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Research Article

Evaluation of Antibiotics Used in Pediatric Outpatients with Acute Respiratory Infection at a Private Hospital in Yogyakarta

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ABSTRACT

Ensuring patient safety and optimal health outcomes in the healthcare system requires appropriate and rational use of medicines. One of the prescription issues noted in the pediatric clinic at a private hospital is the high use of antibiotics for acute respiratory infections. This study aimed to improve antibiotics used in outpatient pediatric clinic. This study was a descriptive analysis with a cross-sectional study design, combining quantitative and qualitative methods. The population was all prescriptions in January - March 2023. By using a purposive sampling method, there were 340 prescriptions obtained. The instruments of the study were data collection sheets and in-depth interview guidelines. Data were analyzed using the triangulation method. The antibiotic prescription rate was 64% (n=340). There were patients with Azithromycin and Erythromycin who received antibiotics below the dosing recommendations. Observation of patients' treatment process showed that prescribers did not always suggest the laboratory examinations. Based on in-depth interviews of prescribers, they prescribed antibiotics based on the patient's clinical examination. Based on in-depth interviews with the hospital managers, there was a tendency to choose a strategy which was a combination of educational and managerial strategies. The strategies to improve the quality of the antibiotics used include conducting training programs for the prescribers and developing standard treatment guidelines.

INTRODUCTION

Ensuring patient safety and optimal health outcomes in the healthcare system requires appropriate and rational use of medicines. This involves administering medicines that are suitable for the patient's medical needs, in the correct dosage, for the right duration, and at an affordable cost. Conversely, irrational medicine use can lead to negative consequences such as antibiotic resistance, adverse medicine reactions, high medicine therapy costs, and a decline in the quality of medicine therapy (Nyabuti *et al*., 2020). Irrational medicine use can manifest in various forms, including the inappropriate use of antibiotics, polypharmacy, and failure to comply with standard treatment guidelines (STG). It is essential to improve medicine use practices to reduce the morbidity and mortality associated with irrational medicine use (Nyabuti *et al*., 2020). The World Health Organization (WHO) has developed indicators to assess rational medicine use. For instance, the prescription indicator measures the proportion of patients prescribed antibiotics in healthcare facilities (Mamo and Alemu, 2020).

Hospitals play a vital role in providing comprehensive healthcare services, including inpatient, outpatient, and emergency care (Sutriyati Tuloli *et al*., 2021). A private hospital in Yogyakarta is committed to provide high-quality healthcare services, is accredited by KARS with the highest level of excellence and has a capacity of 345 beds. The hospital's pharmacy department serves prescriptions from 30 outpatient clinic services, which provide care to an average of 75 pediatric patients per day. This clinic is served by seven pediatricians. One of the prescription issues noted in the pediatric clinic is

the high usage of antibiotics for Acute Respiratory Infections (ARI). In September 2022, approximately 45% of 60 patients were prescribed antibiotics, with 64% among others receiving antibiotics for ARI. In addition, the hospital currently lacks the STG for pediatric ARI, according to the head of the clinical practice guidelines team.

This study aimed to improve the antibiotics used in outpatients of the pediatric clinic by determining the profile of antibiotics used, identifying the underlying factors of antibiotics prescribed, and selecting strategies to improve the quality of antibiotics used in pediatric ARI.

METHODS

This study was a descriptive analysis with a cross-sectional study design. This study was conducted using a combined quantitative and qualitative method. The quantitative method was used to measure antibiotic used and the qualitative method was used to determine the underlying factors of the antibiotics used by the prescribers and to select the strategy for improving the quality of the antibiotics used (Management Sciences for Health, 2012a). The population of this study was all prescriptions in January - March 2023. The daily average number of prescriptions in the pediatric clinic at a private hospital was 75. The determination number of samples by statistical calculation using the Slovin formula n=N/1+N(e)2 (Ismail *et al*., 2022), were 340 prescriptions. Data collection was done using a purposive sampling method (Tandi *et al*., 2018) to determine the prescribers as the study subjects. The instruments of this study were the data collection sheet and the in-depth interview guideline for the prescribers and the hospital managers.

The inclusion criteria of the study subjects were pediatric patients aged between 2-12 years old (Hardin and Hackell, 2017) with ARI and respiratory tract infections ranging from upper to lower respiratory tract infections with symptoms occurring within 1 to 14 days. Upper respiratory tract infections include rhinitis, pharyngitis, tonsillitis, sinusitis, and otitis media. Lower respiratory tract infections include epiglottitis, laryngotracheobronchitis, bronchitis, bronchiolitis, and pneumonia (Rahajoe *et al*., 2010). The exclusion criteria of this study was the prescription from the pediatrician's consultant. Data collection included patient name initial, gender, age, weight, number of antibiotics, type of antibiotics, duration of antibiotic used, symptoms, diagnosis, and laboratory assessment.

The study was divided into four stages: review of prescribing documents; observation of the prescribing process; in-depth interviews to the prescribers and the hospital managers; and selection of the strategy to improve the antibiotics used (Management Sciences for Health, 2012b). The in-depth interview was designed by first developing its instrument. The instrument for in-depth interviews used the in-depth interview guidelines to the prescribers and the hospital managers which were developed based on data obtained from previous stages of the study. Several points were checked to assess whether the guidelines were sufficient to obtain the necessary information. The questions in the in-depth interview were open-ended. Seven respondents were included for in-depth interviews, comprising four prescribers from the pediatric clinic and three hospital managers, including the head of the antimicrobial stewardship program team, head of the clinical practice guidelines team, and the medical director. Interviews were conducted with each respondent after obtaining their signed informed consent. The results of the in-depth interviews were recorded using a voice recorder and then transcribed.

The underlying factors of the antibiotics used were identified through in-depth interviews with the prescribers, review of prescribing documents, and observations of the prescribing process. The strategy to improve the antibiotics used was selected based on the results of the in-depth interviews with the hospital managers. The educational strategy would be chosen if the underlying factor was related to prescribers' inadequate information. The managerial strategy would be chosen if the underlying factor was related to the problem in management. The regulatory strategy would be chosen if the underlying factor was related to the prescribers' behavior. The strategy selected could be one or a combination of two or three strategies (Management Sciences for Health, 2012b, 2012c).

Triangulation methods were used to analyze the data obtained (Kaufmann et al., 2015), based on the observation results of pediatric ARI prescription pattern; observations of the prescribing process; and prescribers and hospital managers points of view regarding the antibiotics used. The triangulation methods were employed to ensure the accuracy and validity of the data obtained. Consequently, the study could achieve comprehensive approaches for strategic selection in improving the antibiotics used. The study has passed the ethical review by the Hospital Ethics and Legal

Committee of Panti Rapih Hospital in Yogyakarta as shown by the certificate of ethical eligibility number: 117/SKEPK-KKE/VII/2023.

RESULTS AND DISCUSSION

ARI is an acute infection affecting the upper and lower respiratory organs that can be caused by viruses, fungi, or bacteria (Mirino *et al.,* 2022). The antibiotic prescription rate in pediatric outpatients with ARI was 64% (n=340) (Figure 1). The other 36% of pediatric patients who were not prescribed antibiotics received symptomatic medicines, which were given for 4-6 days, regarding symptoms of fever, cough, and flu (Table 1). These medicines included Paracetamol, Ibuprofen, Triamcinolone, Salbutamol, Ambroxol, Cetirizine, Loratadine, Pseudoephedrine/Triprolidine, and others.

Characteristics of patients were used to determine the diversity of patients who received antibiotics based on gender, age, symptoms, patient's laboratory assessment, and the antibiotics used in pediatric outpatients with ARI. Most of the patients in this study are male (55.25%). The patients' ages were divided into two categories: 2-5 years old (54.79%) and 6-12 years old (45.21%). Patients' symptoms included fever, cough, and flu (33.70%). The number of patients who were not required to do the laboratory assessment before receiving antibiotics was 80.82%. The most commonly used antibiotic was Cefixime (40.18%). The complete result is summarized in Table 1.

Results of the study showed that there were five types of antibiotics used. The most common antibiotic used in pediatric outpatients with ARI was Cefixime (40.18%), which was used every 8-12 hours. This was followed by Azithromycin (36.07%) which was used every 24 hours, Cefadroxil (14.61) which was used every 12 hours, then Amoxicillin (4.57%) and Erythromycin (4.57%) which were used every 8 hours. The antibiotic doses prescribed were stratified based on the patient's weight into three categories: range from 9-20 kg, 21-40 kg, and 41-60 kg. The antibiotics prescribed followed the dosing recommendations from the Pediatric Dosing Handbook of the Indonesian Pediatric Association. The complete antibiotics dosage prescribed in pediatrics with ARI are summarized in Table 2.

Results of the study showed that most of the patients followed the dose recommendation. However, there were patients with Azithromycin and Erythromycin in weight 21-40kg who received antibiotics below dosing recommendations, which heightened the risk of developing antibiotic-resistant strains of bacteria (Muliana, 2017; Paul *et al.,* 2014). In addition, it could lead to a lack of effectiveness in achieving the desired therapeutic outcome (Angin *et al*., 2021; Titami *et al.,* 2022). The treatment outcome of bacterial ARI was also significantly influenced by the right choice of antibiotic used (Paul *et al*., 2014).

Amoxicillin should be the initial preference for oral treatment when the antibiotic is considered necessary. Macrolide antibiotics like Erythromycin or Azithromycin should be used only when there is a known allergy to penicillin or resistance to Amoxicillin (Paul *et al.,* 2014). Another choice is Cephalosporin medicine, e.g. Cefadroxil and Cefixime. Cefadroxil is from the first generation of Cephalosporins, and Cefixime is from the third generation (Shahbaz, 2017).

Observation of the patient's treatment process was conducted during a single period when the prescriber was engaged in clinical practice. Four prescribers were observed and the number of pediatric patients with ARI observed was 28. Observations of the patients' treatment process showed that the process was started by making the diagnosis. Making the diagnosis included the anamnesis step,

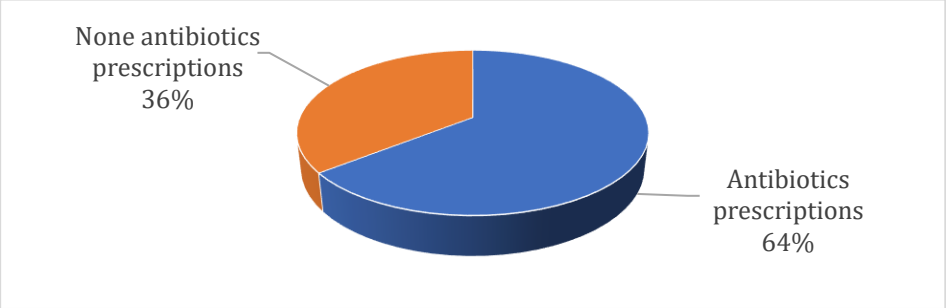

Figure 1. The Antibiotics Prescription Number of Pediatric Outpatients with ARI

Table 1. Characteristics of Patients who Received Antibiotics

Characteristics of Patients	Patients (n= 219)	
	n	%
Gender		
Male	121	55.25
Female	98	44.75
Age (years)		
2-5	119	54.34
6-12	100	45.66
Symptom(s)		
Fever	2	0.91
Cough	25	11.42
Flu	4	1.83
Fever, cough	41	18.72
Fever, flu	5	2.28
Cough, flu	68	31.05
Fever, cough, flu	74	33.79
Patient's laboratory assessment		
Laboratory assessment	43	19.63
Non-laboratory assessment	176	80.37
Type of Antibiotics Used / Duration (days)		
Amoxicillin / 4-7	10	4.57
Azithromycin / 3-6	79	36.07
Cefadroxil / 5-10	32	14.61
Cefixime / 3-7	88	40.18
Erythromycin / 4-8	10	4.57

physical examination, and laboratory examination. Upon the patient's arrival at the clinic, during the anamnesis stage, information was collected about the patient's identity, the patient's signs and symptoms, the current treatment, current and past medical history, and measurements of weight and vital signs. These vital signs include body temperature, blood pressure, and heart rate. Subsequently, the prescribers conducted the physical examination by assessing the patients' signs and symptoms, e.g., fever, cough, flu, and other physical examinations needed, e.g., lung examination. If laboratory examination was deemed necessary, the doctor would recommend it before prescribing antibiotics. Then, the prescribers considered the therapeutic options to achieve therapeutic goals, prescribing medicines for the patient's treatment and determining the necessity of antibiotics, counseling the patient and the patient's family, and monitoring the patient's treatment outcome.

Table 2. Antibiotics Dose in Pediatrics with ARI

Antibiotic Used	Weight (kg)	Dose and administration used (peroral)	% (n=219)	Dosing recommendations (*Ikatan Dokter Anak Indonesia*, 2016)	Note (*)
Amoxicillin	9-20	3x100-250mg, every 8 hours	3.65	40-45 mg/kg/day, divided every 8 hours	✓
	21-40	3x500mg, every 8 hours	0.45		✓
	41-60	3x450mg, every 8 hours	0.45		✓
Azithromycin	9-20	1x80-300mg, every 24 hours	20.55	10 mg/kg/day, every 24 hours	✓
	21-40	1x150-500mg, every 24 hours	12.78		X
	41-60	1x350-500mg, every 24 hours	2.74		✓
Cefadroxil	9-20	2x125-250mg, every 12 hours	8.67	30 mg/kg/day, divided every 12 hours	✓
	21-40	2x250-375mg, every 12 hours	5.94		✓
	41-60	-	0.00		-
Cefixime	9-20	2x25-100mg, every 12 hours, or 3x25-60mg, every 8 hours	23.74	8 mg/kg/day, every 24 hours or divided every 12 hours	✓
	21-40	2x60-125mg, every 12 hours, or 3x65-75mg, every 8 hours	12.79		✓
	41-60	2x100-200, every 12 hours	3.65		✓
Erythromycin	9-20	3 x 100-200mg, every 8 hours	3.66	50 mg/kg/day, divided every 6-8 hours	✓
	21-40	3 x 185-200mg, every 8 hours	0.91		X
	41-60	-	0.00		-

* ✓: antibiotics used followed the dosing recommendation;
X: some antibiotics used did not follow the dosing recommendation.

Observation of the patient's treatment process was conducted during a single period when the prescriber was engaged in clinical practice. Four prescribers were observed and the number of pediatric patients with ARI observed was 28. Observations of the patients' treatment process showed that the process was started by making the diagnosis.

Observation of the patient's treatment process showed that the prescribers followed the process of rational prescribing. Rational prescribing includes making a diagnosis, consideration of treatment options by establishing the goals of therapy, selecting the most appropriate treatment, and monitoring the effects of the treatment (Maxwell, 2016). Based on the Pediatric Respirology Textbook as the guidelines provided by the Indonesian Pediatrician Association, the diagnosis step is the important step to decide whether the ARI is caused by bacteria or not. Making the diagnosis includes the anamnesis step, physical examination, and laboratory examination. However, the prescribers did not always suggest the laboratory examination to the patients. The number of patients who were not required to do the laboratory assessment during observation of the patient's treatment process was 71,43% (n=28).

The laboratory examination is an important step to take that supports the examination of whether the ARI is caused by bacteria or not. The primary principle of antibiotic selection is that the targeted bacteria should be sensitive to the prescribed antibiotic. However, due to various constraints, most antibiotic treatments are prescribed empirically. In many cases, determining the exact causative bacteria is challenging, leading to the use of broad-spectrum antibiotics (Rahajoe *et al.,* 2010). Prescribers employ their clinical judgment and clinical skills when treating patients. Using their expertise and work experience, the prescribers make decisions about whether to use antibiotics or symptomatic therapy (Chan *et al.,* 2019; Paul *et al*., 2014). Therefore, it is particularly important to understand the factors that influence the antibiotics prescribed (Zanichelli *et al*., 2019).

Consideration of prescribing antibiotics due to possible infection by bacteria was obtained from the in-depth interview with the four prescribers. In-depth interviews of the prescribers were conducted to identify the underlying factors of the antibiotics prescribed.

The prescribers said that they would prescribe antibiotics when they considered the possibility of bacterial infection in ARI, based on the patient's clinical examination. These clinical conditions included sore throat, enlarged and red tonsils, purulent nasal discharge, coughing up green sputum, and a fever persisting for more than three days. As the prescribers expressed as follows "… *The bacterial infection was suspected when the patient exhibited symptoms such as cough, runny nose with purulent snot, high fever, shortness of breath, and rhonchi. Additionally, the antibiotics were considered in ARI when the patients appeared more toxic and unwell, the throat showed signs of redness and inflammation, with enlarged and red tonsils, and the sputum could not be easily expelled within three days*. …" (P1, P2, P3, P4).

Additionally, two of the prescribers considered the administration of antibiotics for acute lower respiratory tract infections based on lung exams, which showed lower respiratory tract infection symptoms, including the presence of rhonchi, crepitation, and high fever lasting more than three days. As the prescribers expressed as follows "… *Signs of bacterial infection when the pulmonary examination showed the lower respiratory tract infection, e.g., rhonchi, crepitation and high fever for more than 3 days. Therefore, I considered giving antibiotics for the first 3 days.* …" (P1, P2).

Laboratory examination also supported the assessment of bacterial infection with the markers of bacterial infection such as leukocytes, neutrophils, and monocytes. The prescribers said that they would suggest a laboratory examination before prescribing antibiotics when the patient had symptoms of ARI for more than three days. As the prescribers expressed as follows "… *When the patient had symptoms such as shortness of breath, wheezing, runny nose, cough, high fever for more than 3 days, I typically advised the family to conduct a blood laboratory examination before prescribing antibiotics. The markers of bacterial infection typically showed elevated neutrophil levels, while leukocyte levels might sometimes remain normal. Elevated monocyte levels also tended to point toward a bacterial infection*. …" (P1, P2, P3, P4).

There was one prescriber who used another assessment to consider the possibility of bacterial infection caused by Streptococcus bacteria without having a laboratory examination. The prescriber said that using an assessment called the Centor score could promptly administer antibiotics on the first day of examination without the laboratory assessment. The prescriber expressed this as follows "… *The Centor score was used to identify suspected Streptococcus bacterial infection. It was characterized by high fever, absence of cough, throat pain, age-based criteria, and a tonsil examination revealing tonsil detritus or exudate. The prescriber could promptly administer antibiotics during the initial examination on the first day without the laboratory assessment*. …" (P1).

Furthermore, every prescriber stated that they were confident in their clinical judgment and work experience. Prescribers used their clinical judgment and abilities when deciding the administration of antibiotics. Since they always updated their knowledge by attending workshops, seminars, and symposiums. As the prescribers expressed as followed "… *I follow scientific developments in pediatrics to update my knowledge through seminars, symposiums, and workshops from the Indonesian Pediatric Association*. …" (P1, P2, P3, P4).

Based on Pediatric Respirology Textbook as the guidelines provided by the Indonesian Pediatrician Association, antibiotics must be promptly and appropriately administered if an ARI is suspected to be caused by bacteria. "Promptly" in this context means administering antibiotics immediately when symptoms, signs, and other examinations support a bacterial infection. "Appropriately" implies selecting the type of antibiotic following the causative bacteria or, at the very least, the suspected causative bacteria. Certain types of ARI are significantly influenced by bacteria. Many bacteria can cause ARI, with the two most crucial ones being *Streptococcus pneumoniae*, a gram-positive bacterium, and *Hemophilus influenzae*, a gram-negative bacterium. Furthermore, other bacteria that require attention include *Streptococcus pyogenes* (Rahajoe *et al*., 2010).

In this study, some patients received antibiotics below the dosing recommendations by the Indonesian Pediatrician Association, as shown in the result of reviewing the prescribing documents, specifically, patients prescribed Azithromycin and Erythromycin with a weight range of 21-40kg. Based on the results of in-depth interviews with the prescriber, it was revealed that the prescriber also used another reference for the dosing recommendations, as the prescriber expressed as follows, "… *The reference that I used to determine the dosage of Azithromycin and Erythromycin was from the Royal Children's Hospital in Melbourne, Australia. The dosage of Azithromycin I referred to was 7.5mg/kg/day once daily, while the dosage of*

Erythromycin I referred to was 25mg/kg/day divided into 3 doses. These dosages were chosen to minimize the risk of side effects from both drugs, such as discomfort or stomach pain. …" (P2). This result indicated that there was a difference in the references used by the prescribers. The dosing recommendations referred to by the prescriber were lower than the reference in this study, which was from the Pediatric Dosing Handbook of the Indonesian Pediatric Association. Therefore, there is a clear need for strategies to improve the quality of antibiotics used in ARI.

Selecting strategies were obtained from the in-depth interviews to the 3 hospital managers. The tendency of the strategies chosen from the three respondents was a combination of educational and managerial strategies. The educational strategy included engaging in scientific discussions and developing guidelines for antibiotic selection. This educational strategy could be conducted in collaboration with pediatricians, pharmacists, and the antimicrobial stewardship program team. As the head of the antimicrobial stewardship program team expressed as follows, "… *The antimicrobial stewardship program team could hold an updated knowledge discussion related to the selection of antibiotics. The antimicrobial stewardship program team's role was to keep up with the latest knowledge in antibiotics and to concentrate on antibiotic selection to help prescribers choose the proper antibiotics used through scientific discussion and guidelines provided by flowcharts*. …" (P5)

One of the discussions involved guidelines therapy for ARI. Among the various options or alternative therapies available, prescribers could discuss and agree on the guidelines to be referred to for ARI. This was necessary because the results of in-depth interviews indicated that there was a difference in the references used by the prescribers. The educational strategy was also related to the managerial strategy recommended by hospital management. The managerial strategy included developing Standard Treatment Guidelines (STG) for ARI. Based on the hospital management point of view, STG for a disease are very important to make because they are used in hospitals as a reference by prescribers, to provide excellent services following the guideline. As head of the clinical practice guidelines team as follows, "… *It was essential to create comprehensive guidelines for diseases, including ARI. These guidelines were crucial, as they served as a reference and a framework for clinical colleagues to deliver services by established standards*. …" (P7)

Managers were ready to support funding and other aspects needed for the implementation of both educational and managerial strategies to improve the quality of antibiotics used. As the medical director expressed as followed, "… *Antibiotic resistance is a crucial factor to consider because it is essential to ascertain whether the drugs administered are resistant or not, and also to determine whether the drugs administered contribute to resistance. The accuracy of antibiotic used was monitored by the hospital's antimicrobial stewardship program team. Therefore, the management would support what was needed, both the updating knowledge for the prescribers about the current treatment regarding the use of antibiotics and the developing the STG for ARI.* …" (P6)

The strategies to improve the quality of antibiotics used based on in-depth interviews to the hospital managers was a combination of educational and managerial strategies. The educational strategy can be developed by the antimicrobial stewardship program team. The antimicrobial stewardship program team plays a role in preventing or reducing the incidence of antibiotic resistance that is caused by the incorrect use of antibiotics (Karuniawati *et al.,* 2021) and is involved in developing antibiotic policies and guidelines that lead to a reduction in both antibiotic prescriptions and the incorrect selection of antibiotics (Lutfiyati *et al*., 2022). Utilizing antimicrobial stewardship programs is deemed a foundational strategy for reducing the emergence and escalation of antimicrobial resistance within hospital settings (Setiawan *et al*., 2022). Therefore, the antimicrobial stewardship program team can fulfill these roles through education and training programs (Menteri Kesehatan Republik Indonesia, 2015).

The managerial strategy that was recommended by the managers was developing the STG for ARI that could be agreed upon by prescribers, especially regarding the selection and dosage of antibiotics in ARI. Consequently, patients can be treated with a standardized therapy (Management Sciences for Health, 2012c). Furthermore, there is a need for well-coordinated interventions and the implementation of STG at the point of care to reduce the adverse effects associated with the overuse of antibiotics (Hassan *et al*., 2021). A pressing demand exists for comprehensive interventions to address both the over-prescription of antibiotics and the selection of appropriate antibiotics (Nguyen *et al*., 2023).

CONCLUSIONS

Based on the results of the study, the strategies to improve the quality of antibiotics used in pediatric outpatients with ARI of a private hospital are conducting training programs for the prescribers with material education on refreshment the utilization of standard treatment guidelines in the diagnosing process of ARI by developing simple and applicable standard treatment guidelines. Further study needs to develop and implement the new standard treatment guidelines.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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