ORIGINAL ARTICLE

Antibiotic Prescription Patterns among Pediatric Patients with Pneumonia in Primary Care – A Retrospective Cohort Study

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ABSTRACT

Background and Objectives. The etiology of pneumonia in the pediatric population varies by age group. Among patients one month to 59 months old, viral pathogens are the most common cause of lower respiratory infections. The study aims to determine the frequency distribution of antibiotic prescription among patients one month to 59 months old and to determine the adherence of primary care facilities to local guidelines with recommended antibiotics.

Methods. A descriptive retrospective study using electronic medical records was conducted at two primary care sites. Patients aged 1 month to 59 months old seeking consult via telemedicine or face-to-face diagnosed with community acquired pneumonia from April 2019-March 2020 in the rural facility and May 2019-April 2020 in the remote facility were included in the study. The primary outcome was to determine the patterns of antibiotic use in pneumonia in remote and rural areas and adherence to the recommended antibiotics by the 2016 Philippine Academy of Pediatric Pulmonologists pediatric community-acquired pneumonia clinical practice guidelines (CPG).

Results. There were 30 pediatric patients diagnosed with pneumonia in the rural facility and 213 in the remote facility. Of these patients with pneumonia, 96.7% and 94.8% were prescribed antibiotics in the rural and remote sites, respectively. The most commonly prescribed antibiotic in the rural facility was co-amoxiclav (26.7%), while amoxicillin (51.6%) was the most common in the remote facility. Adherence to the CPG in the rural site was lower at 23.3% (n=8/30) compared to the remote site which was 55.9% (n=119/213).

Conclusion. Primary care physicians prescribed antibiotics in over 90% of the time upon the diagnosis of pneumonia in children aged one month to 59 months old, despite viral pneumonia being the more common in primary care setting. Adherence to recommended antibiotics was higher in the remote setting than in the rural setting. Use of EMR to monitor quality of care can improve patient outcomes and safety, pointing out the importance of improving the quality of documentation in the study sites.

Keywords: pediatrics, pneumonia, primary care, antibiotic prescription, adherence to guidelines

INTRODUCTION

Irrational antibiotic use leads to the emergence of drug-resistant bacteria, higher treatment costs, prolonged hospitalization, and adverse drug reactions. Antibiotic resistance was directly related to the rate of antibiotic use in the community[1]; hence, there is a need to highlight intervention measures and antimicrobial stewardship initiatives in primary care. The inappropriate prescription of antibiotics by trained and untrained healthcare workers for conditions with no

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proven benefit of such therapy, such as in viral infections, increases antimicrobial resistance and unnecessary expense to patients and the healthcare system.[2,3]

Pediatric community-acquired pneumonia (PCAP) is the leading cause of infant and under-five morbidity and mortality, accounting for 14% for all causes of mortality. Most deaths attributed to pediatric pneumonia primarily occurred in developing countries.[4] The World Health Organization (WHO) developed strategies and recommendations for limited resource settings to identify simple signs in classifying the severity of pneumonia.[4] These recommendations were made to assist national health programs in revising local pneumonia guidelines. Implementation of childhood immunization programs with pneumococcal and Hib conjugate vaccines resulted in a shift in bacterial etiology. The empiric antibiotic choice for PCAP per setting largely depends on the most common bacterial etiology, host factors, local resistance patterns, and immunization status.[5]

The etiology of pneumonia in the pediatric population varies by age group. For infants and children older than one month and younger than five years old, viral pathogens are the most common cause of lower respiratory infections. Multiple studies reported that respiratory syncytial virus (RSV), influenza and rhinoviruses were the most identified pathogens in our local setting.[6,7] In a study by Singh, virus was found in 37% and bacteria in 18% of patients with pneumonia.[8] *Streptococcus pneumoniae* and *H. influenzae* was the most common bacteria isolated, and RSV was the most common virus isolated.[8] A study by Ning et al. stated that 40% of the virus detected in patients with pneumonia was RSV.[9] Studies showed that unvaccinated children are at risk of pneumonia due to *S. pneumoniae and H. influenzae* type B (Hib).[10,11] Among children given Hib and pneumococcal vaccines, viruses, particularly RSV, were the predominant cause of hospitalization; but bacteria continued to cause 25% of the cases based on the PERCH study.[12] A study conducted by Nascimento-Carvalho et al. determined the frequency distribution of viral and bacterial pneumonia in hospitalized children—46.4% were viral, 14.4% were bacterial and 25.4% were co-infection.[13] In a study done by Suzuki et al. in Tacloban, of 819 patients, 501 patients (61.2%) were identified with at least one virus. The most common isolated viruses were human rhinovirus (n= 189, 23%) and RSV (n=165, 20.1%). Only 31 patients (3.8%) were positive for bacteria in blood culture, and of which *S. pneumoniae* (n=4) was the most common.[7]

The Philippine Academy of Pediatric Pulmonologists (PAPP) developed the 2016 3rd PAPP Update in the Evaluation and Management of Pediatric Community-acquired Pneumonia (2016 PAPP CPG). This CPG aimed to standardize the approach to the evaluation and management of uncomplicated community-acquired pneumonia in immunocompetent patients aged three months to 19 years old. In this CPG, PCAP A and B are defined as non-severe pneumonia that can be managed on an outpatient basis; while PCAP C and D are severe to very severe cases. Based on this guideline, the decision to start empiric treatment depends on clinical judgment since bacterial pneumonia was difficult to distinguish from viral pneumonia. The CPG recommended that bacterial pneumonia be presumed in the presence of clinical signs and symptoms of pneumonia plus any of the following parameters—elevated white blood count, C-reactive protein, procalcitonin, or imaging findings of consolidation or alveolar infiltrates. Without these ancillary parameters, the decision to start antibiotics was based on the clinician's judgment.[14]

Based on the 2016 PAPP CPG, amoxicillin is the first-line antibiotic in patients with suspected bacterial non-severe pneumonia regardless of immunization status. Macrolides, such as azithromycin or clarithromycin, may also be given if with hypersensitivity to amoxicillin, or if atypical pathogens are suspected. In cases of severe pneumonia, vaccination status affects the choice of antibiotic. Penicillin G is recommended for those with completed vaccination against *H. influenzae type b*; while ampicillin is recommended for those with unknown or incomplete immunization status.

The WHO Integrated Management of Childhood Illness (IMCI) recommendations for the management of pneumonia advises the use of oral amoxicillin for children with tachypnea or retractions. Among patients with other signs of severe pneumonia, one dose of oral antibiotic should be given before referral to the closest higher-level health facility. The WHO created this approach for countries with limited resources and constrained health systems like the Philippines.

A paradigm shift toward primary care is expected after the universal health care law was signed in 2019. The Philippine Primary Care Studies (PPCS) implemented a model to strengthen the primary care health delivery in three healthcare centers in preparation for universal health care implementation. Three pilot healthcare centers — urban, rural, and remote - provided information on how these systems and methods can be implemented across the country and their impact and challenges. Primary care PhilHealth benefits were provided through primary care facilities, and consultations, tests, and treatments were covered for beneficiaries. The rural site started the program last April 2019, and the remote site started its implementation last May 2019. The rural site was Samal, a fourth-class municipality in Bataan with 35,298 residents. The remote site was Bulusan, a fourth-class municipality in the Province of Sorsogon. This site is considered a geographically isolated and disadvantaged area (GIDA), catering to 23,932 residents. PhilHealth benefits were consistently provided in the first year of implementation. In the succeeding years, only residual funds were available.

This study evaluated the quality of care in the rural and remote primary care facilities of the PPCS. Based on the WHO manual on the utilization of drug use in health facilities, adherence of drug prescription practices to local treatment guidelines is a good measure of quality of care.[15]

There are no local data that describe antibiotic prescription patterns in the primary care setting and the adherence to the national clinical practice guidelines with empiric antibiotics in the pediatric population. Hence, adherence to first-line antibiotics based on the CPG recommendations was used as a measure of quality of care in this study.

The aims of this study are: (1) to determine the frequency distribution of antibiotic prescription among patients aged one month to 59 months old diagnosed with pneumonia at the rural and remote primary care facilities; and (2) to determine the adherence of primary care facilities with recommended antibiotics from local guidelines.

METHODS

Study Design

The study was a retrospective chart review using the electronic medical records (EMR) of the rural and remote primary care sites of the PPCS.

Study Population

Eligibility criteria included all patients aged one month to 59 months old seeking consult via telemedicine or face-to-face diagnosed with community acquired pneumonia with ICD codes J09-J18 in the EMR of two primary care facilities, rural and remote. Patients diagnosed with hospital-acquired pneumonia were excluded from the study.

Data Collection

Sociodemographic data and clinical profiles of pediatric patients diagnosed with pneumonia based on the working assessment of the primary care physician were obtained using EMR from April 2019 to March 2020 at the rural-based primary care facility and from May 2019 to April 2020 at the remote-based primary care facility.

More specifically, the patient demographics and clinical profile of both rural and remote primary care facilities to be extracted from the EMR included the following:

- Patient's sex
- Chief complaint
- Number of clinic consultations for the same complaint in a year
- First consultation
- Total number of hospital admission
- Exposure to tuberculosis
- Past medical illnesses
- Clinical symptoms (history of present illness) – fever, cough, poor appetite, vomiting, loose stools, poor activity, etc.
- Chest physical examination findings – crackles, rhonchi, decreased breath sounds
- Signs of severe pneumonia
- Radiographic evidence
- Laboratory evidence of elevated white blood cell (WBC) for age, procalcitonin, and C-reactive protein (CRP)

Clinical symptoms and significant chest physical examinations (decreased breath sounds and adventitious breath sounds such as crackles and rhonchi) as encoded by the attending physician were to be tabulated. The presence of any of the following — cyanosis, desaturation, increased work of breathing or impending respiratory failure (head bobbing, retractions, apnea, grunting), decrease in sensorium, seizures, signs of shock, inability to tolerate oral intake, signs of dehydration, were considered signs of severe pneumonia warranting hospital admission. Aside from the clinical signs mentioned, terms such as 'increased sleeping time', 'increased fussiness or more irritable', 'poor oral intake', 'vomiting', 'poor skin turgor', 'skin tenting', 'cool tips', 'poor pulse' also indicated severe pneumonia and were to be classified as such.

When available, positive radiograph findings and laboratory evidence of elevated WBC and inflammatory markers (CRP) were included in the study. A value of CRP above 6 was significant and the likelihood of antibiotic prescription would be extracted.

Adherence to CPG

The two most commonly used CPGs in the Philippines is the PAPP CPG and the WHO IMCI guidelines. This study assessed adherence based on recommendations of the 2016 PAPP CPG on empiric antibiotic use for PCAP. We deemed that the local CPG would be more appropriate since this CPG based its recommendations on the local epidemiology and antibiotic resistance patterns. We used the 2016 PAPP CPG since this was the version available during the study implementation, although this CPG was recently updated in the year 2021.

In the 2016 PAPP CPG, first line of treatment for non-severe PCAP, regardless of immunization status, should be amoxicillin. If there was a documented hypersensitivity to penicillin or if atypical pathogens were suspected, azithromycin or clarithromycin may be used. The recommended empiric antibiotic in cases of severe pneumonia is penicillin G (if vaccinated) and ampicillin (if unknown or incomplete vaccination).

Data Analysis

Adherence rates to recommended empiric antibiotics based on the 2016 PAPP CGP in both rural and remote primary care facilities were determined for both severe and non-severe pneumonia. Adherence rate was computed as the total number of patients prescribed with any of the recommended empiric antibiotics based on the 2016 PAPP CPG according to pneumonia severity out of the total number of patients diagnosed with pneumonia, then multiplied by 100.

$$\text{Adherence rate (\%)} = \frac{\text{total \# of patients prescribed recommended antibiotic}}{\text{total \# of pneumonia cases}} \times 100$$

Sociodemographic variables and clinical parameters were summarized as means with standard deviation (SD) or frequency with percentages. The variables included in the study are age, sex, exposure to tuberculosis, number of clinic consultations for the same complaint in a year, and total number of hospital admissions.

From the EMR, we tabulated the antibiotics prescribed to patients diagnosed with pneumonia. The prescription rates of the different antibiotics at the two primary care facilities were also determined. The prescription rate was computed as the number of antibiotic prescriptions divided by the total number of pneumonia cases; the quotient was multiplied by 100. Antibiotic prescription was described as the first prescription of an antibiotic or a change in regimen on follow-up. We excluded prescriptions for metronidazole and nitrofurantoin which are commonly used in intestinal and urinary tract infections, respectively. We were primarily interested in drugs prescribed for respiratory infections.

$$\text{Prescription rate (\%)} = \frac{\text{total \# of antibiotic prescriptions}}{\text{total \# of pneumonia cases}} \times 100$$

Ethical Considerations

This study was carried through as one of the performance indicators of quality of care under the PPCS. The PPCS was granted ethical clearance by the University of the Philippines Manila Research Ethics Board (UPMREB) under study protocol code UPMREB 20-15-489-01. Identities and information of the patients from the EMR remained anonymous throughout the study. Patient information was encoded in MS Excel with only patient identification number and consultation number accessible to the primary investigator. Personal identifiers such as names and contact information were not included in data gathering. Confidentiality of data was ensured throughout the study process. Only the researchers and data gatherers had access to the study information.

RESULTS

There were 30 pediatric patients diagnosed with pneumonia in the rural facility and 213 pneumonia cases in the remote facility during the study period. The socio-demographic profile of these patients is tabulated below (Table 1). Majority of the cases were male patients — 60% (18/30) and 52.1% (111/213) in the rural and remote facilities, respectively. The mean age of diagnosis was 2.1 years old (SD 1.4) for the rural facility and 2.2 years old (SD 1.7) for the remote facility. One patient reported tuberculosis exposure. Only three pneumonia cases in total from the rural and remote healthcare facilities had recorded exposure to second-hand smoking.

Over 90% of diagnosed cases of pneumonia were prescribed antibiotics for both primary care facilities. At the rural facility, the most commonly prescribed antibiotic was co-amoxiclav (26.7% or 8/30). In the remote facility, the most common was amoxicillin, 51.6% (110/213). Table 2 demonstrated the frequency distribution of pediatric patients prescribed with antibiotics and prescription rates.

Table 1. Sociodemographic Profile of Pediatric Patients (aged one month to 59 months) Diagnosed with Pneumonia Seeking Consult at Two Primary Care Facilities

Demographics	Rural (N=30)	Remote (N=213)
Sex Ratio (Male: Female)	18:12	112:101
Child's age in years (mean ± SD)	2.1 ± 1.4	2.2 ± 1.7
Number of clinic consultations in a year (mean ± SD)	2.9 ± 2.8	2.0 ± 1.5
Smoking exposure	1	2
Tuberculosis exposure	0	1

Table 2. Frequency Distribution of Pediatric Patients with Pneumonia Prescribed with Antibiotics and their Prescription Rates

	Rural N = 30 No. of cases (%)	Remote N = 213 No. of cases (%)
With antibiotic prescription	29 (96.7)	202 (94.8)
Recommended empiric antibiotic based on CPG*	8 (26.7)	119 (55.9)
Amoxicillin	1 (3.3)	110 (51.6)
Macrolides	7 (23.3)	9 (4.2)
Unrecommended antibiotic prescribed	21 (70.0)	83 (38.9)
Co-amoxiclav	8 (26.7)	36 (16.9)
Cefalexin	7 (23.3)	28 (13.1)
Cloxacillin	0	10 (4.7)
Cefuroxime	5 (16.7)	9 (4.2)
Cefixime	1 (3.3)	0

** Recommended antibiotics for non-severe pneumonia based on 2016 PAPP CPG*

In both settings, cough, colds, and fever were the most common presenting symptoms that led to the diagnosis of pneumonia. Other associated symptoms were difficulty of breathing or shortness of breath, loose stools, and body pains. There was no data recorded in the EMR on past medical illnesses, physical examination findings, other signs pointing to severe pneumonia, social background, and previous hospitalizations. There was also no available information on laboratory results to assess the need to start empiric antibiotics. Two patients had chest radiographs done, with results stating pneumonia. However, specific descriptions of the chest radiographs were not available. Due to the lack of information in the EMR, we could not determine the severity classification of the pneumonia cases in the study. We therefore assumed that all patients had non-severe pneumonia in calculating the adherence rate.

The PAPP guidelines specify amoxicillin as the first line of treatment for non-severe pneumonia, with conditional statement recommending azithromycin or clarithromycin

if with history of penicillin hypersensitivity. The adherence rate to the recommended antibiotic was higher in the remote setting (55.9%, 119/213) than in the rural setting (26.7%, 8/30).

DISCUSSION

Frequency Distribution of Antibiotic Prescription in the Treatment of Non-severe Pneumonia

In this study, identified pneumonia cases were fewer in the rural than in the remote facility, but this did not necessarily mean the prevalence of pediatric pneumonia was less in the rural community. The disparity in the number of pneumonia cases suggests that the primary care program is considered essential and is being utilized more by the remote community.

Due to insufficient evidence to differentiate bacterial from viral pneumonia based solely on clinical signs and symptoms, there is excessive prescription of antibiotics especially for acute respiratory infections observed worldwide. This is particularly prominent in resource-limited settings. In addition, despite viral pathogens being the predominant etiologic agent in pediatric pneumonia, public health training especially in resource-limited settings employ WHO guidelines that recommend antibiotic use in cases of suspected pneumonia. This may explain why antibiotic prescription rates in this study were very high. In the rural and remote sites, more than 90% of children with pneumonia were given antibiotics. This is an alarming high percentage, especially considering the age group of the study participants where viral pneumonia is more common.

Moreover, local data on etiology of pneumonia is not readily accessible. Based on a study by Suzuki, et al. in Tacloban, virus is the most common etiology in pneumonia at 61% and only 3% of the cases had definitive bacterial etiology.[7] This information may be crucial for providers in their assessment of the microbial etiology of pneumonia. Based on findings of this study, primary care physicians tend to overprescribe antibiotics to manage pediatric pneumonia.[13] The overuse of antibiotics may lead to increased antimicrobial resistance in the Philippines.

The study intended to correlate clinical symptoms, physical examination, laboratory, and radiographic findings with the likelihood of bacterial pneumonia and antibiotic prescription. With the available data encoded in the EMR, the most common symptoms that led to the diagnosis of pneumonia were cough, colds, and fever. One study mentioned that the presence of co-morbidities influenced antibiotic prescription for pneumonia.[16] However, there were no recorded information from the EMR regarding co-morbidities, past illnesses, and environmental exposure to establish an association with antibiotic prescription. Pertinent signs and symptoms, and other relevant information pointing to a diagnosis of severe pneumonia were also not recorded in the EMR. According to the WHO Primary health care measurement framework and indicators, EMRs are one of the main data sources for primary healthcare monitoring capacity and performance indicators. Data from the EMR can help improve quality of care, patient outcomes and safety through improved management, reduction in medication errors, and modernized interactions among primary care providers and others involved in the care of the patient.[3] This highlights the importance of improving the quality of documentation in the study sites.

Adherence to the guidelines

The 2016 PAPP PCAP guidelines recommended two empiric choices for non-severe pneumonia considering the local resistance patterns in the rural and remote settings. Amoxicillin was the first line antibiotic — and in cases of hypersensitivity to amoxicillin, macrolides may be given. However, co-amoxiclav was one of the most commonly prescribed antibiotics in both settings. Cefalexin was another frequently prescribed antibiotic. Traditionally, clinicians commonly presume that oral cephalosporins were more effective than amoxicillin for *Streptococcus pneumoniae*. This assumption might come from the knowledge that penicillin-resistant pneumococci were more susceptible to Ceftriaxone, especially in severe pneumonia; hence, oral cephalosporins were assumed more effective than amoxicillin. However, oral cephalosporins, especially the first generation, have shorter half-lives, are highly protein bound, and need to be administered more frequently.[5] Hence, amoxicillin is still the drug of choice for the pediatric pneumonia. Using the 2021 drug price reference index, the outpatient treatment with amoxicillin costs PhP50,000 per 1000 of the pediatric population.[17] This is in contrast with the estimated cost of the most expensive unrecommended antibiotic, cefuroxime, which is around PhP175,000 per 1000 pediatric population. This is about four times more expensive than what should be the cost for outpatient treatment of pediatric pneumonia.[18] While not as commonly prescribed, macrolides such as azithromycin and clarithromycin might be appropriate if there was information on history of drug allergies. In this age group, atypical pathogens are less common.

In this study, adherence rates with recommended empiric antibiotics were higher in the remote than in the rural site. On the MAREA study based in Liguria, Italy, one common reason for guidelines discordance was on recommended duration of antibiotic use, rather than choice of antibiotic. Macrolides and cephalosporins were highly prescribed in that setting.[19] In another study based in South Africa using the WHO guidelines, only 18% of patients were classified correctly to need antibiotic therapy prior to referral.[20]

Based on a study by Qumsaya et al., possible major barriers to adherence were complexity of guideline documents, high number of weak or conditional recommendations, and time constraints due to clinical responsibilities.[21] Familiarity of clinicians with the clinical practice guidelines also vary depending on training and exposure, which could impact adherence. The 2016 PAPP CPG offered structured

parameters to classify pneumonia severity, but had only equivocal recommendations to starting antibiotics in primary care.

Limitations

The association of antibiotic prescription practices and the clinical profile of patients with pneumonia could not be evaluated because of insufficient data from the EMR. The advantage of EMR in generating data for research and further improvements of the program is well-documented; however, due to lack of recorded data on physical examination findings, specific symptoms, and pertinent ancillary history, this advantage was not fully realized. There is a need to improve the quality of recordkeeping by standardizing the checklist of signs and symptoms for pneumonia cases, or by making relevant response fields required. The importance of proper orientation and training in the use of the EMR should also be emphasized.

The diagnosis of pneumonia was based on physician diagnosis, as identified by the ICD code encoded by the attending physician. We did not review the specific parameters, such as clinical symptoms, physical examination findings, radiographic and laboratory results, to confirm the diagnosis. Thus, the results of this study are heavily reliant on the accuracy of the physician's assessment and encoding into the EMR. The marked difference in the number of pneumonia cases between rural and remote settings suggests that further studies on the knowledge and skills of primary care providers in the diagnosis of pneumonia in different sites in the Philippines may also be explored.

We also could not determine the severity classification given the paucity of information in the EMR. We assumed all patients to have non-severe pneumonia in calculating the adherence rate; however, this may be an overestimation of the actual adherence rate.

Furthermore, we did not evaluate factors that may affect adherence to antibiotic prescription, such as familiarity with existing guidelines, perceived complexity of guideline documents, and which guidelines are commonly used by primary care providers. There are some differences in the approach to pneumonia based on the PAPP guidelines used in this study, and other guidelines commonly used in the Philippines such as the WHO IMCI guidelines. Future research may be done to explore factors affecting antibiotic prescription patterns and adherence among primary care providers.

CONCLUSION AND RECOMMENDATIONS

More than 90% were prescribed antibiotics in both rural and remote facilities upon the diagnosis of pneumonia in children aged one month to 59 months old. In prescribing antibiotics in accordance with the 2016 PAPP CPG, there was low adherence rates in both the rural and remote settings, with the adherence rate in the rural site lower than the remote site. Use of EMR to monitor quality of care can improve patient outcomes and safety, pointing out the importance of improving the quality of documentation in the study sites.

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Disclaimers

Views expressed by the authors in the submitted article are their own and not an official position of the institution or funder.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors have no conflicts of interest to declare.

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