ethiopia. *BMC Pediatr*. 2016;16:81. doi:10.1186/s12887-016-0619-5
30. Zed PJ, Black KJ, Fitzpatrick EA, et al. Medication-related emergency department visits in pediatrics: a prospective observational study. *Pediatrics*. 2015;135(3):435–443. doi:10.1542/peds.2014-1827
31. Adem F, Abdela J, Edessa D, Hagos B, Nigussie A, Mohammed MA. Drug-related problems and associated factors in Ethiopia: a systematic review and meta-analysis. *J Pharm Policy Pract*. 2021;14(1):36. doi:10.1186/s40545-021-00312-z

32. Gebretekle GB, Mariam DH, Mac S, et al. Cost-utility analysis of antimicrobial stewardship programme at a tertiary teaching hospital in Ethiopia. *BMJ Open*. 2021;11(12):e047515. doi:10.1136/bmjopen-2020-047515
33. Gebretekle GB, Haile Mariam D, Abebe W, et al. Opportunities and barriers to implementing antibiotic stewardship in low and middle-income countries: lessons from a mixed-methods study in a tertiary care hospital in Ethiopia. *PLoS One*. 2018;13(12):e0208447. doi:10.1371/journal.pone.0208447
34. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191–2194. doi:10.1001/jama.2013.281053

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