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146

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RESEARCH ARTICLE

Antibiotic Surveillance in the Pediatric Intensive Care Unit (PICU) at Sanglah Hospital Denpasar in the Year of 2015-2017

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Abstract:

Background:

Antibiotic surveillance in hospital settings is mandatory for optimal antibiotic therapy for the patient. Only a small number of studies have focused on antibiotic surveillance in hospitalized newborns, infants, and children.

Objectives:

The goal was to evaluate antibiotic use in our Pediatric Intensive Care Unit (PICU) and evaluate it for a possible association with the length of PICU stay.

Methods:

A retrospective, observational, cohort study was conducted from January 2015 to April 2017, involving subjects who were hospitalized in the PICU at Sanglah Hospital. The inclusion criteria were children aged between 1-month-12-years old, who had a blood culture and antibiotic sensitivity test result in their medical record. The exclusion criteria were incomplete medical records, blood cultures showing 2 types of bacteria at the same time (gram-positive and negative), or contaminated blood results. Factors associated with mortality were analyzed using a Chi-square test, with $p < 0.05$ considered to be statistically significant and the Risk Ratio (RR) of the associated factors was determined by 95% CI.

Results:

Multivariate analysis showed that the significant predictors of PICU length of stay were the appropriate continuation of antibiotics (RR 1.19; 95% CI 1.043 to 1.373; P = 0.047). There were also significant results for antibiotic compatibility and length of stay (RR 3.6; 95% CI 0.869 to 15.428; P = 0.049).

Conclusion:

Appropriate continuation of antibiotics and the compatibility of continuation antibiotics were significant predictors of length of PICU stay based on multivariate analysis.

Keywords: Antibiotic, Sensitivity, Resistance, Surveillance, Children, PICU.

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1. INTRODUCTION

Antibiotics are commonly used in the hospital settings, especially in the pediatric intensive care unit. Some reasons for the administration of antibiotics are the risk of infection because of critical conditions, chronic comorbid conditions, surgical procedures, and exposure to invasive procedures and tools as a port of entry for various kinds of microorganisms [1, 2]. Moreover, patients with critical conditions, especially children, may have impaired immune systems, which facilitate the occurrence and spread of infection [3]. Without the intervention of appropriate antibiotics [4], the condition of the patients may worsen to the point of organ damage or even

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death.

Grohskopf *et al.* [5] stated that as many as 71% of PICU patients received one or more types of antibiotics. Similar results were reported by Briassoulis *et al.* [6] who did a cohort study on the use of antibiotics. They found that as many as 67.2% of PICU patients received antibiotics on the first day of treatment and 80.5% received at least one antibiotic during PICU treatment. In addition, Ding *et al.* [7] reported that in three PICUs in China, the use of antibiotics reached 95%, with 30% of them using a combination of more than one antibiotic.

The use of antibiotics in PICU patients is often empirically based upon vital signs and laboratory results. Toltizs *et al.* [8] evaluated the use of antibiotics in children admitted to the PICU with fever (axillary temperature > 38.3°C). They found that only 3.3% did not receive parenteral antibiotics. Broad-spectrum antibiotics are often used as empirical therapy, with third-generation cephalosporins, vancomycin, and second generation cephalosporins most often used, according to Grohskopf *et al.* [5]. Ding *et al.* [7] found that they often used the second and third generation cephalosporins as empirical therapy. However, Tjekyan [9] reported that the three broad-spectrum antibiotics most often used were ampicillin (53.4%), ceftriaxone (31.1%), and meropenem (7.3%). Additionally, in Indonesia, the most commonly used antibiotics in the Cipto Mangunkusumo Hospital (RSCM) PICU were cefotaxime (30.1%), amikacin (14.46%), and piperacillin-tazobactam (12.10%) [10]. Unfortunately, the use of antibiotics is still largely inappropriate. Hadi *et al.* [11] conducted a study in two teaching hospitals and reported that 84% of patients received antibiotic therapy, of whom 60% received treatment that was unsuitable or without indication.

In addition, studies have mentioned the negative effects of antibiotic resistance on patient clinical outcomes. Hence, we conducted a retrospective study in one center to determine the appropriateness of antibiotic use, microbe patterning, and possible associations with patient clinical outcomes. The suitability of antibiotic use was based on the 12-step prevention of antimicrobial resistance by the Centers for Disease Control (CDC) [12]. The primary objective of this study was to determine the relationship between appropriate antibiotic use and the mortality rate of children treated in the PICU. The secondary objective of this study was to identify the degree of appropriate antibiotic use in the PICU, microbe patterns, and antibiotic resistance. We also aimed to assess the relationships between microbe pattern and patient mortality, inadequate empirical antibiotic administration and patient mortality, and antibiotic use patterns and microbe patterns. A deeper understanding of antibiotic resistance data will contribute to rational selection of antibiotics for PICU patients.

2. MATERIALS AND METHODS

This retrospective cohort was done in the PICU, Sanglah General Hospital, Denpasar from 2015 to 2017, using patients' medical records. Informed consent was obtained from subjects' parents or guardians.

All children admitted to the PICU of Sanglah Hospital during the study period were screened for study inclusion. Inclusion criteria were children aged 28 days-12 years when treated at the PICU, Sanglah Hospital, who had undergone blood culture examination (growth of bacteria and antibiotic sensitivity test). Patients with congenital abnormalities, incomplete medical record data (missing blood culture or sensitivity test results), or those who underwent non-standard blood culture screening procedures were excluded from the study.

Age was defined as the chronological age at the time of treatment in the PICU, expressed in months. The subjects were aged 28 days to 12 years. The 12-year age limit was used because Sanglah Hospital policy stipulates that patients' ≤12 years of age are to be treated in the PICU (except for neonates, who should be treated in the neonatal intensive care unit).

Antibiotic sensitivity tests were determined using the Kirby-Bauer disc diffusion technique, with interpretation by the National Committee for Clinical Laboratory Standards (NCCLS) is called as the Clinical and Laboratory Standards Institute (CLSI) [4]. The results of the bacterial sensitivity tests were based on the germicidal value of various types of antibiotics, and the assessment was performed by a competent expert [4, 13].

Use of antibiotics was defined as the administration of one or more types of antibiotics during PICU treatment. The use of antibiotics was classified as 1) empirical (antibiotic therapy for signs of infection, but no microbe-sensitivity test results yet), 2) definitive (antibiotic therapy for pathogenic pathogens), or 3) prophylactic (antibiotic therapy for patients without signs of infection, but have immune-compromised conditions, anatomical defects, indwelling device, or planned surgery [14, 15].

The appropriateness of antibiotic use was an assessment of the precision of antibiotics based on a 12-step recommendation by the CDC [12]. The assessment focused on two points, that were the diagnosis and efficient handling of infection and the wise use of an antibiotic. Use of antibiotic therapy was considered appropriate if it did not deviate from institutional therapy guidelines and the CDC step assessments. The antibiotic conformity was evaluated twice, i.e., at initiation and 2 days after initiation. Incompatibilities in antibiotic therapy were expressed when one of the following criteria was met: 1) there was no strong justification for initiation of antibiotics; 2) empirical therapy was continued for more than 3 days, unless there was a documented, strong reason for continuing empirical antibiotic therapy; 3) Empirical therapy was continued or antibiotics were not replaced, despite conflicting microbe-sensitivity test results; 4) the choice of definitive therapy was inconsistent with the sensitivity test, or 5) prophylactic therapy was resumed 24 hours after surgery [16].

Specifically, empirical antibiotics were adequate if the antibiotics in isolated cultures were sensitive *in vitro*, and empirically administered within 24 hours after the culture was taken. The microbe pattern was the proportion and number of microbes found based on the blood culture results for each patient. We recorded microbial type (gram-negative or positive) and sensitivity to the antibiotic.

Patients treated during a predetermined time range were included in the study. All patients' medical records were screened. The research sample data included general character-

istics: name, address, age, biological sex, nutritional status, duration of PICU hospitalization, a primary underlying disease in the PICU, infection marker, comorbidity (malignancy/HIV), and patient outcome. In addition, blood culture results in the antibiotic susceptibility test results were also obtained from the medical records.

From patients' medical record, antibiotic usage and antibiotic appropriateness were evaluated and recorded, in accordance with the above-described criteria. The determination of the suitability of antibiotics was evaluated progressively from the development sheets from the day the patient was first admitted to the PICU. As a guide to determine the appropriate use of antibiotics, we used a checklist adapted from Stocker *et al.* [15] with necessary modifications. The checklist asks for clinical indications and possible infection at the start of antibiotic therapy. Then, this checklist was used to evaluate therapy at 48 hours and 5 days after antibiotic discontinuation, when the blood culture results were available.

The minimum required sample size was calculated by the large sample formula to test the difference of two proportions [17]. By setting the rate of type I error at 5%, a type II error at 20%, and the proportion of appropriate antibiotic therapy (not considered a risk factor) according to the literature to 18%, 24 and relative risks considered significant at 2, the required sample size was estimated to be 95 patients.

Za = error rate of type I, set at 5%, equal to 1.64

Zb = value of type II error is set at 20%, equal to 0.84

P2 = proportion of patients receiving appropriate antibiotic therapy, set at 0.18 [15].

RR = relative risk considered significant, set at 2.

p1 = p2 x RR [17], is set at 0:36

Subjects' data were collected and processed by 2007 Microsoft Excel software, then analyzed with *SPSS 16.0* software. Results are presented as the mean and Standard Deviation (SD) for continuous and median (continuous interquartile) for continuous non-distributed continuous data. Absolute numbers (percentages) indicated categorical or nominal data.

A *Chi-square* test was used for bivariate analysis to assess for associations between the suitability of the antibiotics and patient mortality, microbial patterns and mortality, as well as the use of antibiotics and microbial patterns. The two-tailed Fisher Exact test was used when the expected frequency was less than 5. A p value of < 0.05 was considered to be statistically significant. The study was approved by the Ethics Committee of Udayana University Medical School, Sanglah Hospital, Denpasar.

3. RESULTS

From the 692 subjects included in the PICU register at Sanglah Hospital Denpasar, 95 (13.7%) patients had complete medical records and were included in the study. We separated the subjects' based on the mean length of stay by local insurance in the PICU. As shown in Table **1** with the 95 subjects, 14 had less than 4 days treatment in the PICU and male subjects were dominant and represented 11 of the 14 (78.6%). It was similar for the subjects whose treatment was for more than 4 days, and the males were also dominant with 49 (60.5%). The largest categories of subjects were in the normal body weight category (35.7% and 48.1%). Bacterial growth was seen in a total of 60 patients and were separated into 9 patients with a length of stay less than 4 days and 51 patients with more than 4 days (Table **1**).

The appropriate use of antibiotics during initiation and continuation is displayed in Table **2**. We found that 80% of subjects used appropriate antibiotic during initiation and 70.5% of subjects used antibiotics appropriately during continuation (Table **2**). In this study, we also found that 40% of subjects died and we found an association between mortality and the appropriate use of antibiotic during initiation (p = 0.021; RR = 0.542; CI = 0.341-0.9861) (Table **3**). Meanwhile, we did not find an association between mortality and the appropriate use of antibiotic during the continuation (p = 0.408; RR = 0.855; CI = 0.578-1.264) (Table **4**).

In this study, we also looked for an association between mortality and the microbial gram status (Table **5**) and there was no significant association (p = 0.090; RR = 0.584; CI = 0.311-1.110). The length of stay variable was found to be associated with the compatibility of antibiotic use, although the association was not very strong in the population (p = 0.049; RR = 3.661; CI = 0.869-15.428). Not only was compatibility associated with length of stay, but also the appropriate continuation variable (p = 0.047; RR = 1.196; CI = 1.043-1.373). However, no other variable was associated with the length of stay, including mortality (p = 0.813; RR = 1.125; CI = 0.424-2.985), appropriate use of antibiotic during initiation (p = 0.563; RR = 1.500; CI = 0.366-6.144), and microbial gram status (p = 0.971; RR = 1.023; CI = 0.304-3.438) (Table **6**).

Table 1. Characteristic of subjects.

No.	Characteristics	Length of Stay (n)	
	–	< 4 days	≥4 days
1	Sex, n (%)		
	Male	11 (78.6%)	49 (60.5%)
	Female	3 (21.4%)	32 (39.5%)
2	Mean age (SD) Months	28.3 (31.6)	27.0 (36.3)
3	Mean weight (SD), kg	13.9 (14.0)	11.9 (11.1)

(Table 1) contd.....

No.	Characteristics	Length of Stay (n)	
	–	< 4 days	≥4 days
4	Mean height (SD), cm	76.3 (28.7)	77.01 (27.9)
5	Nutritional status, n (%)		
	Over Weight	3 (21.4%)	12 (14.8%)
	Normal Weight	5 (35.7%)	39 (48.1%)
	Underweight	4 (28.6%)	24 (29.6%)
	Malnourished	2 (14.3%)	6 (7.4%)
6	Primary Disease, n (%)		
	Respiration	8 (57.1%)	45 (55.6%)
	Cardiovascular	0 (0%)	3 (3.7%)
	Infection	1 (7.1%)	12 (14.8%)
	Hepatic/Gastrointestinal	2 (14.3%)	8 (9.9%)
	Neurology	0 (0%)	2 (2.5%)
	Hematology/Oncology	0 (0%)	3 (3.7%)
	Immunology	0 (0%)	2 (2.5%)
	Post Surgery	1 (7.1%)	4 (4.9%)
	Metabolic	2 (14.3%)	2 (2.5%)
	Others	0 (0%)	0 (0%)
7	Mean WBC (SD), 10^3 µ/L	10.9 (7.0)	17.4 (12.7)
8	Mean Procalcitonin (SD), ng/ml	10.4 (26.9)	33.8 (55.7)
9	Mean CRP (SD), mg/l	54.0(106.2)	64.9 (91.6)
10	Comorbidity, n (%)		
	Malignancy	1 (7.1%)	6 (7.4%)
	HIV	0 (0%)	5 (6.2%)
	None	13 (92.9%)	70 (86.4%)
12	Mean duration of definitive antibiotic (SD), day	4.1(4.7)	4.1(4.7)
13	Mean length of stay in PICU (SD), day	2.1(0.7)	10.4 (5.5)
14	Sum of patient with empirical antibiotic, n (%)	15 (83.3%)	69 (89.6%)
15	Sum of patient with definitive antibiotic, n (%)	5 (27.8%)	22 (28.6%)
16	Mortality, n (%)	6 (42.9%)	32 (39.5%)
17	The appropriate antibiotic during initiation, n (%)	12 (85.7%)	64 (79.0%)
18	The appropriate antibiotic during continuation, n (%)	13 (92.9%)	54 (66.7%)
19	Culture Growth, n (%)		
	No Growth	5 (35.7%)	30 (37.0%)
	Bacteria	9 (64.3%)	51 (63.0%)
	Fungi	0 (0%)	0 (0%)

Table 2. Analysis of the level of appropriate of antibiotic usage.

Variable	N (%)
Appropriate use of antibiotic during initiation	
• Appropriate	76 (80.0%)
• Not Appropriate	19 (20.0%)
Appropriate use of antibiotic during continuation	
• Appropriate	67 (70.5%)
• Not Appropriate	28 (29.5%)

Table 3. Association between appropriate use of antibiotic during initiation and mortality.

Variable	Mortality		RR	95% CI	p value
	Yes	No			
Appropriate use of antibiotic	–	–	–	–	–
• Appropriate	26 (34.2%)	50 (65.8%)	0.542	0.341-0.861	0.021
• Not Appropriate	12 (63.1%)	7 (36.9%)	–	–	–

Table 4. Association between appropriate use of antibiotic during continuation and mortality.

Variable	Mortality		RR	95% CI	P value
	Yes	No			
Appropriate use of antibiotic	–	–	–	–	–
• Appropriate	25 (37.3%)	42 (62.7%)	0.855	0.578-1.264	0.408
• Not Appropriate	13 (46.4%)	15 (53.6%)	–	–	–

Table 5. Analysis of microbial pattern and mortality.

Variable	Mortality		RR	95% CI	P value
	Yes	No			
Gram Status	–	–	–	–	–
• Positive Gram	10 (30.3%)	23 (69.7%)	0.584	0.311-1.110	0.090
• Negative Gram	14 (51.9%)	13 (48.1%)	–	–	–

Table 6. Association between the length of stay and mortality, appropriate use during initiation, appropriate use during continuation, the pattern of bacteria, and compatibility of continuation antibiotics.

Variable	Length of Stay		RR	95% CI	P value
	< 4 days	≥4 days			
Mortality	–	–	–	–	–
Yes	6 (15.8%)	32 (84.2%)	1.125	0.424-2.985	0.813
No	8 (14.0%)	49 (86.0%)	–	–	–
Appropriate use during initiation	–	–	–	–	–
Appropriate	12 (15.8%)	64 (84.2%)	1.500	0.366-6.144	0.563
Not Appropriate	2 (10.5%)	17 (89.5%)	–	–	–
Appropriate use during continuation	–	–	–	–	–
Appropriate	13 (19.4%)	54 (80.6%)	1.196	1.043-1.373	0.047
Not Appropriate	1 (3.6%)	27 (96.4%)	–	–	–
Pattern of bacteria	–	–	–	–	–
Positive gram	5 (15.2%)	28 (84.8%)	1.023	0.304-3.438	0.971
Negative gram	4 (14.8%)	23 (85.2%)	–	–	–
Compatibility of Continuation antibiotic	–	–	–	–	–
Compatibility	12 (20.3%)	47 (79.7%)	3.661	0.869-15.428	0.049
Not Compatibility	2 (5.6%)	34 (94.4%)	–	–	–

Table 7. Percentage of gram sensitivity to several antibiotics (%).

Bacteria	Meropenem	Piperacilin Tanobactam	Tetracyclin	Tigecyclin	Trimetropin Sulfa	Vancomycin
S. epidermidis	100	–	100	100	–	100
S. hominis	0	0	50	100	33.33	100
S. cohnii	0	100	100	–	–	100
S. haemolyticus	0	–	100	100	100	100

(Table 7) contd.....

Bacteria	Meropenem	Piperacilin Tanobactam	Tetracyclin	Tigecyclin	Trimetropin Sulfa	Vancomycin
Coagulase negative staphylococcus	0	0	100	100	–	100
S. aureus	–	100	100	–	100	–
P. aerogenosa	100	–	–	–	–	–
Aachromobacter xylosidans	100	100	100	100	100	–
Salmonela SSP	100	100	–	–	–	–
E. cloacae	100	66.67	–	–	100	–
Aerococcus viridans	–	–	100	–	–	100
Salmonela typi	100	100	–	100	100	–
K. pneumoniae	100	–	–	100	100	–
Bacteria	**Ceftazidime**	**Ciprofloxacin**	**Cotrimoxazole**	**Dicloxacili**	**Levofloxacin**	**Linezolid**
S. epidermidis	–	–	–	50	–	100
S. hominis	0	60	50	33.33	100	100
S. cohnii	0	50	50	100	100	100
S. haemolyticus	0	0	50	33.33	0	100
Coagulase negative staphylococcus	0	100	–	0	100	100
S. aureus	–	100	–	100	100	–
P. aerogenosa	100	100	–	–	–	–
Aachromobacter xylosidans	100	0	100	–	–	–
Salmonela SSP	100	100	100	–	–	–
E. cloacae	0	100	50	–	100	–
Aerococcus viridans	–	0	–	–	0	100
Salmonela typi	100	100	–	–	100	–
K. pneumoniae	0	50	0	–	50	–
Bacteria	**Cefotaxime**	**Ceftriaxone**	**Ampicilin**	**Aztreonam**	**Cloxacilin**	**Gentamicin**
S. epidermidis	–	–	–	–	50	33.33
S. hominis	0	0	100	–	33.33	100
S. cohnii	–	–	0	100	100	66.66
S. haemolyticus	–	–	–	–	25	25
Coagulase negative staphylococcus	0	0	–	–	0	100
S. aureus	–	100	–	–	100	100
P. aerogenosa	–	–	0	–	–	100
Aachromobacter xylosidans	–	–	0	0	–	0
Salmonela SSP	–	100	100	100	–	0
E. cloacae	0	0	0	0	–	66.66
Aerococcus viridans	–	–	–	–	–	50
Salmonela typi	–	100	100	100	–	0
K. pneumoniae	0	50	0	0	–	50
Bacteria	**Amikacin**	**Ampicilin Sulbactam**	**Cefalotine**	**Cefepime**	**Cefoperazone**	**Cefoperazone Sulbactam**
Stapylococus epidermidis (MRSE)	–	–	100	100	–	–
Staphylococus hominis	–	25	50	0	0	–
Staphylococcus cohnii	0	0	100	100	–	–
Staphilococcus haemolyticus	–	–	0	–	–	–
Coagulase negative staphylococcus	–	0	–	0	–	–
Staphylococcus aureus	–	100	100	–	–	–
Pseudomonas aerogenosa	100	0	–	100	100	100
Aachromobacter xylosidans	0	100	–	100	–	–
Salmonela SSP	0	100	–	100	–	–
Enterobacter cloacae	100	0	–	66.66	–	–
Aerococcus viridans	–	–	–	–	–	–
Salmonela typi	0	100	–	100	100	–
Klebsiela pneumoniae	100	100	–	50	100	100

4. DISCUSSION

The extensive use of antibiotics has been closely linked to the subsequent problem of antibiotic resistance [18]. Antibiotic resistance occurs as a result of continuous use of antibiotics over a longer time period. In addition, the empirical use of antibiotics, not based on bacterial sensitivity results, also contributes to antibiotic resistance [7]. To date, antibiotic resistance remains a threat, particularly in PICU patients [14]. Erbay *et al.* [3] found that antibiotic use was not appropriate in 47.3% of the cases (OR = 3.8; 95% CI: 1.1-13.1), as the empirical use of antibiotics often does not conform to definitive antibiotic therapy (corresponding to culture and sensitivity test results). Isolation of antibiotic-resistant bacteria is more often found in patients who received prior antibiotic therapy, with the highest prevalence of antibiotic-resistant bacteria in hospitals with the highest antibiotic use [14]. In addition, Sritippayawan *et al.* [13] reported that two weeks of broad-spectrum antibiotic therapy increased the risk of bacterial infection by Multidrug-Resistant (MDR) bacteria by 9.7 times (95% CI: 1.8 to 53.4). Additionally, Soroush *et al.* [20] reported resistant *Acinetobacter baumannii* in patients previously given broad-spectrum antibiotics.

For years, studies have shown increased infection rates by antibiotic-resistant microbes and their corresponding negative effects. Kapoor *et al.* [21] showed that 100% of *Acinetobacter baumannii* cases were resistant to ampicillin-sulbactam, ceftriaxone, cefotaxime, cefipime, ceftazidime, and levofloxacin. Soroush *et al.* [20] reported a decrease from 2001 to 2007 in the sensitivity of *Acinetobacter baumannii* to ceftriaxone (43.7% *vs*. 16.2%, respectively), ceftazidime (50% *vs*. 14.7%, respectively), ampicillin (18.7% *vs*. 10.4%, respectively), gentamicin (50% *vs*. 34.3%, respectively), and amikacin (81.2% *vs*. 41.5%, respectively). In addition, Johnson [22] noted an increase in the proportion of isolates of Methicillin-resistant *Staphylococcus Aureus* from blood samples in Wales and the UK, where the proportion of methicillin-resistant *Staphylococcus aureus* (MRSA) in 1992 was <5%, which significantly increased in 2001 to more than 40%. Similarly, gram-negative bacteria, which are confirmed carbapenemase producers, increased dramatically from 2005 to 2013 (Table **7**).

Cosgrove [23] reported the negative effects of antibiotic-resistant bacterial infection to-include an increase in the mortality of patients infected with MRSA compared to those infected with methicillin-susceptible *Staphylococcus aureus* (MSSA) (OR = 3.4; P = 0.003). The duration of hospitalization was also elevated in MRSA-infected patients (mean 29.1 days) and compared with MSSA-infected patients (mean 13.2 days). In addition, patients with MRSA required higher treatment costs (US $118,414) than those with MSSA (US $73,165). Similarly, infection with *Enterobacter* resistant to third-generation cephalosporins increased the risk of death by 5.09 times (P = 0.01), increased the duration of hospitalization by 1.47 times (P < 0.001), and increased treatment costs up to 1.5-fold (P < 0.001). In addition, Roberts *et al.* [24] reported that in 2009, the maintenance costs because of antibiotic-resistant infections ranged from US $18,588 to $29,069 in a teaching hospital in Chicago. The duration of hospitalization for these patients was also longer, ranging from 6.4-12.7 days. The mortality from this study caused by gram positive 41.6%, gram negative 58.3% and 3 from gram positive was from MRSI category.

Therefore, to decrease the high rate of antibiotic resistance, which in recent years has gained worldwide attention, antibiotic use should be justifiable, based on microbe-sensitivity data available in the treatment room, especially in the PICU [10]. To reduce inappropriate antibiotic use, the CDC issued a 12-step recommendation to limit resistance to antimicrobials, educate clinicians about antibiotic resistance, and provide a variety of strategies to change clinical practice, including the prescription of antibiotics [12]. This recommendation has been widely adopted, according to the previous studies [15, 16, 25]. Stocker *et al.* [15] mentioned that the 12-step CDC Guideline is useful for evaluating the therapeutic use of antibiotics in PICU patients, even in settings with limited funding and resources. The study also suggested that the proportion of conformity of antibiotic therapy in patients with negative culture results increased, ranging from only 18% before implementation to 74% after implementation. Similarly, the proportion of empirical antibiotic use for <3 days increased from 18% to 35%, and the precision of definitive therapy increased from 58% to 83%.

CONCLUSION

In conclusion, an appropriate continuation of antibiotic therapy is a significant predictor of length of PICU patient stay, based on the bivariate analysis. However, multivariate analysis revealed that appropriate continuation of antibiotics was not a significant predictor.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical clearance of this study was approved by the Ethical Committee with the reference number 1774/UN.14.2/KEP/2007.

HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Informed consent was obtained from subjects'parents or guardians.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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