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Original Article

Antibiotic use in children before and after an e-learning intervention

Maulana Rosyady, Mulya Rahma Karyanti, Novie Amelia Chozie

Abstract

Background Antibiotic resistance is a global health threat. E-learning can be used to increase the knowledge of medical staff and the effectiveness of antibiotic use.

Objective To evaluate the impact of e-learning intervention for pediatric doctors and residents on antibiotic use in pediatric patients.

Methods This single-arm intervention study involved all pediatric doctors and residents from the Department of Child Health, Faculty of Medicine at Universitas Indonesia/Dr. Cipto Mangunkusumo Hospital (FMUI-CMH). Staff and residents underwent e-learning intervention on the topic of antimicrobial stewardship (AMS) via the *E-learning Management System Universitas Indonesia* (EMAS UI) website, followed by comparison of their pre- and post-intervention knowledge. The appropriate use of antibiotics pre- and post-intervention at October and December 2022, respectively, by was assessed by Gyssen's flowchart.

Results A total of 135 (54.4%) antibiotic uses in the pre-intervention period and 170 (72.24%) in the post-intervention period were considered appropriate. A significantly greater proportion of subjects received appropriate antibiotic use after the intervention compared to before (95%CI 0.363 to 0.795; P=0.002). Forty-two out of 56 pediatricians and 119 out of 123 pediatric residents participated in the e-learning program. There was a significant improvement in knowledge levels between the pre- and post-intervention periods among pediatricians, with more passing the post-intervention assessment compared to the pre-intervention assessment (1 *vs.* 29, respectively; P=0.001). Similarly, a significant increase was observed among pediatric residents (10 *vs.* 66, respectively; P=0.001).

Conclusion There was a significant increase in appropriate antibiotic use in pediatric patients at CMH after pediatric doctors and residents underwent e-learning interventions. **[Paediatr Indones. 2025;65:XXX; DOI: https://doi.org/10.14238/pi65.5.2025.XXX**].

Keywords: *e-learning; intervention; antibiotic; Gyssens; antimicrobial stewardship*

Antimicrobial resistance is a global health threat. The rapid reproduction of microorganisms, selective pressure from antibiotics, and unculturable organisms challenge antibiotic effectiveness. Bacterial resistance is driven by excessive, prolonged, and broad-spectrum antibiotic use, often without proper justification, as well as defensive medical practices.[1-4] Moreover, the rate of antibiotic development has slowed over the past 20 years. According to the *Food and Drug Administration* (FDA), the approval of new antibiotics declined by 56% from 1983 to 2002.[1]

Dr. Cipto Mangunkusumo Hospital (CMH) Jakarta, reported in 2011 that 48.3-49.2% of antibiotic use in pediatric inpatient wards was inappropriate, and in 2013, only 53% of antibiotic use in the pediatric intensive care unit at CMH was appropriate (Gyssens algorithm category 0).[3] United States studies indicated that around 2 million illnesses and 23,000 deaths occur annually due to resistant bacteria.[1,4] The risk of antibiotic-related adverse effects varies by antibiotic

From the Department of Child Health, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Corresponding author: Maulana Rosyady. Department of Child Health, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo Hospital. Jl. Salemba Raya No. 6, Jakarta Pusat 10430, Indonesia. Email: maulana.rosyady@gmail.com

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class , with an overall incidence of around 20%.[5-9] These side effects range from mild clinical symptoms (e.g., diarrhea) to life-threatening conditions (e.g., anaphylaxis).[5,8,10] Approximately 1 in 1,000 antibiotic prescriptions results in an emergency room visit due to adverse drug effects. Sulfonamides and clindamycin have the highest rate of adverse effects per prescription.[6,7] Antibiotics are also a major risk factor for Clostridium difficile infection, with nearly half a million cases and 15,000 deaths annually.[4,11] Klein et al. found that physicians who are aware of the potential dangers of antibiotic use during clinical decision-making prescribe fewer antibiotics.[8]

Antibiotic resistance lowers the quality of healthcare services and increases healthcare costs, leads to more complex disease complications, prolongs hospital stays, and adds to the financial and emotional burdens on patients' families.[12-15] This antibiotic resistance exacerbates the burden on hospitals and the government.[16] Appropriate antibiotic prescribing, including correct dosage, duration, and timing, is key to optimizing healthcare services. Insufficient knowledge among attending staff reduces effective antibiotic administration.[9,17-19] Strengthening the medical staff's understanding and adherence to guidelines can be achieved through both offline and online education. The use of technology in information dissemination has positively impacted various fields, including medicine.[10,20-23]

Pediatric doctors and residents at CMH need to improve their knowledge of prudent antibiotic use. Our findings are expected to serve as a reference and guideline for further actions in the rational control of antibiotic use.

Methods

This interventional study had a pre- and post-study design. Total sampling methodology was used for data collection. Evaluation of antibiotic use was conducted one month before (October 2022) and one month after (December 2022) the intervention by assessing the appropriateness of antibiotic use using the Gyssens algorithm.3 The study sample included all pediatric patients who received systemic antibiotics prescribed by attending pediatricians from the Department of Child Health, FMUI-CMH, based on electronic and manual medical records across the general ward, pediatric intensive care unit, and perinatology ward during the study period and who met the inclusion criteria. The e-learning was conducted in November 2022 for all pediatric doctors and residents of the Department of Child Health, FMUI-CMH. Inclusion criteria were pediatric patients receiving systemic antibiotics within the age range of 0-18 years. Exclusion criteria were pediatric patients receiving systemic antibiotics from a primary attending physician in another department or patients receiving only oral antibiotics. The study was approved by the Ethics Committee of the Faculty of Medicine, Universitas Indonesia.

The characteristics of all subjects (antibiotic use) were collected both pre- and post-intervention. Antibiotic use was then evaluated using the Gyssens algorithm. Antibiotic use was considered appropriate if it corresponded with Gyssens category 0, and inappropriate if it fell within Gyssens categories I through VI. Additionally, we assessed the knowledge level of pediatric doctors and residents with pre- and post-test evaluations. The e-learning intervention was provided through an online lecture module accessible via the EMAS UI website, covering the topic of antimicrobial stewardship (AMS) during the intervention period.

Data analysis was performed descriptively using the *Statistical Package for the Social Sciences (SPSS) 28 for Windows®*. Bivariate analysis was conducted using the unpaired T-test for pre- and post-intervention findings of numerical variables, or the Mann-Whitney test if the data were not normally distributed. Bivariate analysis of categorical nominal variables was performed using the Chi-square test or Fisher's exact test. Pre-test and post-test results were analyzed using the paired T-test for normally distributed data or the Wilcoxon test for non-normally distributed data.

Results

Data collection was performed in October and December 2022, evaluating antibiotic use before and after the e-learning intervention. Of the total inpatients for each month, 55.87% of pre-intervention patients received antibiotics and 53.52% of post-intervention patients received antibiotics. The number of subjects included in the analysis were 90.45% of pre-intervention and 92.11% of post-intervention patients. Each patient's antibiotic use was assessed for appropriateness using Gyssens criteria (**Figure 1**).

After the e-learning intervention, residents also regularly participated in weekly antibiotic audit activities using the Gyssens algorithm alongside the AMS team. The intervention for 56 pediatric doctors and 123 residents was conducted via the EMAS UI website, incorporating a pre-test before the learning session, a post-test, and an evaluation form upon completion. A recorded version of the e-learning material was made available post-session for participants to review as needed. Further details on the selection process for pediatric doctors and residents can be seen in **Figure 2**.

The study included 143 pediatric patients in the pre-intervention period and 140 in the post-intervention period, with a total of 248 antibiotic courses used pre-intervention and 229 antibiotic courses used post-intervention. There were more female than male pediatric patients in the pre-intervention period (80 *vs.* 63, respectively), while there were more males in the post-intervention period (83 *vs.* 57, respectively). Most subjects were in the age groups of 0-1 year and 2-5 years. Additionally, the majority of patients were hospitalized for seven days or fewer. IV antibiotics were most commonly administered for bloodstream infections, with 81 cases (32.66%) pre-intervention and 75 cases (32.75%) post-intervention. Based on data from surviving subjects, the use of antibiotics in the pre-intervention group was 174 (70.16%) antibiotic courses, and in the post-intervention group was 158 (69.00%) antibiotic courses. The characteristics of pediatric patients and antibiotic use in the study are presented in **Table 1**.

Table 2 shows a significant increase in the percentage of appropriate antibiotic use post-intervention compared to pre-intervention (54.4 *vs.* 74.2%, respectively; P=0.002). The most frequent error in antibiotic use was in category V (52 cases pre-intervention and 32 cases post-intervention), where there was no indication for antibiotic use. Inappropriate use of antibiotics in each Gyssens category also decreased, specifically in categories Gyssens I, IIA, IIB, IIIA, IIIB, IVA, and IVB. No cases were found in Gyssens category VI in either the pre-intervention or post-intervention periods.

Based on the total sampling method used to assess the success of the intervention among pediatric doctors and residents, we expected that 56 pediatric doctors and 123 pediatric residents would complete the pretest, posttest, and evaluation form. However, in practice, 14 pediatric doctors and 4 residents did not complete the assessment due to time constraints, access issues with the website, absence from work, or unknown reasons. A total of 42 pediatric doctors and 119 residents participated in the e-learning session, which included video viewing and independent study by accessing lecture materials in pdf format. The video viewing duration ranged from 20 to 25 minutes of a total 30-32 minutes per video per topic. Participants watched the entire video content as was mandatory before accessing the post-test questions. Post-intervention, the mean scores improved among pediatric doctors [44.05 (SD 14.0) pre-intervention vs. 74.32 (SD 12.1) post-intervention] and residents [44.37 (SD 15.9) pre-intervention vs. 68.1 (SD 11.9) post-intervention]. The pass rates also improved significantly post-intervention as seen in **Table 3**.

In this study, 151 specimens were confirmed to contain microorganisms, including a total of 125 Gram-negative bacteria and 44 Gram-positive bacteria, with 18 specimens containing two different types of bacteria. The three most frequently identified microbes were *Klebsiella pneumoniae* (43), *Pseudomonas aeruginosa* (23), and *Escherichia coli* (19). The total number of antibiotic courses used during the study was 477. The most frequently used antibiotics, in order, were ceftriaxone (18.1%), ceftazidime (10.9%), ampicillin-sulbactam (10.3%), gentamicin (9.6%), cefoperazone-sulbactam and cefotaxime (9.4%), meropenem (6.3%), metronidazole (5.5%), amikacin (4.3%), and piperacillin-tazobactam (3.6%) as seen in **Figure 3**.

Discussion

Most subjects were aged 1 month to 1 year, as well as 2 to 5 years. Similarly, a previous study noted the mean age of hospitalized patients was four years, with the highest admission frequency in the 1 month to 1 year age group.[24,25] More than half of our subjects were hospitalized for 7 days or fewer; however, in some cases, the length of hospitalization exceeded 14 days.

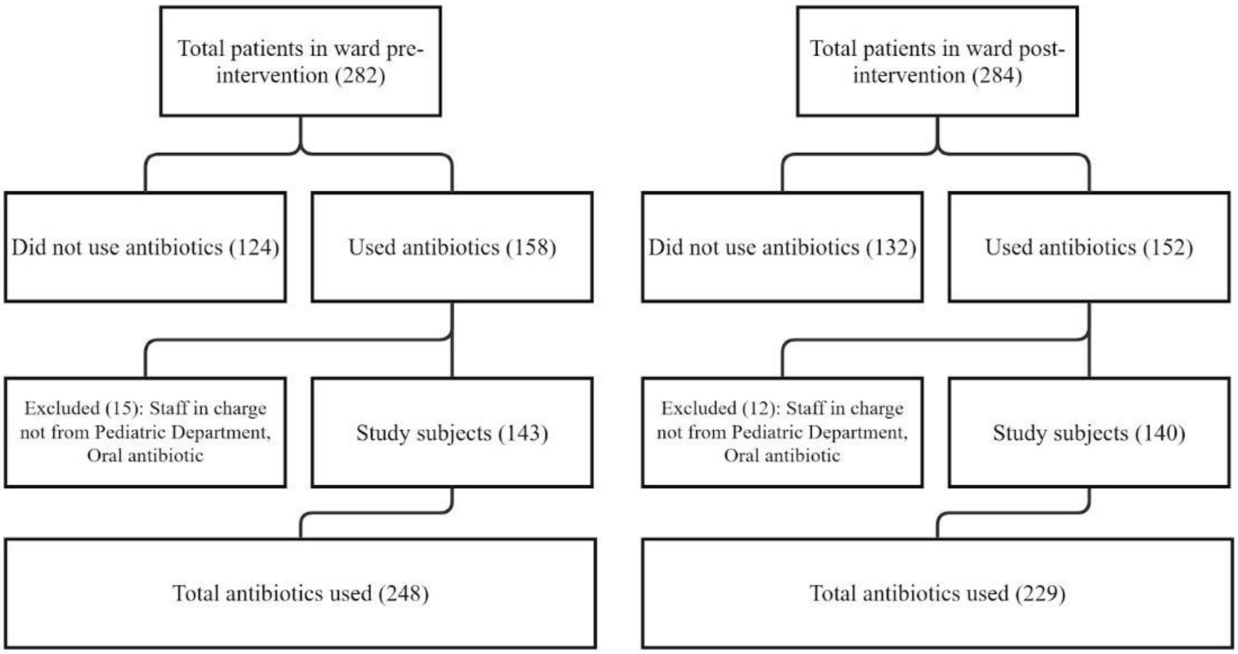

Figure 1. Subject selection process. All pediatric patients in the ward were recorded regardless of antibiotics use

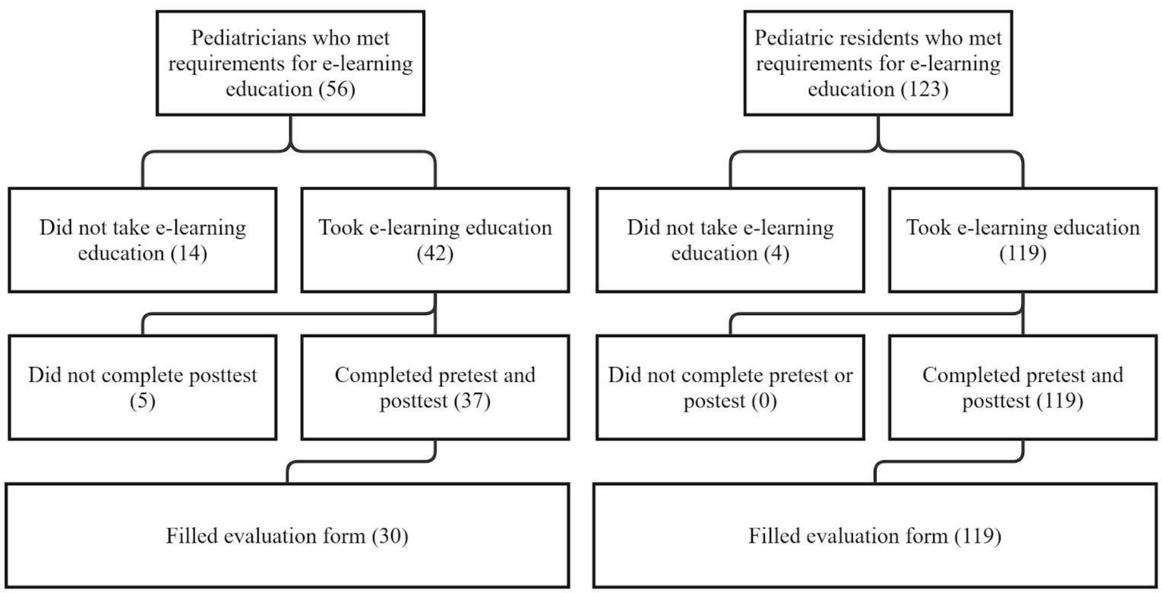

Figure 2. Data collection process from pediatricians and residents

This variation in duration may have been due to other factors that influenced the severity of the patient's condition and length of stay.

According to a study, neonates and pediatric patients with hospital-acquired infections are at a higher risk of extended hospital stays. Additionally, neonates born prematurely or with low birth weight face a higher risk of prolonged hospitalization.[26] Baniasadi et al. suggested that patient's distance from the hospital, admission time (on holidays or regular days), the time (e.g., morning, afternoon, evening, etc) of patient admission, and the physician's qualifications

Table 1. Pediatric patient and antibiotic characteristics

Characteristics	Pre-intervention	Post-intervention
Pediatric patient	(n=143)	(n=140)
Sex, n (%)		
Female	80 (55.94)	83 (59.3)
Male	63 (44.01)	57 (40.7)
Age, n (%)		
<1 month	21 (14.7)	20 (14.3)
0-1 year	40 (28.0)	36 (25.7)
2-5 years	37 (25.9)	38 (27.1)
6-12 years	28 (19.6)	21 (15.0)
13-18 years	17 (11.9)	25 (17.9)
Median body weight (1st-3rd quartile), kg	11.9(6.3-20.5)	12.0 (5.73-22.85)
Length of stay		
<7 days	74 (51.7)	85 (60.7)
> 7 -14 days	42 (29.4)	40 (28.6)
>14 days	27 (18.9)	15 (10.7)
Number of antibiotics used		
Median (1st-3rd quartile)	1 (1-2)	1 (1-2)
1	88 (61.5)	88 (62.9)
2	34 (23.8)	36 (25.7)
3	6 (4.2)	5 (3.6)
>3	15 (10.5)	11(7.7)
Antibiotic characteristics	(n= 248)	(n-229)
Indication for antibiotic use		
Neutropenic fever	10 (4.0)	9 (3.9)
Bloodstream infection	82 (33.1)	79 (34.5)
Skin/soft tissue infection	4 (1.6)	15 (6.6)
Gastrointestinal tract infection	21 (8.5)	24 (10.5)
Urinary tract infection	19 (7.7)	10 (4.4)
Respiratory tract infection	57 (23.0)	49 (21.4)
Central nervous system infection	3 (1.2)	11 (4.8)
No indication	52 (21.0)	32 (14.0)
Clinical outcomes		
Recovered	174 (70.2)	158 (69.0)
Died	74 (29.8)	71 (31.0)

Table 2. Appropriate and inappropriate use of antimicrobial stewardship guidelines

Gyssens category	Pre-intervention	Post-intervention	Changes	OR (95%CI)	P value
Appropriate, n (%)					
0	135 (54.4)	170 (74.2)	↑	0.537 (0.363 to 0.795)	0.002
Inappropriate, n (%)	113 (45.6)	59 (25.8)	↓		
I: administration time not appropriate	2 (0.8)	0 (0)	↓		
IIA: administration dosage not appropriate	23 (9.3)	13 (5.7)	↓		
IIB: administration interval not appropriate	2 (0.8)	0 (0)	↓		
IIC: administration route not appropriate	0 (0)	0 (0)			
IIIA: administration duration too short	4 (1.6)	0 (0)	↓		
IIIB: administration duration too long	9 (3.6)	7 (3.1)	↓		
IVA: more effective alternative is available	20 (8.1)	7 (3.1)	↓		
IVB: less toxic alternative is available	1 (0.4)	0 (0)	↓		
IVC: more cost-effective alternative is available	0 (0)	0 (0)			
IVD: narrower spectrum is available	0 (0)	0 (0)			
V: not indicated	52 (21.0)	32 (14.0)	↓		
VI: insufficient data	0 (0)	0 (0)			

Table 3. Analysis of pre-test and post-test results in pediatricians and residents who underwent e-learning

Categories	Pre-test		Post-test		P value
	Pass	Fail	Pass	Fail	
Pediatricians, n (%)	1 (2.5)	41 (97.5)	29 (80)	8 (20)	<0.001
Residents, n (%)	10 (8.48)	109 (91.53)	66 (55.93)	53 (44.92)	<0.001
Junior	1 (7.14)	13 (92.86)	9 (64.29)	5 (35.71)	0.021
Intermediate	5 (9.43)	49 (90.57)	25 (46.30)	29 (53.70)	<0.001
Senior	4 (7.84)	47 (92.16)	32 (62.74)	19 (37.26)	<0.001

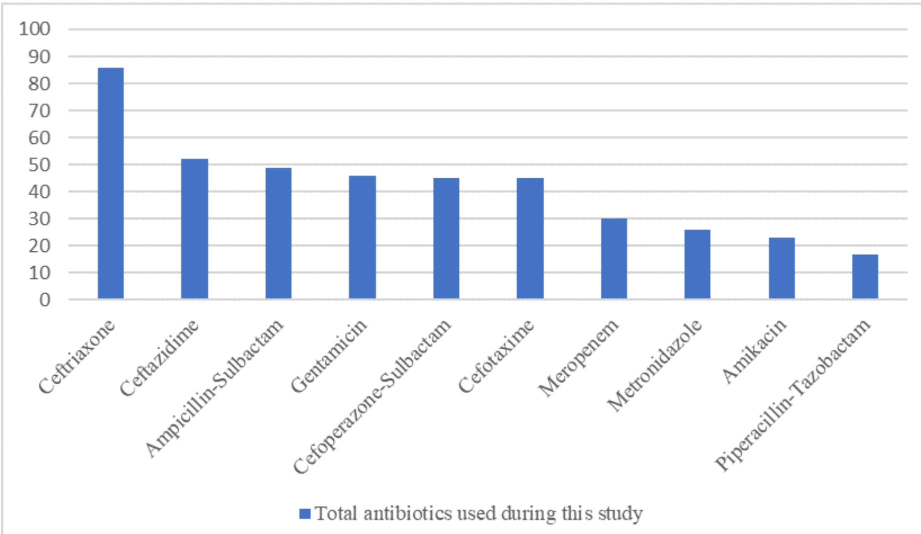

Figure 3. Most frequently used antibiotics during this study

(specialist or subspecialist) may also impact length of hospitalization.[27]

It is important to note that the use of various antibiotics has been aligned with WHO guidelines for prudent antibiotic use. These guidelines prioritize antibiotics with low resistance risk, such as amoxicillin and ampicillin; caution is advised when prescribing antibiotics like cefixime, ceftriaxone, cefotaxime, and ceftazidime due to their high resistance potential. Furthermore, the use of fosfomycin, polymyxin B, and other antibiotics is restricted to multidrug-resistant microbes and considered a last-resort treatment. These measures are critical in preventing drug resistance, a key objective of the *Antibiotic Stewardship Program* (ASP).[28]

A significant increase in appropriate antibiotic use (Gyssens 0) was observed among post-intervention patients (from 54.4% appropriate use pre-intervention to 74.2% appropriate use post-intervention), accompanied by a decrease in antibiotic prescription errors in Gyssens categories I, IIA, IIB, IIIA, IVA, and V for appropriate antibiotic use pre-intervention compared to post-intervention (OR 0.537; 95%CI 0.363 to 0.795; P=0.002). In comparison to a previous study on urinary tract infections (UTI) in patients treated at CMH, the pre-intervention period generally showed a higher percentage of appropriate antibiotic use. This suggests a potential improvement in appropriate antibiotic use without intervention over the past four years, although this hypothesis cannot be conclusively confirmed, as no specific evaluation was performed to assess the rationality of antibiotics used for UTI in this study.[29]

Another study also demonstrated an increase in appropriate antibiotic use, although the improvement was only 9%. This further reinforces the notion that there is a correlation between the e-learning intervention and improved antibiotic prescribing accuracy.[30] The participation of pediatricians and the higher attendance rate for e-learning in our study, may be contributing factors to the more substantial improvement in antibiotic appropriateness.

Gyssens category 5, indicating the absence of a valid indication for antibiotic use, dominated the instances of inappropriate antibiotic prescribing. Antibiotic use in this category was 21% in the pre-intervention group and 14.0% in the post-intervention group. These findings aligned with a previous study which found that 27.4% of antibiotic use in children at M. Yunus Hospital, Bengkulu in 2014 was inappropriate and fell under Gyssens category 5. Most of the Gyssens category 5 antibioticswere administered in post-operative conditions without a clinical assessment (pre-, intra-, or post-surgery) supporting the need for antibiotics, despite the surgeries being major and requiring general sedation and mechanical ventilation post-operatively. The rationale for prescribing antibiotics in such cases included concerns about the risk of post-operative infections, the use of numerous medical devices on patients, and reducing hospital stay duration.[31]

An improvement in post-test scores compared to pre-test scores was observed ($P<0.001$) for both pediatric doctors and residents. According to the WHO, various methods can be applied, including problem-based learning, case-based learning, and team-based learning, all of which can be implemented in workshops, discussion sessions, or simulation sessions. According to the *Australian Commission on Safety and Quality in Health Care*'s ASP guidelines, ASP education for clinicians should be conducted at least once a year or more frequently, depending on the changes in clinical rotations. The main goal of the ASP program is to reduce inappropriate prescribing. Through repeated education, clinicians are expected to continue improving their rational and appropriate antibiotic use for patients.[32,33]

Gram-negative bacteria were the most commonly cultured microbes, accounting for 82.8% of the microbial findings. The most commonly grown microorganisms were *Klebsiella pneumoniae* (42 isolates), *Pseudomonas aeruginosa* (23 isolates), and *Escherichia coli* (19 isolates), consistent with the results from Karyanti et al. four years earlier at CMH.[34] Gram-positive bacteria found were *Staphylococcus epidermidis* (19 isolates), methicillin-resistant *Staphylococcus epidermidis* (MRSE) (8 isolates), and methicillin-resistant *Staphylococcus aureus* (MRSA) (4 isolates). There was a noticeable pattern of alignment between the dominant microbial findings and indications for antibiotics, with bloodstream infections and respiratory tract infections being the two leading indications for antibiotic use. The dominance of gram-negative bacteria aligns with several previous studies in which *Pseudomonas aeruginosa* and *Escherichia coli* were most prevalent.[24,30,34]

The most commonly used antibiotic was ceftriaxone (18.1%), followed by ceftazidime (10.9%) and ampicillin-sulbactam (10.3%) from total 477 antibiotics used in this study. The majority of these antibiotics were used for seven days or less. In other studies conducted at CMH, the most commonly used antibiotics were cefotaxime, ceftazidime, and ceftriaxone, with a duration of use under seven days in 47.2% of cases in 2018.[34-35] These observations suggest a shift in the pattern and duration of antibiotic use at RSCM over the past four years. This shift may be influenced by varying clinical conditions of patients during this period.

This study is the first to use e-learning interventions to evaluate the appropriateness of antibiotic use in pediatric patients at the Department of Child Health, CMH. The e-learning sessions were flexible, allowing participants to replay missed sessions and adjust to their schedules. Pre- and post-test assessments showed the intervention improved the knowledge of pediatric doctors and residents. The evaluation involved infectious disease consultants and the AMS Team, including pharmacology, microbiology, and pharmacy experts. However, some participants did not complete the sessions due to absence from work, website access issues, or personal reasons. Additionally, the study lacked data on infection sources (community- or hospital-acquired) and other factors that could worsen infections, which could have been explored through multivariate analysis.

In conclusion, appropriate antibiotic use significantly improved after an e-learning education intervention among pediatric doctors and residents. Inappropriate antibiotic administration in the pediatric care units at CMH is generally caused by errors in dosage, the availability of more effective alternative antibiotics, and the lack of indications for antibiotic use based on the findings of this study. The use of antibiotics in accordance with the AMS

Guidelines has an impact on clinical outcomes, both in the pre- and post-intervention periods.

Conflict of interest

None declared.

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