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Original Article

Antibiotic Use among Vietnamese Children Hospitalized with Pneumonia

Bui Thi Xuan[1,*], Pham Van Dem[1,2], Nguyen Thanh Nam[2]

[1]*VNU University of Medicine and Pharmacy, 144 Xuan Thuy, Cau Giay, Hanoi, Vietnam*
[2]*Bach Mai Hospital, 78 Giai Phong, Kim Lien, Hanoi, Vietnam*

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Abstract: Background: The use of antibiotics in the treatment of community-acquired pneumonia in children from 2 months to 5 years old at a tertiary hospital in Vietnam still has many shortcomings. Materials & Methods: A cross-sectional descriptive study was carried out based on retrospective data and information collected from 154 inpatient medical records for community-acquired pneumonia at the Department of Pediatrics - Bach Mai Hospital, Hanoi, Vietnam, in 2021. Clinical and laboratory information, information on antibiotic use in community-acquired pneumonia in pediatric patients, and information on the appropriateness of antibiotic use were collected and analyzed. Results: There were 12 antibiotic regimens initially selected to be used to treat community-acquired pneumonia at the hospital, of which four regimens used one antibiotic and eight regimens used combined antibiotics. The rate of combination regimen gradually increased with disease severity, which was 22.3%, 38.5%, and 50% for mild pneumonia, severe pneumonia, and very severe pneumonia, respectively. The most commonly used antibiotic groups in the initial regimen are penicillin/β-lactamase inhibitor (alone regimen) and penicillin/β-lactamase inhibitor in combination with macrolides (combination regimen). The rate of initial treatment regimens that were not suitable according to the recommendations accounted for 99.4%. There were 83/154 cases where patients were prescribed antibiotics inappropriately in terms of dose and rhythm or both. Conclusion: The use of antibiotics in the treatment of community-acquired pneumonia in children at a tertiary hospital still has shortcomings. It is necessary to develop a system of assessment and monitoring of antibiotic use, from which timely adjustments and controls can be made, to limit the ability of bacteria to develop drug resistance.

Keywords: Bacteria, antibiotics, pneumonia, children, hospital.

* Corresponding author.
E-mail address: xuanbt.ump@vnu.edu.vn

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1. Introduction

Pneumonia is one of the main causes of mortality in children, especially in developing countries. According to statistics from the World Health Organization (WHO), about 15% of children under 5 years old died from pneumonia in 2017 [1]. Every 39 seconds, a child dies from pneumonia [2]. Vietnam is ranked as one of the 15 countries with the highest number of new pneumonia cases annually in the world, estimated at 2.9 million cases a year, and the incidence of pneumonia is about 0.35 episodes/child/year [3]. In Vietnam, according to statistics from health facilities, pneumonia is the leading cause of children's hospital visits for examination and treatment [4].

Causes of pneumonia vary and include bacteria, viruses, parasites, fungi, etc. According to WHO statistics, these groups of causes change with age. In older children, atypical bacterial pneumonia is common, represented by *Mycoplasma pneumonia*, while *Streptococcus pneumonia* is the leading cause of community-acquired pneumonia in children under 5 years of age. In developing countries, bacteria are the most common cause of disease, most commonly *S.pneumoniae,* and *H.influenzae* [1]. Therefore, antibiotics play an important and indispensable role in the treatment of pneumonia. However, improper usage of antibiotics has been increasing the population of drug-resistant bacteria and reducing the effectiveness of treatment. The analysis of the current situation of antibiotic use plays an important role in the development and implementation of a safe, effective, and reasonable antibiotic use strategy, which is also a solution to improve the effectiveness of the treatment of community-acquired pneumonia for children. This study was conducted to describe the current status of antibiotic use in the treatment of community-acquired pneumonia in children aged 2 months to 5 years in a tertiary hospital in Vietnam.

2. Materials and Methods

2.1. Study Settings and Participants

Bach Mai Hospital Pediatric Center has 120 beds. The center examines and treats about 200 outpatients per day. However, 2021 is a year with complicated developments of the COVID-19 epidemic, so the number of patients coming for examination and treatment has decreased sharply. The total number of patients hospitalized for treatment related to pneumonia is only about 250 patients.

A cross-sectional descriptive study was carried out based on retrospective data and information collected from inpatient medical records for community-acquired pneumonia at the Department of Pediatrics - Bach Mai Hospital, Hanoi, Vietnam, in 2021. The selected patients were children aged 2 months to 5 years old, diagnosed with community-acquired pneumonia, and receiving inpatient treatment for at least 3 days or more at the Pediatrics Department - Bach Mai Hospital, with a discharge date of January 1, 2021, to December 31, 2021. Ethical approval from the hospital ethical committee was obtained. The selection criteria included are as follows: i) The patients were aged from 2 months to 5 years old; ii) Having a confirmed diagnosis of pneumonia and antibiotics were prescribed; and iii) Receiving inpatient treatment for 3 days or more. Exclusion criteria included are as follows: i) Patient's medical history with hospital-acquired pneumonia or pneumonia diagnosis 48 hours after admission; ii) Patients whose medical treatment regime does not include antibiotics; iii) Medical records of patients treated for less than 3 days (withdrawal of treatment, or transferred to another hospital); and iv) Blurred, torn, incomplete medical records. A total of 154 cases were selected during the study period.

2.2. Data Collection

The collected information was collected in the form of a medical record collection form to survey predefined criteria.

Clinical and laboratory information included: age, gender, the severity of pneumonia, comorbidities, and microbiological characteristics.

Information on antibiotic use in community-acquired pneumonia in pediatric patients:

hospital-acquired resistance status, initial treatment regimens, changes in antibiotic regimens, patterns of regimen changes antibiotics.

Information on antibiotic use: Comparison with the Ministry of Health's Antibiotic Use Guidelines (2015) [5] on dosage and dosage ratio compared to recommendations in patients with normal renal function and patients with renal failure. The regimen is considered appropriate when the antibiotics in the regimen are used for patients according to the regimen in the Treatment Guidelines. The regimen is considered inappropriate when there is an excess/deficiency of at least 1 drug in the regimen compared to the recommended regimen. The appropriateness of dosage and drug delivery ratio is compared based on several documents in the following order of priority: Antibiotic regimens for treatment of community-acquired pneumonia in children at the Ministry of Health's Antibiotic Use Guidelines Health 2015 [5], British National Formulary for Children 2021 [6], Vietnam National Pharmacopoeia 2018 [1], and the Hospital's Medication Guide.

2.3. Statistical Analysis

Data was entered and processed on Microsoft Office Excel 2016 and SPSS 23.0. Qualitative variables were described by frequency and percentage. Continuous variables were described by mean ± standard deviation if the data followed a normal distribution, or represented by the median and interquartile range if the data were not normally distributed.

3. Results

Table 1 shows that among 154 samples, the majority were male (52.6%) and aged 2-12 months (53.2%). Most of the paediatric patients had mild pneumonia (61%) and severe pneumonia (33.8%), and the proportion of paediatric patients with very severe pneumonia was low (5.2%). There were 31 patients (20.1%) with 1-2 comorbidities, mainly ear-nose-throat diseases such as acute rhinitis (51.6%), and otitis media (38.7%) - diseases associated with upper respiratory tract infections, which could lead to pneumonia.

Table 1. Clinical and laboratory characteristics of the study sample

Characteristics		Freq (n)	Percentage (%)
Age (n=154)	2-12 months old	82	53.2
	>12-24 months old	45	29.2
	>24-36 months old	17	11.0
	>36-48 months old	6	3.9
	>48-60 months old	4	2.6
Gender (n=154)	Female	73	47.4
	Male	81	52.6
Severity of pneumonia (n=154)	Mild pneumonia	94	61.0
	Severe pneumonia	52	33.8
	Very severe pneumonia	8	5.2
Number of comorbidities (n=154)	No comorbidities	123	79.9
	1-2 comorbidities	31	20.1
Comorbidities (n=31)	Acute otitis media	12	38.7
	Acute rhinitis	16	51.6
	Immunodeficiency	4	12.9
	Malnutrition	3	9.7
	Diarrhea	2	6.5
	Myeloproliferative disorder	1	3.2

Table 2 shows that the rate of being tested for bacteria was 94.8% (146 patients), of which 50.7% (74 patients) gave positive results. The specimen used was mainly nasopharyngeal fluid (97.9%). Bacterial culture results showed that 3 out of 6 bacteria found in the study sample, with the highest frequency, were *H. influenzae* (63.5%), *S. pneumoniae* (29.7%), and *M. catarrhalis* (12.2%). In addition, some rare strains of bacteria, such as *E. coli* and multidrug-resistant *K. pneumoniae*, were found with a very low frequency. There were 17 out of 154 patients assigned to test for *Mycoplasma pneumoniae* by Real-time Poly-chain Reaction technique, of which 1 case was positive (accounting for 5.9%).

Table 2. Microbiological test characteristics in the study sample

Characteristics			Freq (n)	Percentage (%)
Indication of a test for bacteria (n=154)	Have		146	94.8
	Is not		8	5.2
Specimen (n=146)	Translation of the pharynx		143	97.9
	Blood		5	3.4
Test results for bacteria (n=146)	Positive		74	50.7
	Negative		72	49.3
Bacterial strains identified (n=74)	*H. influenzae*		47	63.5
	S. pneumoniae		22	29.7
	M. catarrhalis		9	12.2
	S. aureus		1	1.4
	K. pneumoniae		1	1.4
	E. coli		1	1.4
Indications for making antibiograms for bacterial strains (n=74)	Yes		60	81.1
	No		14	18.9
Indications to test for *Mycoplasma pneumoniae* (n=154)	Yes		17	11.0
	No		137	89.0
	Result	Positive	1	5.9
		Negative	16	94.1

Out of 74 cases with positive bacterial culture results, 60 cases were subjected to an antibiogram. Quinolone antibiotics maintained their susceptibility to most isolates. Amoxicillin/clavulanate antibiotics maintained 100% sensitivity to the *M.catarrhalis* strain. *H.influenzae* bacteria had a high rate of sensitivity to C3G antibiotics. *S.pneumoniae* bacteria were resistant to the macrolide group at a very high rate, with 100% to clindamycin, 90% to erythromycin, and 86% to azithromycin. The *S. aureus* strain was also sensitive to doxycycline, linezolid, and trimethoprim/sulfamethoxazole. *K.pneumoniae* and *E.coli* strains were resistant to most antibiotics and only sensitive to carbapenem and fosfomycin antibiotics.

There were 12 active antibiotics belonging to the β-lactam, macrolide, and aminoglycoside groups used in the study sample. There were three groups of mainly used antibiotics: Penicillin/β-lactamase inhibitor, 3rd generation cephalosporin, and macrolide. Specifically, ampicillin/sulbactam antibiotics belonging to the group of Penicillins/β-lactamase inhibitors were indicated the most, with a rate of 38.08% of the orders. Next was the antibiotic ceftriaxone, belonging to the 3rd generation cephalosporin group, which was also used relatively commonly, with 26.2% of the orders. In terms of route of administration, intravenous antibiotics predominated at 80.6% of the indicated times. The rest were oral antibiotics, mainly azithromycin, with 14.8% of the indicated times (Table 4).

Table 3. Sensitivity levels of bacteria in the study sample

Antibiotics	Number of times of sensitization/Number of times of making an antibiogram					
	H. influenzae	*M. catarrhalis*	*S. pneumoniae*	*S. aureus*	*E. coli*	*K. pneumoniae*
Ceftazidime/Avibactam					1/1	1/1
Imipenem					1/1	1/1
Amikacin					1/1	1/1
Meropenem				0/1	1/1	1/1
Cefoxitin					1/1	
Ampicillin				0/1	0/1	
Cefuroxime				0/1	0/1	0/1
Ceftriaxone	38/38		15/17		0/1	0/1
Ceftazidime	38/38				0/1	0/1
Gentamycin					0/1	0/1
Trimethoprim/Sulfamethazole			4/13	1/1	0/1	0/1
Amoxicillin/Clavulanic acid	25/36	4/4		0/1		
Levofloxacin	2/2		15/16			0/1
Penicillin G			12/16	0/1		
Clindamycin			0/10			
Moxifloxacin	36/36		13/13			
Doxycycline	1/1			1/1		
Linezolid				1/1		
Cefotaxime	37/37			0/1		
Oxacillin				0/1		
Erythromycin			1/10			
Azithromycin			1/7			
Ertapenem						1/1
Fosfomycin						1/1

Table 4. The proportion of antibiotics used in the study sample

Antibiotic		Name of antibiotics	Route	Indication times	Percent (%)
β-lactam	Penicillin/β-lactamase inhibitor	Ampicillin/sulbactam	Intravenous injection	90	38
		Amoxicillin/clavulanate	Oral	2	0.8
	C2G	Cefuroxime	Intravenous injection	3	1.3
		Cefoxitin	Intravenous injection	1	0.4
	C3G	Ceftriaxone	Intravenous infusion. Intravenous injection	62	26.2
		Cefoperazone/sulbactam	Intravenous injection	11	4.6
		Cefotaxime	Intravenous injection	2	0.8
		Oral	Oral	2	0.8
Macrolide		Azithromycin	Oral	35	14.8
		Clarithromycin	Oral	7	3.0
Aminoglycoside		Gentamicin	Intravenous injection	2	0.8
		Amikacin	Intravenous infusion, Intravenous injection	20	8.5
Total				237	100

There were 12 antibiotic regimens initially selected to be used to treat community-acquired pneumonia at the hospital. Of which, four antibiotics were used alone, and eight antibiotics were used in combination. It was found that the rate of choosing the combination regimen gradually increased with disease severity, which was 22.3%, 38.5%, and 50% respectively, for mild pneumonia, severe pneumonia, and very severe pneumonia. In which the most commonly used antibiotic groups in the initial regimen were penicillin/β-lactamase inhibitor (alone regimen) and penicillin/β-lactamase inhibitor in combination with macrolides (combination regimen) (Table 5).

Table 5. Initial antibiotic regimens when the patient was first admitted to the hospital

	Regime	Mild pneumonia		Severe pneumonia		Very severe pneumonia	
		N	%	N	%	N	%
Alone		73	77.7	32	61.5	4	50
1	Penicillin/ β-lactamase inhibitor	45	47.9	21	40.4	3	37.5
2	C2G	1	1.1				
3	C3G	27	28.7	10	19.2	1	12.5
4	Macrolide			1	1.9		
Combination		21	22.3	20	38.5	4	50
1	Penicillin/ β-lactamase inhibitor + macrolide	9	9.6	5	9.8	1	12.5
2	Penicillin/ β-lactamase inhibitor + aminoglycoside	3	3.2	2	3.8		
3	Penicillin/ β-lactamase inhibitor + macrolide + aminoglycoside			1	1.9		
4	C2G + macrolide	1	1.1				
5	C2G + aminoglycoside + macrolide			1	1.9		
6	C3G + aminoglycoside	4	4.2	1	1.9	1	12.5
7	C3G + macrolide	4	4.2	6	11.5	1	12.5
8	C3G + aminoglycoside + macrolide			4	7.7	1	12.5
Total		94	100	52	100	8	100

The number of patients who kept the original regimen was 107 patients, accounting for 69.5%. The average number of regimen changes was 1.2±0.4. Out of 54 regimen changes, the reason for the change was mainly due to improved clinical symptoms, which accounted for 53.7%. The cases where the regimen was changed due to slow improvement of clinical symptoms accounted for 29.6%. There were 16.7% of regimen changes due to the results of microbiological tests and antibiograms. There were 23 types of alternative regimens encountered in the study sample. The two most common alternatives were from penicillin/beta-lactamase inhibitor plus macrolide to penicillin/beta-lactamase inhibitor alone (16.7%) and from penicillin/beta-lactamase inhibitor to C3G (9.3%) (Table 6).

Table 6. Number of times of change of antibiotic regimen and reasons for change

Characteristics		Freq (n)	Percentage (%)
Not change the regimen		107	69.5
The average number of regimen changes		1.2±0.4	
Reason for change of regimen	Clinical symptoms slowly improve	16	29.6
	Clinical symptoms improved	29	53.7
	Results of microbiological tests and antibiograms	9	16.7
Total		54	100

Table 7. Comparison with recommendations in the selection of initial antibiotic regimens

Regime	Mild pneumonia		Severe pneumonia		Very severe pneumonia		Total	
	N	%	N	%	N	%	N	%
According to recommendations	1	1.1					1	0.6
Amoxicillin/clavulanate	1	1.1					1	0.6
Not as recommended	93	98.9	52	100	8	100	153	99.4
Ampicillin/sulbactam	44	46.8	21	40.4	3	37.5	68	44.2
Ampicillin/sulbactam + aminoglycoside	3	3.2	2	3.8			5	3.3
Ampicillin/sulbactam + macrolide	9	9.6	5	9.6	1	12.5	15	9.8
Ampicillin/sulbactam + macrolide + aminoglycoside			1	1.9			1	0.6
Cefuroxime	1	1.1					1	0.6
Ceftriaxone	20	21.3	7	13.5			27	17.5
Cefoperazone/sulbactam	4	4.2	3	5.8	1	12.5	8	5.2
Cefotaxime	3	3.2					3	2
Macrolide			1	1.9			1	0.6
C2G + macrolide	1	1.1					1	0.6
C2G + aminoglycoside + macrolide			1	1.9			1	0.6
C3G + aminoglycoside	4	4.2	1	1.9	1	12.5	6	3.9
C3G + macrolide	4	4.2	6	11.6	1	12.5	11	7.2
C3G + aminoglycoside + macrolide			4	7.7	1	12.5	5	3.3
Total	94	100	52	100	8	100	154	100

Table 8. Comparison with recommendations for antibiotic doses and rates in patients with normal renal function

Characteristics		Freq (n)	Percentage (%)
According to recommendations	Yes	150	64.4
	No	83	35.6
Not as recommended	Total daily dose (mg/kg/24h)	83	100.0
	Higher than recommended	75	90.4
	Ampicillin/sulbactam	3	3.6
	Azithromycin	11	13.3
	Ceftriaxone	57	68.7
	Amikacin	1	1.2
	Clarithromycin	1	1.2
	Cefixime	2	2.4
	Lower than recommended	8	9.6
	Ampicillin/sulbactam	1	1.2
	Azithromycin	2	2.4
	Amikacin	3	3.6
	Clarithromycin	2	2.4
	The rhythm of drug delivery	18	21.7
	More than recommended	16	19.3
	Ceftriaxone	16	19.3
	Less than recommended	2	2.4
	Clarithromycin	2	2.4

Table 7 shows that the rate of initial treatment regimens not in accordance with the recommendations was very high at 99.4%. There was one case of a patient with mild pneumonia who was selected for the recommended initial treatment regimen. In cases of mild pneumonia and severe pneumonia, initial treatment regimens not in accordance with the guidelines accounted for more than 93 cases, mainly using ampicillin/sulbactam and ceftriaxone. Among cases of very severe pneumonia, antibiotics prescribed not in accordance with the recommendations were 100%, mainly ampicillin/sulbactam at 37.5%.

Table 8 shows that 83/233 patients with normal renal function were prescribed antibiotics at non-recommended doses or rates or both, accounting for 35.6%. Regarding dosage, 57/83 cases of ceftriaxone were prescribed at higher than recommended doses. Regarding drug rates, 18 cases were not as recommended. Of these, 16 cases had higher than recommended rates for ceftriaxone, and 2 cases had lower than recommended rates for clarithromycin.

4. Discussion

In Vietnam, the use of non-prescription drugs has become a common and uncontrolled phenomenon, of which antibiotics are a typical example[8]. Arbitrary use of antibiotics can cause consequences for patients, such as unwanted effects, and the most serious consequence is increasing antibiotic resistance of bacteria, affecting the treatment results of the patient. Culturing and detecting bacteria is necessary for more effective and safer use of antibiotics. In this study, 50.7% of cases tested positive for bacteria, mainly *H.influenzae*, *S.pneumoniae*, and *M.catarrhalis*. These are the main bacterial strains causing pneumonia [1, 9, 10]. In this study, we have not mentioned viral agents. This is also the agent that causes pneumonia in children and has the risk of causing antibiotic resistance. And using antibiotics on children infected with viruses can cause many potential risks [11, 12]. This agent should be considered in future studies.

The results of our study showed that ampicillin/sulbactam antibiotics belonging to the group of penicillins/β-lactamase inhibitors were the most indicated, with 38.08% of indications for treatment for inpatients with community-acquired pneumonia in the study setting. In another study in central Vietnam, the preferred antibiotic was single-component cefuroxime [13]. Although there is a difference in the order of priority between the penicillin and cephalosporin groups, our research and many other studies show that these two groups are most indicated when treating community-acquired pneumonia in children. Specifically, in our study, ampicillin/sulbactam and ceftriaxone were the two antibiotics with the most indications. Ampicillin/sulbactam is a broad-spectrum antibiotic that is active against many strains of bacteria, including *H. influenzae*, *S.pneumoniae*, and *M. catarrhalis*. These are also the bacteria that account for a large proportion of community-acquired pneumonia in Viet Nam. The antibiotic ceftriaxone also has a good effect on *S. pneumoniae* and shows absolute sensitivity against *H. influenzae*. This is also the reason why these two antibiotics were used with the highest frequency in our study. The third most common antibiotic used in our study was a macrolide antibiotic (17.8%). This group of antibiotics is less toxic, with few side effects; thus, it is often used in pediatrics. However, currently, the situation of drug resistance to macrolides in Vietnam tends to increase [14]; hence, the macrolide group is often used in combination with the beta-lactam group to treat suspected cases of atypical pneumonia. Meanwhile, some publications show the opposite trend [10]. The group of antibiotics that accounted for the lowest percentage in our study was the aminoglycoside group (9.3%), mainly amikacin and gentamicin. Aminoglycoside antibiotics were rapidly bactericidal and were indicated for the treatment of severe or life-threatening infections. However, amikacin, as well as other antibiotics of the aminoglycoside

group, had nephrotoxic side effects, which should only be indicated in cases of severe pneumonia. In terms of routes of administration, intravenous antibiotics predominated 80.6% of the indicated times, and the rest were oral antibiotics, mainly azithromycin, with 14.8% of the indications.

Most patients were given the regimen alone at the time of admission, accounting for 109/154 patients (70.8%). The proportion of patients using the combination regimen accounted for 29.2%. In which the single most used regimen is a penicillin/β-lactamase inhibitor (44.8%), followed by C3G (24.7%). According to the guideline for the treatment of CAP in children of the Ministry of Health, antibiotic C3G is not recommended in the treatment of community-acquired pneumonia in the first place. When using antibiotics by injection, ampicillin and penicillin G are the initial choices [15]. Given the high prevalence of β-lactamase-producing *H.influenzae* and *M.catarrhalis* strains in Vietnam, using penicillin in combination with a β-lactamase inhibitor may be an alternative [5]. Of note, according to the 2015 Antibiotic Use Guidelines, aminoglycosides should only be combined in very severe cases of pneumonia [5]. However, in our study, the rate of 7.4% of mild pneumonia cases and 15.3% of severe pneumonia cases were assigned to use an aminoglycoside combination. Research in some other countries also shows that using only single-component antibiotics to treat pneumonia still gives very positive results [16]. Therefore, more research is needed to evaluate the effectiveness of monotherapy and combination antibiotic regimens in Vietnam.

The rate of combination of beta-lactam antibiotics with macrolide antibiotics in cases of mild, severe, and very severe pneumonia was 9.6%, 9.8%, and 12.5%, respectively. The rate of combination of cephalosporin and macrolide antibiotics in cases of mild, severe, and very severe pneumonia was 5.2%, 11.5% and 12.5%, respectively. The combination of macrolide antibiotics with initial antibiotics in the treatment of atypical bacterial pneumonia has been mentioned in the Ministry of Health Antibiotic Use Guidelines 2015 [5] and BTS 2021 [6]. In particular, macrolides could be added at any age if there was no response to initial treatment or if *Mycoplasma* or *Chlamydia pneumonia* is suspected, or in very severe cases. Besides, in our study, another initial regimen was penicillin/β-lactamase inhibitor or C3G in combination with macrolides and aminosides, which was found in 1/52 of patients with severe pneumonia. The ratio of C3G in combination with macrolides and aminoglycosides was 4/52 patients in severe pneumonia and 1/8 patients with very severe pneumonia.

The number of patients who kept the original regimen was 107, accounting for 69.5%. The average number of regimen changes was 1.2±0.4. Among 54 regimen changes, the main reason for the change was due to improved clinical symptoms, accounting for 53.7%. The cases where the regimen was changed due to slow improvement of clinical symptoms accounted for 29.6%. There were 16.7% of regimen changes due to the results of microbiological tests and antibiograms. The rate of change of the initial antibiotic regimen in the study sample was 30.5%.

The reason for the high rate of change of the initial antibiotic regimen in the study sample may be due to the high prevalence of severe and very severe pneumonia at the time of admission in the study setting. The use of antibiotics in hospitals in the lower level of the health system, or the patient's self-administration of antibiotics before admission, can cause false negatives in microbiological tests or lead to decreased sensitivity of bacteria to antibiotics. That forces doctors to use broad-spectrum antibiotics or expand the spectrum of action by combining multiple antibiotics, specifically, a combination regimen of penicillin/beta-lactam inhibitor or ceftriaxone in combination with amikacin or macrolide. When the patient's clinical symptoms improve and the duration of amikacin and macrolide antibiotics used is shorter than the penicillins/beta-lactam and C3G inhibitors, physicians could switch from the initial

combination antibiotic regimen to a single antibiotic regimen. This could be used to explain the matter that the improvement in clinical symptoms could be the main reason for the change of regimen.

The results showed a high rate of non-use of penicillin/β-lactamase inhibitors as recommended. In the mild pneumonia group, only 1 case of penicillin/β-lactamase inhibitor was prescribed exactly according to the guidelines (0.6%). Inappropriate antibiotic use in pediatric pneumonia remains quite common in many countries [17]. In the severe pneumonia group, 21/52 children were prescribed intravenous ampicillin/sulbactam instead of ampicillin alone as recommended. However, another recommendation suggested that, given the high prevalence of β-lactamase-producing *H. influenzae* and *M. catarrhalis* strains in Vietnam, the use of penicillin in combination with a β-lactamase inhibitor could be an alternative. In the very severe pneumonia group, 3/5 times intravenous ampicillin/sulbactam was prescribed was not according to the guidelines.

The results showed that 83/233 cases of patients with normal renal function were prescribed antibiotics that were not as recommended in terms of dose and rhythm, or both, accounting for 35.6%. Regarding dosage, 75 cases were prescribed doses higher than the recommended dose, mainly ceftriaxone, with 57 cases. Of these, it should be noted that one case prescribed a dose of amikacin higher than the recommended dose. For aminoglycoside antibiotics, the use of high doses even in people with normal renal function can cause undesirable effects on the kidneys and hearing. In contrast, aminoglycosides are concentration-dependent antibiotics, and the ability to achieve the Cpeak/MIC ratio (Cpeak is the peak concentration in serum of the drug, MIC is the minimum inhibitory concentration), the time factor is no longer considered. The Cpeak/MIC ratio is a factor to evaluate the treatment efficacy; therefore, using a lower dose of amikacin than the recommended dose does not guarantee the treatment efficacy because the desired Cpeak has not been achieved. In our sample, there were 3 times that amikacin was prescribed at a lower dose than the recommended dose, accounting for 3.6%. Regarding the drug use rate, there were 18 cases not as recommended, of which 16 cases were higher than the recommended dose of ceftriaxone and 2 cases were lower than the recommended dose of clarithromycin. With time-dependent antibiotics such as beta-lactams and macrolides, the decisive factor for efficacy is the time the drug concentration is above the minimum inhibitory concentration (MIC). The drug delivery rate affects the drug concentration maintained in the blood; therefore, failure to ensure the number of doses can lead to unachievable drug concentration in the blood, reducing the treatment efficacy.

Limitations of the study:

- The data collection time of the topic in the context of the complicated developments of the COVID-19 epidemic, so the sample size is not large enough. Medical records related to COVID-19 are also not mentioned.
- The study was only conducted on retrospective data in medical records, so there may be information that is incomplete and unclear.

5. Conclusions

The use of antibiotics in the treatment of community-acquired pneumonia in children at a tertiary hospital still has shortcomings. It is necessary to develop a system of assessment and monitoring of antibiotic use, from which timely adjustments and control can be made, to limit the ability of bacteria to develop drug resistance.

Conflicts of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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