Original Article

Point Prevalence Survey of Antimicrobial Prescription Patterns in a Pediatric Tertiary-Care Unit in Thailand 2019

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Background: Surveillance data is an essential part of antimicrobial stewardship programs (ASP).

Objective: To describe and compare prescription patterns of antibiotics after a 3-years implementation of an ASP using prospective audit and feedback.

Materials and Methods: The authors conducted a point prevalence survey (PPS) of antibiotic prescriptions at a 200-bed pediatric unit at King Chulalongkorn Memorial Hospital. A standardized study protocol from the Global Antimicrobial Resistance, Prescribing, and the Efficacy in Neonates and Children (GARPEC) project was used. The authors reviewed medical charts of hospitalized children of less than 18 years of age, using a point prevalence method on the 15 of February, May, August, and November 2019. Endpoints measures included rate of antimicrobial prescriptions and type of antimicrobial use, stratified by neonatal and pediatric ward types. Rate of antimicrobial prescriptions will be compared with historical data form PPS in the same institute collected in 2016.

Results: In 2019, the medical records of 269 neonates and 409 children hospitalized were reviewed. The proportion of children receiving antibiotics in neonatal units overall was 18.6% (95% CI 14.1 to 23.8), of which ampicillin or gentamicin (52.0%) was the most common regimen. Rate of antibiotic prescriptions in general pediatric wards was 46.5%, with third generation cephalosporins being the most used antibiotics. Prescription rate in the oncology ward was 52.9% with antipseudomonal agents or meropenem being the most prescribed antibiotics. Prescription rates in the pediatric intensive care unit (PICU) was 88.9%, with meropenem being the most used antibiotic. Compared to a previous PPS study in 2016, prevalence of antimicrobial use was higher in general pediatric wards at 46.5% versus 37.2% (p=0.02) and PICU at 88.9% versus 67.7% (p=0.007).

Conclusion: The prevalence rates of antimicrobial use in pediatric wards increased despite implementation of a prospective audit and feedback antibiotic stewardship program. Other measures are needed to reduce the unnecessary prescriptions.

Keywords: Antimicrobial; Antimicrobial stewardship program; Pediatric; Point prevalence survey.

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Antimicrobial resistance (AMR) is a major global healthcare challenge. The Centers for Disease Control and Prevention (CDC) estimates a burden of more than 2.6 million antibiotic-resistant infections and approximately 44,000 deaths each year in the U.S.[1,2]. In Thailand, antimicrobial resistant infections resulted in an addition of at least 3.24 million days of hospitalizations and 38,481 deaths[3]. Irrational use of antimicrobials is an important factor leading to antibiotic resistance, especially overuse and inappropriate use. Approximately one-third of the inpatient antibiotic prescriptions are either unnecessary or inappropriate[4]. Consequently, drug toxicity and the selection of pathogenic organisms such as *Clostridium difficile* including the emergence of drug-resistant organisms are increasing[5].

Due to the emergence of multidrug-resistant pathogens in the past 20 years, many countries have established strategies to reduce the prevalence of such pathogens for several years[6]. In Thailand, common multidrug resistant bacterial pathogens in community-acquired infections include *Streptococcus pneumoniae*, *Salmonella* spp., and *Enterobacterales*. In hospital-acquired infections, common multidrug-resistant pathogens are gram-negative organisms such as extended-spectrum beta-lactamase (ESBL)-

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producing *Enterobacterales*, carbapenem-resistant *Pseudomonas aeruginosa*, and carbapenem-resistant *Acinetobacter baumannii*, and gram-positive organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant coagulase-negative *Staphylococcus* (MR-CoNS)[7-10]. Antimicrobial stewardship programs (ASP) are one of the recommended interventions to reduce AMR[2]. One of the core elements of hospital ASP is tracking and reporting[11].

Point prevalence surveys (PPS) of antimicrobial use is a standardized tool to study the prescribing patterns and indications for antibiotic treatment over time[12]. The strength of PPS is their ability to quantify the rate of antimicrobial use and patterns of types of antibiotics used as a cross-sectional study[12]. It is less time consuming with minimal cost, which is implementable even in resource-limited settings. From a previous global PPS study, the rates of antimicrobial use in children were 36.7%, compared to 40.9% in the U.K., and 68% in China[13-15]. In Thailand, a study in King Chulalongkorn Memorial Hospital (KCMH) in 2016 found that 43.3% of hospitalized children received at least one antimicrobial[7]. Interventions are reported to reduce the rate of antimicrobial agents in many settings. A study in pediatric settings in the United States showed that using two strategies of prospective audit and feedback plus prior authorization for selected antibiotics had a significant impact on reducing antibiotic uses[16]. A study in Japan also reported that prospective audit and feedback contributed to the reduction of antimicrobial therapy prescription[17].

The objectives of the present study were to describe the rates and patterns of antimicrobial prescriptions in pediatric wards after a 3-year implementation of an antibiotic stewardship program using prospective audit and feedback at KCMH.

Materials and Methods

Settings

The present study was conducted at the Department of Pediatrics, King Chulalongkorn Memorial Hospital, Bangkok, Thailand. It has 200 pediatric beds and receives an average of 500 admissions per month. Neonatal units include general neonatal wards and an 18-bed neonatal intensive care unit (NICU). Pediatric wards consist of nine general pediatric wards, one oncology ward, two pediatric intensive care units (PICUs), and one surgical ward. An ASP has been practiced at this center since May 2017. The program provides clinical practice guidelines training for pediatric residents, regular antibiotic stewardship ward rounds twice a week by an ASP team made up of pediatric infectious diseases physicians, pharmacists, and microbiologists. The ASP provide prospective audit and feedback among cases that were prescribed broad spectrum antimicrobial agents including carbapenem, colistin, and vancomycin. It reviews appropriateness of antibiotic use and provides suggestions of antibiotic use to attending physicians. There are an average 50 cases per month of ASP consultations provided, equating to approximately a quarter coverage of all prescriptions[18].

Data collection process

A cross-sectional point prevalence survey on antimicrobial prescription was conducted on the 15 of February, May, August, and November 2019, using the standardized study protocol from the Global Antimicrobial Resistance, Prescribing, and Efficacy in Neonates and Children (GARPEC) project[19]. All inpatient children aged under 18 years admitted to the pediatric units at 8:00 a.m. on the day of the survey were included in the present study. Medical records were reviewed on the survey date to determine patient demographics, underlying comorbidities, and prescribed antimicrobials including agent, route, dose, and reason for use, but did not include duration of antimicrobial prescription. The GARPEC PSS data collection forms were used. Antimicrobial agents referred to any antimicrobials including antibiotics, antifungal, and antiviral agents with intravenous, oral, or intramuscular routes of administration, and excluded topical antimicrobial agents. Point prevalence survey data from KCMH in 2016 pre-ASP were used to compare changes over time[7].

Definitions

Prevalence of antimicrobial prescription was defined by the number of patients receiving antimicrobial agents at the time of the survey divided by the total number of surveyed patients. Antimicrobial use at the study hospital during the time when the study was conducted, were grouped into the third-generation cephalosporin group such as ceftriaxone and cefotaxime, antipseudomonal agents such as ceftazidime and piperacillin/tazobactam, carbapenems, and other antimicrobial agents. Classification of antimicrobial prescriptions was grouped into monotherapy or combination therapy, the latter defined as usage of more than one prescribed antimicrobial agent. These groupings were

Table 1. Demographic of neonates and pediatric patients who had antibiotic prescriptions

	Total (n=262); n (%)	Neonatal; n (%)		Pediatric; n (%)			
		General (n=29)	ICU (n=21)	General (n=127)	ICU (n=40)	Oncology (n=27)	Surgical (n=18)
Age (months); median (range)	19 (1 to 73)	4 days (3 to 6)	10 days (4 to 25)	24 (11 to 85)	6 (1 to 55)	49 (19 to 122)	43 (24 to 97)
Sex: male	136 (51.9)	15 (51.7)	14 (66.7)	61 (48.0)	17 (42.5)	18 (66.7)	11 (61.1)
Birth weight (g); median (range)	2,760 (1,970 to 3,105)	2,885 (2,565 to 3,330)	1,176 (842 to 2,091)	Not applicable			
Ventilator support	61 (23.3)	1 (3.5)	16 (76.2)	14 (11.0)	29 (72.5)	1 (3.7)	0 (0.0)
Underlying diseases	217 (83.1)	8 (27.6)	21 (100)	112 (88.9)	37 (92.5)	26 (96.3)	13 (72.2)
Cardiovascular	46 (17.6)	1 (3.5)	4 (19.1)	18 (14.2)	23 (57.5)	0 (0.0)	0 (0.0)
Malignancy	36 (13.7)	0 (0.0)	0 (0.0)	16 (12.6)	2 (5.0)	18 (66.7)	0 (0.0)
Neuromuscular	29 (11.1)	1 (3.5)	1 (4.8)	15 (11.8)	5 (12.5)	4 (14.8)	3 (16.7)
Respiratory	27 (10.3)	1 (3.5)	3 (14.3)	13 (10.2)	9 (22.5)	1 (3.7)	0 (0.0)
Hematologic	22 (8.4)	0 (0.0)	0 (0.0)	13 (10.2)	0 (0.0)	9 (33.3)	0 (0.0)
Gastrointestinal	22 (8.4)	0 (0.0)	2 (9.5)	15 (11.8)	3 (7.5)	1 (3.7)	1 (5.6)
Other	41 (15.7)	1 (3.5)	0 (0.0)	32 (25.2)	3 (7.5)	2 (7.4)	3 (16.7)

ICU=intensive care unit

performed to compare data to a PPS in 2016 in which the same method of PPS was performed but used a different timeframe, which was combined six months in 2016. A PPS in 2016 was conducted and received approval from the Institutional Review Board, Faculty of Medicine, Chulalongkorn University (IRB no. 466/59) and data collection in 2019 were collected as part of the quality improvement of clinical services in antimicrobial stewardship program.

Data analyses

The authors used percentages and 95% confidence intervals (CIs) to describe prevalence rates of antimicrobial prescriptions. The present study used percentages to describe commonly prescribed antimicrobials and common reasons for use categorized by ward type. To compare antibiotic prescription rates between 2016- and 2019-point prevalence surveys used the chi-square test. Statistical analyses were performed using IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA).

Results

Study population

Six hundred seventy-eight hospitalized children were surveyed in 2019 and were made up of 269 neonates and 409 children. Baseline characteristics of patients who received antimicrobial agents are shown in Table 1. The median (interquartile range, IQR) age of neonates was 7 (3 to 11) days and children 2.6 (0.9 to 8) years. Fifty-one-point-nine percent were male, 23.3% required ventilation, and 83% had underlying medical conditions.

Rate of antimicrobial prescriptions

Neonatal wards: The proportion of children receiving antibiotics overall in the neonatal unit was 18.6% (95% CI 14.1 to 23.8) (Table 2). Antibiotic use could be broken down into 14.6% use in the general neonatal ward, and 29.6% in the NICU. The most used antimicrobial regimen in the general neonatal unit was ampicillin or gentamicin (72.4%). The main reasons for antimicrobial use in general neonatal wards were neonatal sepsis (34.5%) and newborn prophylaxis for maternal risk factors (27.3%). The main reasons for treatment in the neonatal intensive care unit were neonatal sepsis (28.1%) and pneumonia (18.8%).

Pediatric wards: The proportion of children receiving antibiotics in pediatric wards was 51.8% (95% CI 46.9 to 56.8) The highest percentage of patients receiving an antimicrobial agent was in the PICUs (88.9%), followed by the oncology ward (52.9%), general wards (46.5%), and surgical ward (45.0%). The main reasons for antimicrobial prescriptions in pediatric ICU were bacterial lower respiratory tract infection (19.2%) and sepsis or bacteremia (15.4%). On the oncology ward, the main reasons were febrile neutropenia (16.5%) and medical prophylaxis (12.6%).

Patterns of antimicrobial agents

In the general pediatric wards, third generation cephalosporins were the most prescribed antimicrobial agents (22.0%), followed by antipseudomonal antibiotics (21.2%). Respiratory tract infection was the main reason (14.8%) for antimicrobial use. At the oncology ward, meropenem and antipseudomonal

Table 2. Point prevalence of antimicrobial prescription at neonatal and pediatric wards at King Chulalongkorn Memorial Hospital in 2019

Ward type	No. of patients hospitalized*	No. of patients receiving antimicrobial agents; n (%) (95% CI)	Rank 1	Rank 2	Rank 3
Neonatal unit					
General ward	198	29 (14.6) (10 to 20.4)	Ampicillin + gentamicin (72.4%)	Coamoxiclav (13.8%)	Cloxacillin (6.9%)
Intensive care unit	71	21 (29.6) (19.3 to 41.6)	Vancomycin (38.1%)	Ampicillin + gentamicin (23.8%)	Meropenem (23.8%)
Pediatric service					
General pediatric wards	273	127 (46.5) (40.5 to 52.6)	3rd generation cephalosporin (22.0%)	Antipseudomonal agents (21.2%)	Meropenem (14.2%)
Oncology ward	51	27 (52.9) (38.5 to 67.1)	Antipseudomonal agents (25.9%)	Meropenem (25.9%)	Cotrimoxazole (14.8%)
Intensive care unit	45	40 (88.9) (75.9 to 96.3)	Meropenem (45.0%)	Antipseudomonal agents (27.5%)	3rd generation cephalosporin (20.0%)
Surgical ward	40	18 (45.0) (29.3 to 61.5)	3rd generation cephalosporin (38.9%)	Cefazolin (33.3%)	Metronidazole (11.1%) Antipseudomonal (11.1%)

CI=confidence interval

* Total number of hospitalized patients on 15th of February, May, August and November 2019

• 3rd generation cephalosporin includes ceftriaxone and cefotaxime, • Antipseudomonal agents include ceftazidime and piperacillin/tazobactam

Table 3. Compare rate of antimicrobial prescription among pediatric wards between 2016 and 2019 by point prevalence survey

Pediatric wards	Prevalence of antimicrobial prescription; n (%)			Monotherapy; n (%)			Combination therapy; n (%)		
	2016	2019	p-value	2016	2019	p-value	2016	2019	p-value
Neonatal wards	66/312 (21.2)	50/269 (18.6)	0.44	21/66 (31.8)	13/50 (26.0)	0.49	45/66 (68.2)	37/50 (74.0)	0.49
General pediatric wards	149/400 (37.2)	127/273 (46.5)	0.02	112/149 (75.2)	82/127 (64.6)	0.06	37/149 (24.8)	45/127 (35.4)	0.06
Oncology ward	39/83 (47.0)	27/51 (52.9)	0.81	29/39 (74.4)	16/27 (59.3)	0.37	10/39 (26.0)	11/27 (40.7)	0.37
Intensive care unit	67/99 (67.7)	40/45 (88.9)	0.007	52/67 (77.6)	17/40 (42.5)	<0.001	15/67 (22.4)	23/40 (57.5)	<0.001
Surgical ward	24/62 (38.7)	18/40 (45.0)	0.53	15/24 (62.5)	15/18 (83.3)	0.50	9/24 (37.5)	3/18 (16.7)	0.50

* p-value from chi-square test

antibiotics were the most prescribed antimicrobials. Febrile neutropenia was the main reason for antimicrobial use in the oncology ward (16.3%), which was used as empirical treatment. At the PICU, the most prescribed antimicrobial agents were meropenem (45.0%) and antipseudomonal antibiotics (27.5%). Lower respiratory tract infection was the main issue leading to antimicrobial prescription in the PICU (19.2%). At the pediatric surgical ward, the most prescribed antimicrobial agents were third generation cephalosporins (38.9%), and cefazolin (33.3%). The main reason for antimicrobial use was for surgical prophylaxis (57.1%) (Table 2).

Comparison of antimicrobial prescriptions in 2016 and 2019

Compared to KCMH's 2016 PPS data, prevalence of antimicrobial use in 2019 in neonates decreased from 21.2% to 18.6%, p=0.44. On the contrary, the prevalence of overall antimicrobial use among children was higher in 2019 in the general pediatric wards at 46.5% and 37.2% (p=0.02) and PICU at 88.9% and 66.7% (p=0.007) (Table 3). Proportions of combination therapy in PICU increased significantly from 22.4% in 2016 to 57.5% in 2019 (p=0.001).

Discussion

The present study was the second point prevalence survey of antimicrobial prescription patterns in a pediatric unit at a tertiary care hospital after a 3-years implementation of an ASP. As far as the authors know, the present study is the first study to evaluate the effectiveness of ASP using a prospective and feedback strategy in pediatric setting in Thailand. Overall, the authors found that approximately half of hospitalized children received at least one antimicrobial agent. The prevalence of antimicrobial prescription rates increased from 43.3% in 2016 to 52.6% in 2019.

The prevalence of antimicrobial use was stable in the neonatal ward at 21.2% and 18.6% in neonates. This may have been due to the prevalence of the neonatal complications remaining the same. The main reasons for antimicrobial use at the neonatal department were neonatal sepsis and congenital

pneumonia. Ampicillin plus gentamicin was the most prescribed antimicrobial (52%). This finding complies to the International and Thai guidelines for neonatal sepsis[20]. However, given the need to cover for hospital-acquired multidrug resistance NICU, there was substantial use of broad-spectrum antimicrobials seen, including meropenem (23.8%) and vancomycin (38.1%).

The trends of prevalence of antimicrobial use have increased in the general pediatric wards and PICU. Compared the KCMH's 2016 PPS, statistically significant increased usage in general pediatric wards at 46.5% versus 37.2% and pediatric ICUs at 88.9% versus 67.7% were seen. Increased use of antibiotic seen between 2016 and 2019 PPS could be from bias comparison among different patient characteristics or may have been due to the strategy of ASP interventions, as perspective audit and feedback, which allowed clinicians to prescribe antimicrobials without any suggestions from specialists before the ASP team came to audit and feedback. The preauthorization of some broad-spectrum antimicrobials may have enabled more reduction in rates of usage. A study on the impact of a prospective audit and feedback antimicrobial stewardship program, found favorable outcomes with up to 11% reductions in the U.S.[21]. There has also been a study in the US showing that antimicrobial consumption rates would increase if ASPs changed their strategy from preauthorization to prospective audit and feedback[22].

In the general pediatric wards, as this was at a tertiary care center, 88.9% of patients had underlying diseases. Due to the frequency of treatment of lower respiratory infection at the present study center, third generation cephalosporin use was more common than ampicillin or beta-lactam plus beta-lactamase inhibitor use[23]. On oncology wards, the main reason for antimicrobial use was empirical treatment for febrile neutropenia, the rationale for antipseudomonal agents including piperacillin/tazobactam, ceftazidime, or meropenem to cover multi drug resistance *P. aeruginosa* and *Enterobacterales*. Increased rates of drug resistance will push the use of progressively more broader spectrum antibiotics such as meropenem as a first-line empirical treatment. This situation emphasizes the urgent need to expand ASP programs to optimize appropriate use of antimicrobial agents, aiming to discontinue inappropriate use, and escalation of antibiotics in cases of potential multidrug resistance and serious life-threatening conditions. In the PICU, the most common reason for antimicrobial use was lower respiratory tract infection. Given the high severity of disease seen in intensive care settings, clinicians are more likely to use antimicrobial agents that are most effective and broad-spectrum to manage life-threatening infections. The most prescribed antimicrobial agents were meropenem and antipseudomonal agents. Antimicrobial use in surgical wards was mostly for surgical prophylactic purposes. Type of antimicrobial use corresponded to type and site of surgical procedures, which mostly were third generation cephalosporins, which was recommended for biliary and colonic surgery, and cefazolin.

A study in China by Chang et al, saw a decrease in antimicrobial prescription by 13% after implementation of an ASP program[24], while the present study showed stable prevalence of antimicrobial prescription rates. This result may have been due to the prospective audit and feedback strategy used the ASP in the present study setting that addressed only broad-spectrum antibiotics, which covered only a quarter of hospitalized patients.

A major strength of the present study was that it was the first to compare the prevalence of antimicrobial prescription patterns at different time points in the same tertiary care center in Thailand to evaluate the impact of an ASP intervention. However, the present study also had some limitations. It was done in only one tertiary care medical center, which limited its generalizability to other settings. This could have been expanded given there is a network set up to survey PPS in Thailand. Secondly, the present study is a point prevalence survey that examines a single point of time, so the result can be affected by the variation of antimicrobial usage day-to-day, clinician judgement, and specific seasonal diseases. However, the authors collected data by doing the survey quarterly in one year to reduce the effect of seasonal variation. According to the WHO or CDC, the method of PPS is valid, and the authors used GARPEC tools to increase its comparability with other settings. Lastly, the appropriateness of prescription, duration of antimicrobial therapy, and a correspondence between antimicrobial agents to susceptibility results were not included in the present study, so, further study to define the quality and appropriateness of antimicrobial usage is recommended.

In conclusion, the present study provided information of antimicrobial prescribing patterns in a tertiary care hospital after an ASP intervention as a prospective audit and feedback strategy was implemented. Prevalence of antimicrobial use remained unchanged. Another strategy for ASP such as pre-authorization of broad-spectrum antibiotics

should be considered to decrease the overuse of antimicrobial agents. A follow-up PPS after applying new strategies is an essential part of improvement of antimicrobial prescription in the future.

What is already known on this topic?

PPS of antimicrobial use is a standardized tool to survey antimicrobial use as part of surveillance after an antibiotic stewardship program implementation.

What this study adds?

After a 3-years implementation of ASP intervention using a prospective audit and feedback strategy in a pediatric tertiary-care unit, the prevalence of antimicrobial use remained unchanged. Pre-authorization for broad spectrum antibiotics should be considered and a follow-up PPS should be repeated.

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Conflicts of interest

The authors have no conflicts of interest to disclose.

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