Evaluating antimicrobial appropriateness in a tertiary care pediatric ICU in Saudi Arabia: A retrospective cohort study

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Abstract

Background Two-thirds of antibiotic prescriptions administered in pediatric inpatient care are inappropriate. This inappropriate utilization is associated with the emergence of antimicrobial resistance (AMR) and a decline in antibiotic susceptibility in many pathogenic organisms isolated in intensive care units. Antibiotic stewardship programs (ASPs) have been recommended as a strategy to reduce and delay the impact of AMR. A crucial step in ASPs is understanding antibiotic utilization practices and quantifying the problem of inappropriate antibiotic use to support a targeted solution. We aim to characterize antibiotic utilization and determine the appropriateness of antibiotic prescription in a tertiary care pediatric intensive care unit in Saudi Arabia.

Methods A retrospective cohort study was conducted at King Abdullah Specialized Children's Hospital (KASCH), Riyadh, Saudi Arabia, over a 6-month period. Days of therapy (DOT) and DOT per 1000 patient-days were used as measures of antibiotic consumption. The appropriateness of antibiotic use was assessed by two independent pediatric infectious disease physicians based on the guidelines of the Centers for Disease Control (CDC) 12-step campaign to prevent antimicrobial resistance among hospitalized children.

Results During the study period, 497 patients were admitted to the PICU, accounting for 3009 patient-days. A total of 274 antibiotic courses were administered over 2553 antibiotic days. Ceftriaxone, vancomycin, ceftazidime, and cefazolin were responsible for the highest rates of consumption (164.8, 150.5, 91.7, and 83.1 DOTs per 1000 patient-days, respectively). Forty-eight percent of antibiotic courses were found to be nonadherent to at least 1 CDC step. The top reasons were inappropriate antibiotic choice (empirically or definitive) (31.3%) and inappropriate prophylaxis (30.2%). Infectious disease service consultation decreased the likelihood of inappropriate consumption of antibiotics.

Conclusions Antibiotic consumption was high in our setting, with significant inappropriate utilization mainly due to empiric choices and the duration of prophylaxis. These data could inform decision-making in antimicrobial stewardship programs and strategies. The CDC steps provide a more objective tool and limit biases when assessing antibiotic appropriateness.

Background

Antibiotics are the most common medication prescribed in pediatric intensive care units (PICUs), with up to 50–100% of patients receiving an antibiotic prescription [1–5]. This may be due in part to a high prevalence of community- and hospital-acquired infections in these settings and an overall high risk of morbidity and mortality [6–8]. However, it may also signify a lack of judicious use of antibiotics. It has been found that almost two-thirds of all antibiotics prescribed in a pediatric setting are inappropriate [1, 9]. Such inappropriate utilization is associated with the emergence of antimicrobial resistance (AMR), adverse drug reactions, and additional morbidity and hospitalization costs [10–12]. It has been estimated that AMR will result in 10 million deaths by 2050 if no global action is taken [13]. In 2015, the World

Health Organization (WHO) addressed AMR with a global strategy that incorporated several interventions, including the reduction of inappropriate antimicrobial utilization [14, 15]. In 2016, during the United Nations General Assembly, experts raised the alarm regarding the looming threat of AMR [16]. Saudi Arabia is facing similar challenges with emerging AMR and declining susceptibility in many organisms isolated from ICU patients; this prompted the participation of Saudi Arabia in the WHO global action plan for Containment of Antimicrobial Resistance [17–19].

The Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America recommended the use of antibiotic stewardship programs (ASPs) in a consensus statement in 2007 and 2016 to address the inappropriate utilization of antibiotics [20, 21]. To initiate ASPs and reduce the inappropriate prescription of antibiotics, it is important to first understand antibiotic utilization practices. Balkhy et al. [22] presented data on antibiotic consumption in our institute but did not elaborate on indications, types of infections or the appropriateness of antibiotic prescriptions. Such information helps quantify the problem of inappropriate antibiotic use and identify the main areas that require attention and modification through an ASP strategy. The primary aim of this study was to characterize and determine the appropriateness of antibiotic utilization in a tertiary care PICU.

Methods

Setting

This retrospective cohort study was conducted at King Abdullah Specialized Children's Hospital (KASCH), an academic governmental tertiary center in Riyadh, Saudi Arabia. The hospital's bed capacity is currently 220, with 25 beds assigned to a closed medical and surgical PICU that has approximately 1000 admissions per year. During the daytime, the PICU is staffed by two intensivist attendants, at least two fellows/specialists, and five to ten residents. The nurse-to-patient ratio is 1 to 1. At the time of this study, there were no approved local antimicrobial guidelines, and no antibiotic stewardship program or strategies were implemented.

Population

All pediatric patients aged 0-14 years who were admitted to the PICU and initiated antibiotic therapy during the study period were included. Patients > 14 years of age or known to have an immunocompromising condition (including all post-transplant patients and all oncological patients receiving chemotherapy at the time of evaluation to up to 6 months prior), to be on an immune-compromising medication, or to require antifungal or antiviral agents were excluded from the study.

Study design

A retrospective cohort study of data was conducted from January to June 2017 (6 months).
Our Institutional Review Board (IRB) at King Abdullah International Medical Research Center (KAIMRC) approved the study, and the requirement for informed consent was waived.

Data collection

Data were collected by the investigators from electronic medical records using a standardized data collection form and reviewed by two pediatric infectious disease physicians in the study group. Data were collected on patient demographics, disease comorbidities, admitting and/or infectious diagnoses, admission type (medical, surgical, trauma, burn), indication for antibiotics, microbiological results on documented infections, consultation for infectious disease (ID) service, and antibiotic utilization (type and duration). Identified infections were reviewed, and multidrug-resistant organisms (MDROs) were identified based on susceptibility patterns and resistance to most available antibiotics.

Antibiotic indications were classified as empiric (based on clinical suspicion of infection or positive culture with pending susceptibility), definitive (to treat an identified pathogen with known antimicrobial susceptibility), or prophylactic (mainly used perioperatively to prevent infection in a patient at risk) [23, 24]. For empiric antibiotics, the decision was classified as follows at 72 hours: antibiotics were stopped (i.e., infection ruled out), antibiotics were continued with a planned duration, antibiotics were changed per microbial culture results and clinical condition (i.e., de-escalation to definitive treatment), or no action was taken (i.e., no decision or plan was documented and the same antibiotics were continued).

Outcome definitions

The appropriateness of antibiotic use was independently assessed by two pediatric ID physicians. Consensus agreement was sought in more complex cases and when opinions differed. Appropriateness was based on clinical judgment and classified using the Centers for Disease Control (CDC) 12-step campaign to prevent antimicrobial resistance among hospitalized children [25]. The CDC 12-step protocol covers four main domains: preventing infection, effectively diagnosing and treating infection, using antimicrobials wisely, and preventing transmission. Adherence to 5 of the 12 steps relating to the appropriateness of antibiotics was utilized in the study. The steps included *targeting the pathogen* (step 4), *practicing antimicrobial control* (step 6), *treating infection and not contamination or colonization* (step 8), *knowing when to say no to antibiotics* (step 9) and *stopping antibiotics if infection was treated or ruled out* (step 10). These steps were elaborated on with some examples to improve clarity and unify understanding of each step for the evaluators (Table 1). Additionally, step 5, *accessing the experts* (i.e., consulting the ID service), was also evaluated separately.

Table 1. Definitions of selected CDC 12-step recommendations

CDC Step	Clarification
Step 4: Target the pathogen	· Inappropriate empiric antibiotic choice based on the likely pathogen · Inappropriate definitive antibiotic choice based on identified pathogen susceptibility (need for de-escalation)
Step 6: Practice antimicrobial control	· Inappropriate prophylaxis regimen (drug or duration) · Inappropriate antibiotic combination (redundant coverage) · Inappropriate route of administration (can/should shift from IV to oral) · Inappropriate dose of antibiotic (based on indication, renal function, etc.) (*not assessed in this study)*
Step 8: Treat infection, not contamination or colonization	· Treating contamination or colonization and not a confirmed true infection
Step 9: Know when to say 'no'	· Starting vancomycin or broad-spectrum antibiotics (meropenem, piperacillin/tazobactam, or ceftazidime) unnecessarily (empirically)
Step 10: Stop infection when cured or unlikely	· Continuing antibiotics despite infection being ruled out or negative cultures or duration of appropriate therapy completed

Days of therapy (DOT) per 1000 patient-days was used to quantify antibiotic consumption. DOT was defined as the number of days that a patient received antibiotics regardless of the dose. When a patient received more than one antibiotic simultaneously, one DOT was counted for every antibiotic given [26]. Patient days were defined as the number of days that all patients were at risk for antimicrobial exposure [27]. Only antibiotics received during the PICU stay were calculated. Any courses prior to or after the PICU stay were not included in data collection or assessed for appropriateness.

Statistical methods

IBM SPSS version 25 was used to analyze the data. The median and percentile (*Q1-Q3)* are used to describe quantitative variables, such as age, PICU length of stay, and days of therapy. Frequencies and percentages are used to describe qualitative variables, such as sex, type of admission, and type of antibiotics (Table 2). DOT is reported per 1,000 patient-days for each antibiotic (Figure 1). The chi-square and Mann-Whitney U tests were used to assess the relationships between sample characteristics and inappropriate judgment of antibiotic use. A binary logistic model was used to identify multiple factors associated with inappropriate antibiotic use (Table 3). The goodness of fit for this model was assessed by the Hosmer and Lemeshow test. All statistical tests were 2-tailed, and the significance level was set at $\alpha = 0.05$.

Table 2. Sample characteristics and relation to inappropriate judgment of antibiotic use (univariate and bivariate analysis)

Factor	Range	Overall		Appropriate antibiotic use 131 (50.8%)		Inappropriate use 127 (49.2%)		P
		Median	Q1-Q3	Median	Q1-Q3	Median	Q1-Q3	
Age/months	0.03 – 182.30	23	6-66.5	22.8	6-57.7	24.6	6-81	0.229
PICU length of stay/days	0-91	3	1-6	3	2-6	3	1-6	0.476
Days of therapy	0-42	8	4-13	7	3-10	9	6-14	0.001*
	Levels	**n**	**%**	**n**	**%**	**n**	**%**	
Sex	Female	127	49.0	63	49.6	64	50.4	0.137
	Male	132	51.0	68	51.9	63	48.1	
Admission type	Surgical/Trauma/Burns	87	33.6	28	32.6	58	67.4	0.001*
	Medical	172	66.4	103	59.9	69	40.1	
Antibiotic decision beyond 72 hours	Stopped	98	38.0	58	59.2	40	40.8	0.001*
	Continued with planned duration	98	37.6	56	57.1	42	42.9	
	Changed	11	4.3	5	45.5	6	54.5	
	No action	52	20.2	13	25.0	39	75.0	
ID service consulted	Yes	36	14.1	23	63.9	13	36.1	0.090
	No	219	85.9	106	48.6	112	51.4	
Documented indication	Yes	228	88.4	114	50.2	113	49.8	0.749
	No	30	11.6	16	53.3	14	46.7	
Positive cultures	Yes	56	21.6	30	53.6	26	46.4	0.636
	No	203	78.4	101	50.0	101	50.0	

*. Significant at $\alpha=0.05$.

Table 3. Multivariate factors associated with inappropriate judgment of antibiotic use

							95% C.I.for aOR	
Factor	Ref.	B	SE	Wald	P	aOR	Lower	Upper
Age		0.008	0.004	4.394	0.036*	1.008	1.001	1.016
Female	Male	0.104	0.336	0.096	0.757	1.109	0.575	2.141
PICU length of stay		-0.031	0.024	1.729	0.188	0.969	0.925	1.016
Surgical/Trauma/Burns	Medical	1.585	0.627	6.384	0.012*	4.878	1.427	16.678
Vancomycin	Ceftriaxone	1.082	0.526	4.235	0.040*	2.950	1.053	8.266
Cefazolin	Ceftriaxone	0.860	0.719	1.429	0.232	2.363	0.577	9.674
Ampicillin	Ceftriaxone	-0.246	0.814	0.091	0.763	0.782	0.159	3.854
Others	Ceftriaxone	1.015	0.475	4.560	0.033*	2.760	1.087	7.009
Stopped	No action	-1.438	0.490	8.599	0.003*	0.237	0.091	0.621
Cont with duration	No action	-1.087	0.486	5.012	0.025*	0.337	0.130	0.873
Changed	No action	-1.069	0.913	1.372	0.241	0.343	0.057	2.054
No ID consulted		2.162	0.645	11.230	0.001*	8.684	2.453	30.743
Documented indication	ID consulted	-0.152	0.554	0.075	0.784	0.859	0.290	2.547
Positive culture		-0.247	0.493	0.251	0.617	0.781	0.297	2.053
Constant		-3.987	1.111	12.891	0.001	0.019		

Results

During the study period, 497 patients were admitted to the PICU; these accounted for 3009 patient days. After excluding 238 patients based on the study criteria, 259 patients were included in the review. Table 2 summarizes the cohort demographics and characteristics. One hundred thirty-two (51%) patients were male, and the median age was 23 months (IQR: 6-66.5 months). The median PICU length of stay was 3 days (IQR: 1–6 days). One hundred and seventy-two (66%) of the admitted patients were medical admissions, while 87 (32%) were either surgical, trauma, or burn admissions.

Overall, 259 children received 274 antibiotic courses, resulting in 2553 DOTs during the study period. The median duration of an antibiotic course was 4 days (range, 3–7). The indications for antibiotics at initiation were empiric (n = 187, 68%), prophylactic (n = 61, 22%), or definitive therapy (n = 6, 9%). The reasons for antibiotic initiation were infections of the respiratory system (n = 115, 42%), surgical procedures (n = 74, 27%), bloodstream infections (n = 65, 24%), central nervous system infections (n = 7,

3%), skin and soft tissue infections (n = 5, 2%), and other systemic involvement (gastrointestinal, cardiovascular, renal) (n = 8, 3%). The most common clinical indications for antibiotic initiation were community-acquired pneumonia (20.5%), community-acquired sepsis (10.4%), bronchiolitis (10%), hospital-acquired sepsis (9.3%), and neurosurgical procedures, e.g., drain insertion or tumor resection (8.9%). Appropriate cultures were collected prior to antibiotic initiation in 205 courses. Of these, an infection was isolated in 60 cultures (29.3%). An MDRO was isolated in 27 cultures (45% of positive cultures). The ID service was consulted in 40 of 274 antibiotic courses (equivalent to 14.6%).

In our center, ceftriaxone, vancomycin, ceftazidime, and cefazolin were the most frequently used antibiotics at 164.8, 150.5, 91.7, and 83.1 DOTs per 1000 patient-days, respectively (Fig. 1). Cefazolin, vancomycin, ceftazidime, and ceftriaxone were the most inappropriately used antibiotic therapies, with 50.2, 40.9, 39.5, and 24.3 inappropriate DOTs per 1000 patient-days, respectively. Figure 2 shows inappropriate and appropriate antibiotic use by indications. Compared to other clinical indications, surgical prophylaxis for neurosurgical procedures and gastrointestinal surgery were positively associated with an increased likelihood of inappropriate antibiotic use (P = 0.001) (Fig. 2).

Out of 274 courses, 133 (48%) were found to be nonadherent to at least 1 of the five CDC steps evaluated, leading to 677/3009 (22.5%) inappropriate DOTs. Thirty-one percent of the courses did not target the pathogen (step 4), 30.2% did not include antimicrobial control (step 6), 16.2% inappropriately began with broad spectrum coverage (step 9), and 22.3% did not stop antibiotics when an infection was considered cleared or unlikely (step 10). No antibiotic courses were found to be violating step 8. On reviewing courses that did not target the pathogen and were nonadherent to step 4 (56 courses), we found that 66% of these were due to an inappropriate empiric choice, 27% were due to inappropriate de-escalation to definitive therapy, and 4 cases had an inappropriate empiric and inappropriate definitive choice.

Subgroup analyzes are demonstrated in Table 2. The duration of antibiotic courses was significantly higher in children with inappropriate antibiotic use than in children who had appropriate antibiotic use (median: 9.0 vs. 7.0, P = 0.001). Surgical, trauma, and burn admissions each had a higher percentage of inappropriate antibiotic use than was found in medical patients (67.4% vs. 40.1%, P = 0.001). Cefazolin and vancomycin were associated with a higher percentage of inappropriate judgment of antibiotic use than was found for other antibiotic agents (P = 0.001). The presence of respiratory comorbidity was associated with a lower percentage of inappropriate antibiotic use (P = 0.028). No action taken regarding antibiotics after 72 hours was associated with a higher percentage of inappropriate antibiotic use than was found for other antibiotic decisions (stopped: 40.8%, continued with planned duration: 43.8%, changed based on clinical condition and culture results: 54.5%, no action taken: 75%, P = 0.001). The rest of the sample characteristics were not significantly associated with inappropriate antibiotic use.

Adjusted odds ratios are provided in Table 3. Age was positively associated with inappropriate judgment of antibiotic use (adjusted odds ratio (aOR): 1.012, 95% confidence interval (CI): 1.002 to 1.022, P = 0.016). Compared to ceftriaxone, vancomycin and cefazolin significantly increased the risk of inappropriate judgment of antibiotic use (aOR: 3.781, 95% CI: 1.265 to 11.299, P = 0.017 and aOR: 13.560,

CI: 1.170 to 157.105, P = 0.037, respectively). Compared to cases with infectious disease consultation, in cases where an ID consultation was not carried out, the likelihood of inappropriate antibiotic use was higher (aOR: 7.407, CI: 2.078 to 26.405, P = 0.002). The Hosmer and Lemeshow test indicate that this model fits the data well (P = 0.868).

Discussion

Several studies of pediatric antibiotic consumption have been performed in Saudi Arabia. Balkhy et al. [22] conducted a prospective surveillance study over 33 months in two PICUs and one neonatal intensive care unit (NICU) [22]. They reported that the consumption of cephalosporins (237.3 DOT per 1000 patient-days) and carbapenems (85.8 DOT per 1000 patient-days) was higher in PICU patients in Saudi Arabia than the levels reported in the USA and Canada. Al Matar et al. [28] conducted a point prevalence study on antibiotic consumption using data obtained in 26 hospitals in Saudi Arabia in both adults and children and found that 24% of patients admitted to ICUs received antibiotics, with third-generation cephalosporins the most commonly prescribed agents. AlAwdah et al. [29] reported in a pilot ASP study that 72% of admissions to a tertiary care PICU were prescribed antibiotics. None of these studies addressed the appropriateness of antibiotics, and only Balkhy et al. [22] used the metric DOT per 1000 patient-days to report the consumption of antibiotics. The DOT and DOT per 1000 patient-days are the metrics of choice for measuring antibiotic consumption in the pediatric population as recommended by the National Healthcare Safety Network and CDC [26, 30].

To the best of our knowledge, this is the first report to assess antibiotic appropriateness in pediatric patients admitted to intensive care units in Saudi Arabia. We calculated 3009 total DOTs and 848.5 DOTs per 1000 patient-days, indicating a rising increment with regard for the 708.3 DOTs per 1000 patient-days previously reported between 2012 and 2015 [22]. This difference may be attributable to seasonal variation because prescription rates increased during winter months in our study period [31]. The current antibiotic consumption places in our center are at the higher end of the ranges reported in Switzerland, Canada and the USA, where 550, 750 and 1000 DOTs per 1000 patient-days, respectively, have been reported [2, 4, 32].

On initiation, empiric antibiotics accounted for almost two-thirds of antibiotic prescriptions. This frequency is higher than the international rates reported in Canada and European countries (approximately 40%) and similar to those reported other countries, such as Indonesia (85%) [1, 33, 34]. The high rate of empiric prescriptions may be influenced by a higher burden of infections in PICUs in Saudi Arabia. Almuneef et al. [35, 36] found that the rates of hospital-acquired infections, including central line-related bloodstream and ventilator-associated pneumonia, were higher than those of the National Nosocomial Infection Surveillance system. Another factor may be the difficulty of differentiating between bacterial and viral infections, as reflected in the fact that 26 courses were started empirically in patients diagnosed with bronchiolitis. On review of non-adherence to CDC step 4 (target the pathogen), the majority of such cases were found to be due to inappropriate use of empiric antibiotics. This

suggests a need for a better understanding of common pathogens and local susceptibility patterns, better utilization of diagnostics, and guidelines for the initiation of empiric antibiotics.

The most frequently used antibiotics were ceftriaxone, vancomycin, ceftazidime and cefazolin. Antibiotic choices and top indications for antibiotics in this cohort (pneumonia, sepsis, and surgical prophylaxis) were similar to those in the US and Canada [1, 37]. Forty-eight percent of courses were deemed nonadherent to at least one of the five CDC steps, resulting in a total of 677 inappropriate DOTs (22% from a total of 3009 DOTs). This is lower than the rates reported in Canada by Blinova et al. [1] (62%) and in Turkey by Ceyhan et al. [5] (50%).

Cefazolin was the most inappropriate antibiotic, with a total of 151 inappropriate DOTs and 20% of total inappropriate DOTs for all antibiotics. The main purpose of cefazolin use in our institute is perioperative prophylaxis, with 22% of antibiotics initiated for this purpose. High inappropriate use is largely due to a prolonged duration of postoperative prophylaxis, which had a median duration of 3 days (IQR 2 to 5). This may explain why the rate of inappropriate antibiotics was higher in surgical patients than in medical patients ($P = 0.001$). The misconception of prolonging prophylaxis for specific procedures or the presence of drains may contribute to this finding. Guidelines for perioperative prophylaxis recommend durations not extending beyond 24 hours from initiation irrespective of the surgical procedure or the presence of drains or catheters [23, 24].

A lack of reassessment or action at 72 hours by the treating team was found to be associated with inappropriate antibiotic use ($P = 0.028$). In view of this finding, conducting an antibiotic ‘time out’ would be a suitable intervention. A time out is an ASP intervention recommended by the CDC that standardizes the review of clinical, laboratory and microbiological data at a predefined time (48–72 hours post antibiotic initiation) to identify opportunities for discontinuing or deescalating empiric antibiotics [38]. Adams et al. [27] conducted a quality improvement trial over an 8-month period to evaluate three target antibiotics (vancomycin, meropenem, and piperacillin/tazobactam) and found that the DOT per 1000 days was reduced for both vancomycin and meropenem.

This is the first study to address the appropriateness of antibiotic consumption among PICU patients in Saudi Arabia. We included antibacterial consumption, indications for antibiotic initiation as parameters and, most importantly, assessed the appropriateness of antibiotics by two independent infectious disease physicians based on the CDC 12 step classification. We further quantified and categorized inappropriate antibiotic use, highlighting areas for improvement and allowing for targeted rectification.

The study has several limitations, and data were collected retrospectively; thus, some information influencing decision making could have been missed. In addition, this is a single center report, which limits its generalizability. Decisions regarding antibiotic appropriateness are prone to bias and the subjective interpretation of data despite attempts to unify understanding of the CDC steps and consensus decision-making in more complex cases. This may explain why patients considered to be at a higher risk (i.e., with respiratory comorbidities and younger age) had a higher likelihood of being judged by the reviewing ID physicians to be on appropriate antibiotics. Additionally, due to the retrospective

nature of the study, the accuracy of diagnoses was not confirmed, and the authors accepted all diagnoses made by treating physicians. This meant that we could not assess non-adherence to step 8 (treat infection but not contamination or colonization). In a prospective approach, the necessary information regarding diagnoses could be gathered in real-time. ID consultation decreased the likelihood of inappropriate use and should be utilized in addition to other ASP initiatives.

Conclusions

Throughout our study, we were able to confirm a high prevalence of antibacterial utilization in the PICU with high rates of inappropriate prescriptions, mainly due to inappropriate empiric and definitive antibiotic choices as well as inappropriate perioperative prophylaxis durations. Based on our findings, the main areas for stewardship include the development of empiric antibiotic guidelines, re-education on surgical prophylaxis guidelines, and the introduction of ‘time-out’ moments post-antibiotic initiation. Different approaches to antimicrobial stewardship need to be individualized based on identified concerns. Decisions regarding the appropriateness of antibiotic use could be facilitated by the development of local antibiotic guidelines and the utilization of tools such as the CDC steps to both standardize the process and limit bias and subjectivity.

Abbreviations

PICU Pediatric Intensive Care Unit

AMR antimicrobial resistance

WHO World Health Organization

ICU intensive care unit

ASP Antibiotic stewardship Programs

KASCH King Abdullah Specialized Children’s Hospital

KAIMRC King Abdullah International Medical Research Center's

CDC Centers for Disease Control

DOT Days of therapy

NICU neonatal intensive care unit

Declarations

Ethics approval and consent to participate

The study was approved by the King Abdullah International Medical Research Center (KAIRMC) Institutional Review Board.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YK, NA, HT, BA, and LI conceptualized and designed the study and designed the data collection instruments. HT, BA, and LI collected data. NA and NF coordinated and supervised data collection and carried out antibiotic appropriateness assessments. YK carried out the initial analyses and drafted the initial manuscript. YK, NA, and NF reviewed and revised the manuscript. All authors read and approved the manuscript as submitted and agree to be accountable for all aspects of the work.

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Figures

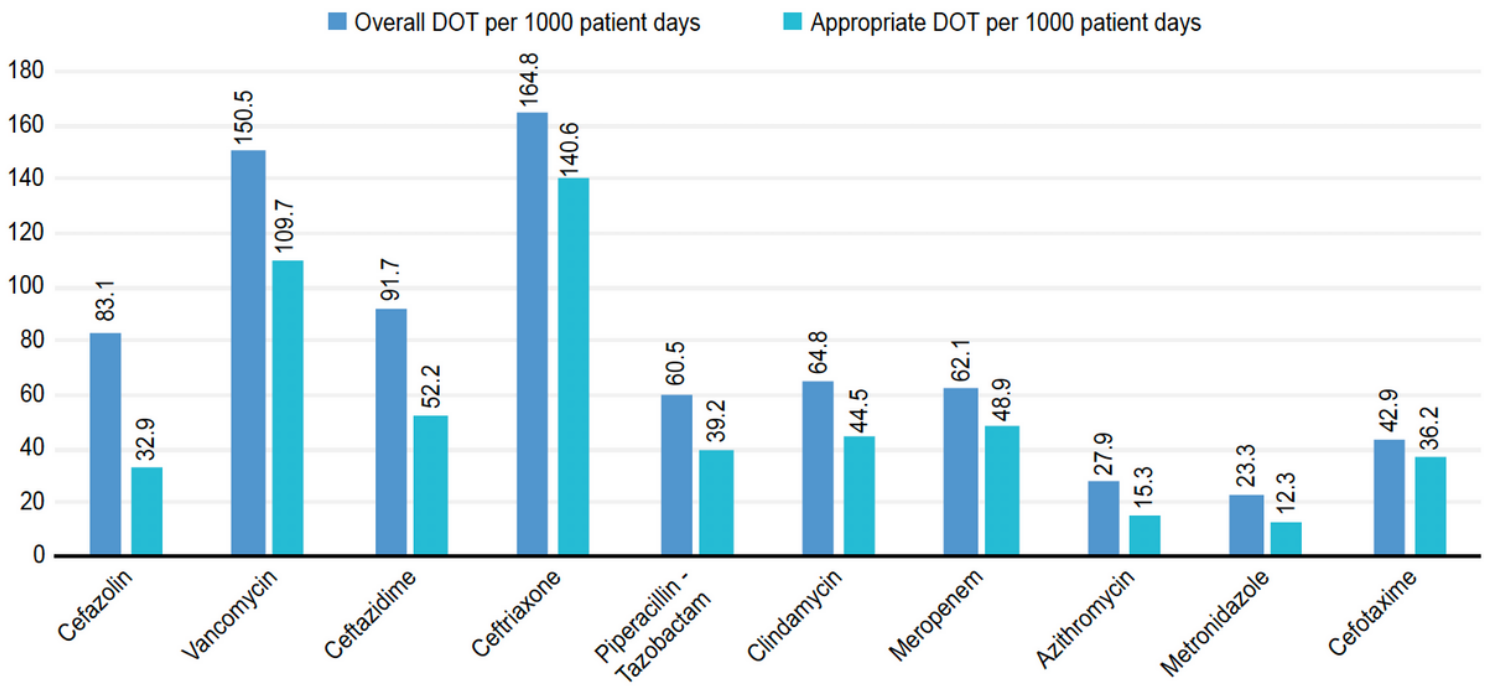

Figure 1

Overall and inappropriate therapy per 1,000 patient days by antimicrobial agent

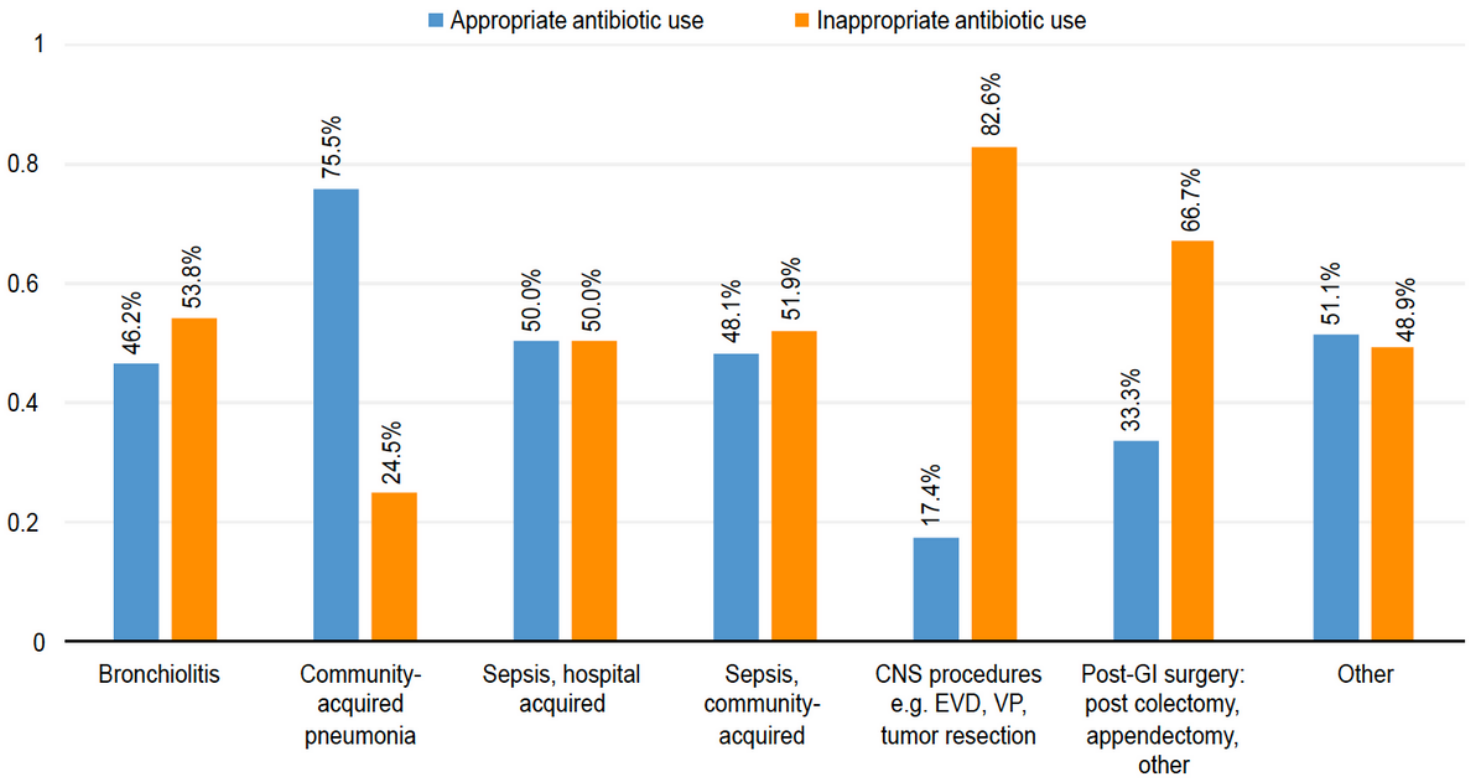

Figure 2

Inappropriate and appropriate antibiotic use by indications