

The rationality of the use of antibiotics towards the mortality and hospitalization period of pediatric patients with pneumonia

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ABSTRACT: Purpose: Antibiotics play an important role in reducing child mortality due to pneumonia. Ineffectiveness in prescribing and using antibiotics will lead to many inappropriate prescribing and inappropriate use of antibiotics that will affect the irrational use of antibiotics in patients. The irrationality of antibiotics for death and length of stay has not been done much. Methodology: This research was an observational research with the cross sectional approach. The population of this study was every pneumonia pediatric patients who were hospitalized in one hospital in Central Java in the inpatient ward or PICU. The sampling technique used is Non-probability sampling technique with purposive sampling method. Secondary data were obtained from medical records. Chi-square tests and logistic regression were used to process the data. Results: The use of antibiotics according to the Gyssens flow evaluation obtained the results of irrational antibiotics most used in category IV A as many as 70 patients (72.2%), in category IV C as much as (3.1%), and rational antibiotics in category 0 as many as 24 patients (24.7%). The mortality outcome for pneumonia pediatric patients was 6 patients (6.2%) and 91 patients (93.8%) went home. There are 74 pneumonia pediatric in-patients (76.3%) with 0-7 days hospitalization period and 23 pneumonia pediatric in-patients (23.7%) with > 7 days hospitalization period.

KEYWORDS: Rationality of the use of antibiotics toward the outcome of mortality do not show a significant correlation, however rationality of the use of antibiotics toward hospitalization period is correlated.

I. INTRODUCTION

Pneumonia is still a fundamental health problem for children, especially in developing countries. The incidence and mortality rates are higher in developing countries than in developed countries. The incidence of pneumonia in infants is estimated at 0.29 episodes per child each year in developing countries and 0.05 episodes per child each year in developed countries (Latumahina et al., 2017). In 2013 there were about 156 million new episodes each year worldwide, of which 151 million were in developing countries. Most cases occurred in India (43 million), China (21 million), Pakistan and Bangladesh (10 million) Indonesia and Nigeria (6 million, respectively) (Fischer Walker et al., 2013).

Every year an estimated 6.9 million children under five in the world die, where 3 million children die in the first month of life and 2 million children die at the age of 1-12 months. Pneumonia is the main cause of death in children under five. Pneumonia is estimated to be the death cause around 920.136 children under 5 years of age in 2015, contributing to 15% of all child deaths under 5 years. Pneumonia has always been ranked top every year as a cause of death for infants and toddlers in Indonesia (Latumahina et al., 2017).

In 2010 pneumonia was included in the top 10 inpatient ailments in which as many as 17.311 patients were hospitalized and approximately 7.6% (1.315 patients) died due to pneumonia. The number of pneumonia cases in

toddlers in Indonesia according to the age group in 2014 was 657.490, age <1 year was 206.363 with severe pneumonia cases as many as 15.997, ages 1-4 years were 419.102 with severe pneumonia cases as many as 16.028. The mortality rate due to pneumonia in infants is 1.19%, whereas in the infant group the mortality rate is higher at 2.89% (Ministry of Health and Long-Term Care, 2018).

The use of antibiotics should be started immediately in children suspected of having Community-Acquired Pneumonia (CAP) due to bacteria (Alzomor et al., 2017; Ostapchuk et al., 2004). Pharmacological therapy in pneumonia is done empirically using broad-spectrum antibiotics with the aim that the selected antibiotic can kill several possible germs that cause pneumonia, whereas the use of broad-spectrum antibiotics that are not controlled can cause problems in the management of patients, especially related to therapy. The widespread use of inappropriate antibiotics is a major issue in public health and patient safety.

Many hospital patients receive antibiotic and more than half of patients receive antibiotics that are not needed (Sachdev et al., 2001). Inappropriate use of antibiotics can cause various problems such as expensive cost for the treatment, toxic side effects of medicines, increased antibiotic resistance and the emergence of superinfection incidence that are difficult to treat so that the rationality of therapy in using antibiotics for pneumonia therapy is needed (Ceyhan et al., 2010; Gerber et al., 2015; Griffith et al., 2019).

The use of antibiotics in primary health care and hospitals reaches 80% in several studies, it was reported that the improper use of antibiotics for illnesses that actually do not require antibiotics ranged from 40-62%, meanwhile in the study, the quality of antibiotic use in hospitals reported to be around 30% to 80% is not based on indications (Ministry of Health and Long-Term Care, 2018).

In the study of Lee et al. (2018), it is known that the use of antibiotics in 43.1% of pneumonia inpatients in Rumkital DR. Ramelan Surabaya received inappropriate dosage. Other studies stated that the use of antibiotics reaches 20% of all medicines sales and about 40-60% reported irrational use. Irrational use of antibiotics in Turkey has caused many problems in the country (Lambrini, 2017; Tunger et al., 2009)

Antibiotics that are used inappropriately and excessively have a contribution in emergencies due to antibiotic resistance. Prevention of inappropriate use of antibiotics is the key to control the incidence of antibiotic resistance (Hashemi et al., 2013; Ministry of Health and Long-Term Care, 2018). Irrational use of antibiotics can affect the failure of therapeutic outcomes that end in a repeat episode of hospitalization and a longer duration of therapy and affect the cost of treatment to achieve the desired therapeutic outcome (Abegunde, 2010).

Several studies have been conducted to assess the prevalence of irrational use of antibiotics in children with pneumonia, which are: Mongolia 56.6% 11 6, Indonesia 24% 12 and India 56% (Sachdev et al., 2001). Based on these data it can be concluded that the prevalence of irrational use of antibiotics in pediatric patients with pneumonia is still quite high.

Risk factors for death in children with pneumonia have been identified, which are: women, young age, very severe pneumonia, poor nutrition, illness longer than 21 days and referral cases from primary care health facilities (Lazzerini et al., 2016). Research in India also identified young age, women, and malnutrition as risk factors that can increase mortality in children with pneumonia. Other risk factors include wheezing, respiratory rate ≥ 70 x/minute, chest retraction, loss of consciousness, seizures, shock, presence of congenital heart disease (CHD), newly acquired measles and the need for the use of additional ventilation devices. Data on the effect of irrational antibiotics on death has not yet been obtained.

The negative impact of the use of antibiotics that are not rational is the emergence of antibiotic-resistant germs (resistant). Resistance found in *Pneumococcus* has increased in the last ten years, especially in penicillin. Failure of therapy is made possible by bacteria that are resistant specifically to penicillin derivatives or fails to identify the bacteria that cause pneumonia (Katarnida et al., 2016).

Management of severe infections in children such as pneumonia, there are several problems that need attention, including initial treatment that is given only empirically, then the possibility of antibiotic replacement is very possible. giving more than one type of drug (multiple drug therapy) will cause problems in increasing medical costs, heightening the risk of side effects and facilitating the resistance process or the administration of drugs sometimes become problematic since blood vessels for parenteral administration are difficult to find or because of incompatibility between drugs (Soedarmo et al., 2012).

Antibiotics play an important role in reducing child mortality due to pneumonia, but information about the use of antibiotics in children is limited, while the mortality rate is still quite high. Ineffectiveness in prescribing and using antibiotics is feared will lead to many inappropriate prescribing and inappropriate use of antibiotics that will affect the irrational use of antibiotics in patients. The irrationality of antibiotics for death and length of stay (LOS) has not been done much.

II. METHODS

This research was an observational research with cross-sectional approach. The population of this study was every pneumonia pediatric patients who were hospitalized in one hospital in Surakarta in the inpatient ward or PICU room in 2014-2014. The sampling technique used was the non-probability sampling technique with purposive sampling method. Inclusion criteria in this research were pediatric patient diagnosed pneumonia who was hospitalized in one hospital in Surakarta from October 2016 to October 2018 and received antibiotics therapy with minimum of 3 x 24 hours. The exclusion criteria of this study were pediatric patients with incomplete medical records, who received two types of antibiotics at one time, and with change of antibiotics. We also excluded pediatric patients with diagnoses besides pneumonia such as sepsis, tuberculosis, urinary tract infection and others that need antibiotic therapy, and with comorbidities such as diarrhea, congenital heart disease, and others. A pediatric patient who died not because of pneumonia was also excluded from this study.

The variables studied in this research included mortality outcome and hospitalization period as the dependent variable, and the rationality of antibiotics use as independent variable. The rationality of antibiotics use was defined as rational if fulfilled category 0, defined as irrational if meets category I-VI (I, IIA, IIB, IIC, IIIA, IIIB, IVA, IB, IVC, IVD, V and VI). We used Gyssens flow chart and dose standard based on Pediatric and Neonatal Dosage Handbook Mortality (Taketomo, Hodding, & Kraus, 2014). Mortality outcome was categorized as death and released, which was determined by death or alive recorded a patient’s medical record. The hospitalization period was categorized as 7 days or less and more than 7 days.

Secondary data were used in this study, obtained from patients’ medical records from the period October 2014 to October 2018, patients’ identity and objective data. Statistical analyses were carried out using descriptive analysis, chi-square test, Fisher exact test, and logistic regression.

III.

IV. RESULTS AND DISCUSSION

Characteristics of Respondents

The characteristics of respondents in this study describe the gender and age groups of respondents. The results of the descriptive analysis for the characteristics of respondents are shown in table 1.

Table 1. Distribution of characteristics of pediatric patients with pneumonia in a private hospital in Surakarta (n=97).

Characteristics	n	%
Gender		
Male	43	43.3
Female	54	55.7
Age		
0-11 months	41	42.3
12 months	21	21.6
≥ 13 months	35	36.1

Characteristics of pediatric patients with pneumonia in a private hospital in Surakarta were mostly female as many as 54 patients (55.7%). Based on the age group, almost half of them were in the age group of less than 1-year-old (42.3%).

Mortality and Hospitalization Period

The results of the descriptive analysis of the mortality and hospitalization period of respondents in this study are shown in table 2.

Table 2. Distribution of mortality and hospitalization period in pediatric patients with pneumonia in private hospital in Surakarta (n=97).

Variable	n	%
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Mortality		
Death	6	6.2
Released	91	93.8
Hospitalization period		
0-7 days	73	75.3
> 7 days	24	24.7

Table 2 shows that six (6.2%) pediatric patients with pneumonia in a private hospital in Surakarta encountered death. The majority of pediatric patients with pneumonia with hospitalization period for 0-7 days were 74 patients (76.3%), and hospitalization period for > 7 days were 23 patients (23.7%).

The Rationality of The Use of Antibiotics

The rationality of the use of antibiotics was divided into two categories in this study. The rational category is code 0 and the irrational category was IV A and IV C. The results of the descriptive analysis for the rationality of the use of antibiotics are shown in table 3.

Table 3. Distribution of rationality use of antibiotics in a private hospital in Surakarta (n=97).

Category	n	%
Rational		
Code 0	24	24.7
Irrational		
IV A	70	72.2
IV C	3	3.1

Table 3 above shows that the majority of rational antibiotic use with category 0 was 24 patients (24.7%), irrational antibiotics use in category IV A or cheaper antibiotics alternative is 70 patients (72.2%) and irrational antibiotics use in category IV C or cheaper antibiotics alternative is 3 patients (3.1%).

The Rationality of The Use of Antibiotics, Mortality and Hospitalization Period

A cross-tabulation of the association between the rationality of antibiotic use toward the outcome of mortality and hospitalization period of pediatric patients with pneumonia in a private hospital in Surakarta can be seen in table 4 and table 5.

Table 4. Association between the rationality of antibiotic use toward the outcome of mortality of pediatric patients with pneumonia in a private hospital in Surakarta (n=97)

Rationality Use of Antibiotics	Outcome			X ² (Chi-square)	p ^a
	Death	Cured	Total		
	n (%)	n (%)	n (%)		
Irrational	4 (5.5)	69 (94.5)	73 (100.0)	0.254	0.635
Rational	22 (8.3)	22 (91.3)	24 (100.0)		
Total	6 (6.2)	91 (93.8)	97 (100.0)		

Note: a. Chi-square test

The use of antibiotics in the irrational category was 73 with 69 patients released (94.5%) and 4 patients died (5.5%). Meanwhile, the use of rational antibiotics in 24 patients with 22 patients released (91.3%) and 2 patients died (29.2%). These results illustrate that rational or irrational use of antibiotics is the percentage of released and

death outcome is very low in number. The results of the analysis of the value of chi-square = 0.254 with a value of p = 0.635 indicate there was no significant association between the rationality of antibiotic use toward mortality outcome of pediatric patients with pneumonia in a private hospital in Surakarta.

Table 5. Association between the rationality of antibiotic use toward the hospitalization period of pediatric patients with pneumonia in a private hospital in Surakarta (n=97)

Rationality Use of Antibiotics	Hospitalization Period			p ^a
	> 7 days	0-7 days	Total	
	n (%)	n (%)	n (%)	
Irrational	23 (31.5)	50 (68.5)	73 (100.0)	0.030
Rational	2 (8.3)	22 (91.7)	24 (100.0)	
Total	25 (25.8)	72 (24.7)	97 (100.0)	

Note: a. Fisher's exact test

Irrational use of antibiotics with a hospitalization period of 0-7 days happened in 50 patients (68.5%) and > 7 days is 23 patients (31.5%). Rational use of antibiotics with hospitalization period of 0-7 days happened in 22 patients (91.7%) and > 7 days is 2 patients (8.3%). The result shows that patients with the use of irrational antibiotics will be released > 7 days longer than patients with the use of rational antibiotics. The chi-square analysis result for table 2 x 2 with cell value under 5 then the Fisher's Exact Test shows the value of p = 0.030 which means there is a significant association of the rationality of the use of antibiotics to the length of hospitalization period of pediatric patients with Pneumonia at the Private Hospital in Surakarta.

We also analyzed the data using logistic regression between age, gender and antibiotics use and mortality and hospitalization period, with the results shown in table 6 and table 7.

Table 6. Association between age, gender and antibiotics use, and mortality of pediatric patients with pneumonia in a private hospital in Surakarta.

Variables	p	95% CI	Exp (B)
Age	0.052	0.011 – 1.020	0.105
Gender	0.278	0.365 – 33.325	3.488
Antibiotics use	0.670	0.224 – 10.258	1.515

Based on table 6, logistic regression analysis results show that overall there was no association between gender, age, and use of antibiotics with the mortality outcome in pediatric patients with pneumonia in a private hospital in Surakarta.

Table 7. Association between age, gender and antibiotics use and hospitalization period of pediatric patients with pneumonia in a private hospital in Surakarta.

Variables	p	95% CI	Exp (B)
Age	0.965	0.353 – 3.973	1.024
Gender	0.932	0.371 – 2.481	0.959
Antibiotics use	0.045	1.034 – 23.722	4.952

Logistic regression analysis results show that antibiotics use was significantly associated with hospitalization period, even after controlled by age and gender variables, in a private hospital in Surakarta (p<0.05).

V. DISCUSSION

The outcome of pediatric patients with pneumonia

The outcome of pediatric patients with pneumonia in a private hospital in Surakarta reveals the death of pediatric patients was 16 patients (16.5%) and released patients were 81 patients (83.5%). The results of this study are in line with one study conducted by Suharjo et al. (2009) showed the percentage of recovered returned patients is more than those who died. One of the objectives of evaluating outcomes is to shorten the duration of treatment and reduce mortality. In research conducted by Sari et al. (2017) that the therapeutic outcome of CAP patients indicates that the administration of appropriate antibiotics will provide good outcomes. From the results of the study it can be concluded that the outcomes obtained from the rational use of antibiotics in pneumonia patients are partly good, although some are still not good because of certain conditions or because these patients have severe degrees of infection.

Hospitalization period of pediatric patients with pneumonia

It is known that pediatric patients with pneumonia with a hospitalization period of 0 – 7 days in 74 patients (76.3%), and hospitalization period >7 days is 23 patients (23.7%). In line with a study by Rahayu et al. (2014) which mentioned a significant correlation between the use of rational antibiotics toward hospitalization period in group with rational use of antibiotics with longer hospitalization period of 5 days more than the total of group with irrational antibiotics with shorter hospitalization period of 3 - 5 days. The duration of treatment of patients suffering from pneumonia is influenced by the degree of pneumonia, the higher the degree of pneumonia, the longer the treatment required (Alzomor et al., 2017; Ostapchuk et al., 2004).

The rationality of the use of antibiotics in private hospital in Surakarta

The rationality of the use of antibiotics in a private hospital in Surakarta known as most of the rational use of antibiotics with category 0 in 24 patients (24.7%), irrational use of antibiotics with category IV A is 70 patients (72.2%) and irrational use of antibiotics with category IV C is 3 patients (3.1%). This study is not in line with what was done by O'Connor (2018) that rational use of antibiotics was 66.3% and irrational use of antibiotics by 33.7%.

Antibiotics are medicines that are used in infections caused by bacteria. Various studies have found that around 40-62% of antibiotics are used incorrectly. In this study the use of antibiotics that are widely used is included in category VI A, which means they use of antibiotics is appropriate but not the right type because there are other antibiotic choices that are more effective while the category VI C is the use of antibiotics is appropriate but not the right type because there are another cheaper alternatives. The use of incorrect antibiotics with high intensity will result in many losses such as side effects, waste of money and resistance that can cause severe infections in the future. Irrational use of antibiotics can affect the failure of therapeutic outcomes that end in a repeat episode of hospitalization and a longer duration of therapy and affect the cost of treatment to achieve the desired therapeutic outcome (Abegunde, 2010).

Association between the rationality of antibiotic use toward the outcome of mortality and hospitalization period

The significance of the association between the use of antibiotics and outcomes based on the chi-square test is 0.635 which means there is no correlation between the use of antibiotics and outcomes for pneumonia patients. The use of antibiotics in the irrational category was 73 with 69 patients released (94.5%) and 4 patients died (5.5%). Meanwhile the use of rational antibiotics in 24 patients with 22 patients released (91.3%) and 2 patients died (29.2%). It is in line with a study by (Kaparang & Tjitrosantoso, 2014) who stated that percentage of recovered released patients is more in numbers than those who are released by perforce. Rational use of antibiotics provides a more significant outcome than the use of antibiotics that are not rational (Soedarmo et al., 2012).

The association of antibiotic use with the hospitalization period of pneumonia patients showed the results of the analysis of Fisher's Exact Test = 0.030 which means there is a significant association of antibiotic use with the hospitalization duration of pneumonia patients. This association also remained significant when analyzed using logistic regression with age and gender variables controlled. Treatments and medication until the patients are released are only last for 5 to 7 days. Most of the illnesses found in patients who are in the hospital are infections. Giving antibiotics must be in accordance with clinical needs and the patient's condition at that time and the right dose for the antibiotics to be useful for patients. Many misunderstandings occur with the duration of antibiotics administration, most doctors and pharmacists assume that the administration of antibiotics with a long duration is better than the administration of antibiotics with a short duration (Van Der Meer & Gyssens, 2001).

The use of irrational antibiotics with hospitalization period of 0 – 7 days in 50 patients (68.5%) and > 7 days is 23 patients (31.5%). Meanwhile, the use of irrational antibiotics with hospitalization period of 0 – 7 days in 22 patients (91.7%) and > 7 days is 2 patients (8.3%). This result is in line with a study by Anastasia Hilda in 2013 which stated that effective treatment period is ≤ 9 days and treatment period ≥ 10 days is considered ineffective.

The response of the use of antibiotics to patients is evaluated 3 days after administering the antibiotics to the patients. If the antibiotics do not respond, it is possible that there is another infection, complication, or antibiotics

resistance. Inappropriate use of antibiotics causes ineffective treatment or therapy, increases resistance and increases the cost of treatment due to the hospitalization period (Soedarmo et al., 2012).

VI. CONCLUSION

There is an association between the rationality of antibiotic use and the hospitalization period in pediatric patients with pneumonia. There is no significant association between the rationality of the use of antibiotics toward the mortality outcome of pediatric patients with pneumonia in private hospitals in Surakarta.

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