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Research Article

Analysis of Antibiotic Use in Outpatient Pneumonia Patients at X Blitar Health Center using the Gyssens Method and the Defined Daily Dose

Hesti Rima Hariyani [1]

Rina Widiyawati [2]

Fauna Herawati [1*]

Nurul Chusna [3]

[1] Department of Pharmacy, Universitas Surabaya, Surabaya, East Java, Indonesia
[2] Doctoral Program of Public Health, Universitas STRADA Indonesia, Kediri, East Java, Indonesia
[3] Department of Pharmacy, Universitas Muhammadiyah Palangkaraya, Palangka Raya, Central Kalimantan, Indonesia

*email: fauna@staff.ubaya.ac.id; phone: +6282149889295

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Abstract

Pneumonia is a respiratory infection that remains a public health problem and requires appropriate antibiotic therapy. However, irrational use of antibiotics has the potential to increase resistance and worsen patient clinical outcomes. This study aims to analyze antibiotic use among outpatient patients with pneumonia at the X Blitar Health Center using the Defined Daily Dose (DDD) and Gyssens methods. This study employed a cross-sectional approach, utilizing secondary data from 109 medical records and prescriptions for pneumonia patients (ICD-10 codes J12-J18) from February 2024 to May 2025. Quantitative analysis was conducted using the DDD per 1,000 patients per day method, while qualitative analysis of prescriptions was performed using the Gyssens method. The results showed that Amoxicillin (J01CA04) was the most widely used antibiotic, namely 232.42 DDD/1,000 patients per day, followed by Cefadroxil (87.04 DDD/1,000 patients per day), Ciprofoxacin (18.35 DDD/1,000 patients per day), and Azithromycin (15.29 DDD/1,000 patients per day). Gyssens' analysis revealed that most prescriptions fell into categories IIA (33.94%), IVA (29.36%), and V (27.52%). Inaccurate dosage and suboptimal antibiotic selection were the leading causes of irrational antibiotic use. Additionally, 30 pneumonia patients were identified who did not receive antibiotics despite having clinical indications for them. The results of this study emphasize the need for rationalization training in therapy, prescription audits, and strengthening the implementation of clinical guidelines in primary care facilities.

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INTRODUCTION

Antibiotic resistance has become a serious threat to public health worldwide. The World Health Organization (WHO) states that antimicrobial resistance (AMR) is one of the top global threats requiring immediate intervention[1,2]. AMR not only threatens the clinical effectiveness of existing treatments but also escalates global disease burden, with mortality projections reaching 10 million deaths annually by 2050 if left unchecked[3]. The inappropriate use of antibiotics, including improper drug selection, incorrect dosing, and inadequate treatment duration, is the primary driver accelerating resistance in pathogenic bacteria responsible for severe respiratory infections, particularly pneumonia[4,5]. Pneumonia remains one of the most prevalent respiratory tract infections and a leading cause of morbidity and mortality globally[6], causing over 2.5 million deaths each year, with young children and the elderly representing the most vulnerable populations[7]. Consequently, pneumonia is a critical focus of global and national efforts to promote rational antibiotic stewardship.

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In Indonesia, primary healthcare centers serve as the main gateway to health services but face distinct operational challenges in managing pneumonia cases. According to data from the Ministry of Health of the Republic of Indonesia, pneumonia consistently ranks among the five most common outpatient diseases, with clinical visits increasing annually[8]. Primary care facilities frequently encounter limitations in rapid diagnostic infrastructure, variability in clinician competence, and high patient-volume pressures[9]. These operational constraints heighten the risk of suboptimal antibiotic prescribing, including inappropriate drug selection, inaccurate dosing, and improper treatment duration. Furthermore, monitoring and evaluation systems for antibiotic stewardship in primary care are not yet standardized. The absence of routine audit and feedback mechanisms hinders effective monitoring of prescribing practices, ultimately accelerating rates of resistance and causing unnecessary healthcare expenditure[10].

A review of the literature reveals that studies evaluating antibiotic use for pneumonia in Indonesian primary healthcare settings remain limited. Existing evaluations predominantly focus on secondary or tertiary hospital inpatient settings and often employ incomplete analytical methods[11]. Standardized internationally recognized auditing frameworks, such as the Gyssens method for qualitative prescribing quality and the Defined Daily Dose (DDD) metric for quantitative consumption, are rarely applied in combination within primary care[12]. If this gap persists, irrational antibiotic prescribing in primary care will remain undetected and unaddressed, predisposing patients to treatment failure, prolonged illness, and adverse drug events. Moreover, the lack of standardized metrics hinders evidence-based policy implementation and restricts the optimization of antimicrobial stewardship programs[13,14].

The Gyssens method provides a structured qualitative framework for evaluating antibiotic appropriateness across categories such as indication, drug selection, dosage, route of administration, interval, and duration of therapy[12]. Concurrently, the DDD system, developed by the WHO Collaborating Center for Drug Statistics Methodology, provides standardized quantitative units (such as DDD per 1,000 patient-days) to measure and compare consumption patterns across health facilities and over time[15]. Integrating these two complementary methodologies provides a comprehensive mapping of both prescribing quality and utilization volume. Previous work, such as that by Syam and Karuniawati[16], demonstrated that combining Gyssens and DDD metrics offers a robust evaluation framework for rational drug use programs. However, comprehensive baseline data on rational antibiotic prescribing for pneumonia in Indonesian health centers remain sparse, despite the need for formulating targeted interventions[11].

Most previous evaluations of antibiotic prescribing in Indonesia have been restricted to inpatient settings or have applied qualitative and quantitative methods in isolation. Studies combining Gyssens and DDD analyses specifically for outpatient pneumonia in primary care remain exceptionally rare. Additionally, existing literature seldom addresses specific pediatric prescribing challenges, such as dosing inaccuracies and under-prescribing patterns, which are highly relevant in primary care populations[10,17]. Therefore, this study was designed to address these research gaps by conducting an integrated qualitative and quantitative evaluation of antibiotic use in outpatient pneumonia at the primary healthcare level. Using the Gyssens method to assess prescribing appropriateness and DDD per 1,000 patient-days to quantify utilization volume, this study identifies key prescribing vulnerabilities to provide an empirical baseline for establishing tailored antimicrobial stewardship programs in Indonesian primary care.

MATERIALS AND METHODS

Materials

This observational study employed a retrospective cross-sectional design to analyze quantitative and qualitative antibiotic utilization among outpatient cases of pneumonia at a primary healthcare center. Ethical approval was granted by the Institutional Ethics Committee of the Universitas Surabaya (Approval Certificate No. 650/KE/VII/2025). The study was conducted at Community Health Center X in Blitar, East Java, Indonesia, between July and August 2025. Purposive sampling was applied to select this facility based on the availability of standardized, archived electronic and physical medical record systems suitable for comprehensive auditing. Medical records covering outpatients diagnosed with pneumonia according to the International Classification of Diseases, Tenth Revision (ICD-10 codes J12–J18) between February 2024 and May 2025 were systematically retrieved. The source population comprised all outpatients presenting with acute respiratory tract infections at Community Health Center X during the observation period. A total sampling

approach was implemented to include all eligible pneumonia cases that met the inclusion criteria, specifically those with complete clinical documentation containing patient demographic profiles, verified ICD-10 diagnoses, prescribed antibiotic agents, individual doses, administration frequencies, and total treatment durations. Patients referred directly to secondary healthcare facilities without receiving initial therapeutic interventions at the health center were excluded. Secondary clinical data were extracted using a structured data collection sheet designed to calculate quantitative consumption metrics and facilitate qualitative Gyssens categorization.

Methods

Quantitative evaluation of antibiotic consumption (defined daily dose)

Quantitative antibiotic consumption was analyzed using the DDD methodology established by the World Health Organization (WHO) Collaborating Center for Drug Statistics Methodology[18,19]. The Defined Daily Dose represents the assumed average maintenance dose per day for a drug used for its main indication in adults. While standard WHO international guidelines recommend reporting consumption as DDD per 1,000 inhabitants per day for population-level evaluations, this study adapted the metric to DDD per 1,000 patients per day due to the unavailability of precise regional population catchment data for the health center. Antibiotic consumption was quantified using **Equation 1**, where Total Drug Consumed represents the aggregate mass of a specific antibiotic prescribed over the study period expressed in grams, WHO Standard DDD denotes the assigned daily dose value according to the WHO Anatomical Therapeutic Chemical (ATC)/DDD index, 1,000 serves as the standardized patient denominator scaling factor, and Total Pneumonia Patients indicates the total number of outpatient pneumonia cases treated at Community Health Center X.

$$\frac{\text{DDD}}{1{,}000}\,patients\ per\ day = \frac{\text{Total drug consumed (g)} \times 1{,}000}{WHO\ standard\ DDD\ (g) \times Total\ pneumonia\ patients} \qquad [1]$$

Qualitative evaluation of prescribing appropriateness (Gyssens method)

Qualitative evaluation of antibiotic appropriateness was conducted using the Gyssens flowchart algorithm[18,19]. Each antibiotic prescription was audited against official national clinical practice guidelines. Prescriptions for pediatric patients under 5 years of age were evaluated in accordance with the Integrated Management of Childhood Illness (IMCI/MTBS) guidelines issued by the Ministry of Health of the Republic of Indonesia. Prescriptions for patients aged five years and older were evaluated using the Decree of the Minister of Health of the Republic of Indonesia No. HK.01.07/MENKES/1186/2022 regarding Clinical Practice Guidelines for Physicians in Primary Healthcare Facilities. To ensure objectivity, the evaluation was conducted independently by two reviewers, both licensed clinical pharmacists with expertise in infectious disease stewardship. Each prescription was evaluated sequentially across clinical parameters, including indication, drug selection, dosage accuracy, administration interval, route, and treatment duration, and assigned to a Gyssens category:

1. Category 0: Appropriate and rational antibiotic use.
2. Category I: Inappropriate timing of administration.
3. Category IIA: Inappropriate dosage (under-dosing or over-dosing).
4. Category IIB: Inappropriate administration interval.
5. Category IIC: Inappropriate route of administration.
6. Category IIIA: Duration of therapy too long.
7. Category IIIB: Duration of therapy too short.
8. Category IVA: An alternative antibiotic is more effective.
9. Category IVB: An alternative antibiotic is less toxic or safer.
10. Category IVC: An alternative antibiotic is more cost-effective.
11. Category IVD: An alternative antibiotic with a narrower spectrum is available.
12. Category V: No valid clinical indication for antibiotic therapy.
13. Category VI: Unassessable due to incomplete medical record documentation.

Data analysis

Quantitative consumption data derived from DDD calculations were compiled and expressed as total DDD and standardized DDD per 1,000 patients per day for each identified antibiotic class and specific drug entity. Qualitative prescribing data obtained from the Gyssens evaluation were summarized as absolute frequencies and percentages across Categories 0 through VI. Inter-evaluator agreement between the two independent reviewers was assessed prior to consensus building. Discrepancies in Gyssens categorizations were discussed collaboratively until a unanimous consensus was reached to ensure analytical validity and reproducibility. Data aggregation and descriptive statistical analyses were performed using Microsoft Excel and SPSS.

RESULTS AND DISCUSSION

The demographic and diagnostic characteristics of outpatient pneumonia cases treated at the primary healthcare center are summarized in **Table I**. Toddlers aged 12 to 59 months represented the most prevalent age cohort (35.78%), followed by children aged 5 to 9 years (23.85%) and mature adults (19.27%). These findings confirm that pneumonia remains an infectious burden among vulnerable populations, particularly young children and the elderly, who exhibit immature or declining immune function. This distribution aligns with previous reports, which establish pneumonia as a leading cause of pediatric mortality and infectious morbidity among older adults in developing nations[20,21].

Physiologically, the underdeveloped immune systems of children under 5 years limit their capacity to clear lower respiratory tract pathogens. Anatomically, smaller pediatric airway diameters increase airflow resistance, predisposing children to lumen obstruction as inflammatory exudate accumulates[22]. This vulnerability is further exacerbated by environmental risk factors, including malnutrition, indoor air pollution, and incomplete immunization[23].

Male patients predominated in this study (55.05%), consistent with epidemiological observations reported by Guma *et al*[24]. Biologically, estrogen enhances humoral immunity by stimulating B-cell differentiation and antibody synthesis, whereas testosterone exhibits mild immunosuppressive effects on cellular immune responses[25]. Additionally, behavioral tendencies among young males, including higher outdoor activity and exploratory play, increase potential exposure to environmental pathogens[18].

Diagnostic coding was dominated by non-specific designations, led by unspecified viral pneumonia (J12.9, 32.11%), pneumonia due to other infectious organisms (J16, 25.69%), and unspecified pneumonia (J18.9, 20.18%). The high frequency of non-specific ICD-10 codes reflects diagnostic infrastructure limitations inherent to primary healthcare centers. A multicenter trial by Rodriguez-Contreras *et al*.[26] demonstrated that point-of-care lung ultrasound (POCUS) exhibits high sensitivity (87.8%) but moderate specificity (58.5%) relative to radiography. Similarly, Htun *et al*.[27] noted that clinical criteria (fever $\geq$ 38°C and tachypnea $\geq$ 20 breaths/min) yield modest positive likelihood ratios (LR+ 3.2-3.5) that are insufficient for definitive microbial differentiation without microbiological or radiological confirmation. Consequently, primary care clinicians rely on broad clinical codes, complicating etiological differentiation between viral and bacterial infections and increasing the risk of empirical over-prescribing[28].

Quantitative antibiotic utilization evaluated using the DDD metric is presented in **Table II**. Total antibiotic consumption across the outpatient cohort was 353.10 DDD per 1,000 patients per day. Amoxicillin was the primary antibiotic prescribed, accounting for 232.42 DDD per 1,000 patients per day (65.82% of total volume). This aligns with national clinical practice guidelines and WHO recommendations, positioning oral amoxicillin as first-line empirical therapy for uncomplicated community-acquired pneumonia. These findings mirror observations by Limato *et al*.[10] and Poutanen *et al*.[29], which documented the predominance of amoxicillin in primary care outpatient respiratory management.

Cefadroxil was the second most-utilized agent (87.04 DDD per 1,000 patients per day; 24.65%), serving as an alternative first-generation cephalosporin. In contrast, broad-spectrum agents exhibited low utilization rates, with Ciprofloxacin contributing 5.20% (18.35 DDD per 1,000 patients per day) and Azithromycin contributing 4.33% (15.29 DDD per 1,000 patients per day). Modest broad-spectrum consumption aligns with stewardship principles that prioritize narrow-spectrum penicillins to minimize selective pressure and disruption of the gut microbiota. National stewardship audits in primary care have demonstrated that active feedback mechanisms can reduce utilization of broad-spectrum fluoroquinolones and

macrolides by 10% to 24%[30,31]. Maintaining low broad-spectrum reliance requires ongoing prescribing audits to ensure narrow-spectrum agents remain effective without under-treating atypical infections.

Table I. Distribution of patient demographic and clinical characteristics (n = 109).

Characteristic Parameter	Sub-category / ICD-10 Designation	Frequency (n)	Percentage (%)
Age Group			
Infants (months)	0–11	8	7.34
Toddlers (months)	12–59	39	35.78
Children (years)	5–9	26	23.85
Adolescents (years)	10–19	5	4.59
Adults (years)	20–59	21	19.27
Elderly (years)	≥60	10	9.17
Gender			
Female	—	49	44.95
Male	—	60	55.05
Primary Diagnosis			
J12	Viral pneumonia, not elsewhere classified	3	2.75
J12.2	Parainfluenza virus pneumonia	1	0.92
J12.9	Viral pneumonia, unspecified	35	32.11
J13	Pneumonia due to *Streptococcus pneumoniae*	1	0.92
J15.8	Other bacterial pneumonia	2	1.83
J15.9	Bacterial pneumonia, unspecified	1	0.92
J16	Pneumonia due to other infectious organisms	28	25.69
J18	Pneumonia, organism unspecified	16	14.68
J18.9	Pneumonia, unspecified	22	20.18

Table II. Quantitative consumption of antibiotics based on defined daily dose (DDD).

ATC Code	Generic Name	Total Mass (g)	Consumption (DDD / 1,000 patients/day)	Proportion (%)	Total Patient Sample
J01CA04	Amoxicillin	25.33	232.42	65.82	109
J01DB05	Cefadroxil	9.49	87.04	24.65	
J01MA02	Ciprofloxacin	2.00	18.35	5.20	
J01FA10	Azithromycin	1.67	15.29	4.33	
Total	—	**38.49**	**353.10**	**100.00**	**109**

The qualitative evaluation of antibiotic appropriateness, conducted using the Gyssens flowchart algorithm, is summarized in **Table III**. Appropriate antibiotic prescribing (Gyssens Category 0) was observed in 6.42% of audited prescriptions (n = 7), indicating low adherence to guidelines across indication, drug selection, dosage, and duration. This low proportion falls below benchmark compliance rates reported in primary care settings (33%–58%)[32], reflecting challenges in implementing antimicrobial stewardship at the primary care level.

Table III. Quantitative consumption of antibiotics based on defined daily dose (DDD).

Gyssens Category	Clinical Interpretation	Frequency (n)	Percentage (%)
Category 0	Appropriate and rational antibiotic use	7	6.42
Category I	Inappropriate timing of administration	0	0.00
Category IIA	Inappropriate dosage (under-dosing or over-dosing)	37	33.94
Category IIB	Inappropriate administration interval	0	0.00
Category IIC	Inappropriate administration route	0	0.00
Category IIIA	Duration of therapy too long	0	0.00
Category IIIB	Duration of therapy too short	0	0.00
Category IVA	Alternative antibiotic is more effective	32	29.36
Category IVB	Alternative antibiotic is less toxic or safer	0	0.00
Category IVC	Alternative antibiotic is more cost-effective	0	0.00
Category IVD	Alternative antibiotic with narrower spectrum available	3	2.75
Category V	No valid clinical indication for antibiotic therapy	30	27.52
Category VI	Unassessable due to incomplete medical record data	0	0.00
Total	—	**109**	**100.00**

Inappropriate dosing (Category IIA) constituted the primary prescribing error, accounting for 33.94% of cases (n = 37). This issue was prominent among pediatric patients, where amoxicillin was frequently prescribed at fixed adult doses or unadjusted flat regimens rather than calculated weight-based doses (mg/kg/day). Weight-based under-dosing risks therapeutic failure and promotes resistant sub-populations, whereas over-dosing increases dose-dependent toxicity risks.

Dosing errors represent a recognized vulnerability in pediatric primary care, with Kurniawan *et al*.[33] and regional audits reporting pediatric dosing inaccuracies ranging from 35% to 56.8% in acute respiratory management[34].
Inappropriate drug selection (Category IVA) accounted for 29.36% of prescriptions (n = 32), where first-line amoxicillin was bypassed in favor of secondary cephalosporins or macrolides without a documented clinical rationale (e.g., penicillin allergy or treatment failure). Broad-spectrum selection without indication deviates from primary care guidelines and contributes to selective pressure for resistance[35]. Category V (no indication) was assigned to 27.52% of cases (n = 30), where patients received antibiotics despite being diagnosed with viral or non-bacterial pneumonia (J12.9 or J16). However, in primary care settings lacking diagnostic facilities, clinicians often prescribe empirically to prevent secondary bacterial superinfections[36]. Diagnostic uncertainty, fear of clinical deterioration, and high patient volume contribute to defensive prescribing practices[37]. Strengthening diagnostic access, promoting weight-based pediatric dosing tools, and implementing audit-and-feedback stewardship programs are essential to improve prescribing quality in primary care facilities.
This study was conducted at a single primary healthcare facility selected via purposive sampling for its record completeness. While this limits the direct generalizability of the absolute consumption metrics to all health centers across Indonesia, the identified prescribing vulnerabilities, specifically pediatric weight-based dosing errors and reliance on non-specific diagnostic codes, provide relevant targets for primary care antimicrobial stewardship interventions in similar resource-constrained settings.

CONCLUSION

This study demonstrates that antibiotic utilization for outpatient pneumonia at Community Health Center X in Blitar was predominantly driven by amoxicillin (232.42 DDD per 1,000 patients per day), followed by cefadroxil, ciprofloxacin, and azithromycin. Despite the appropriate reliance on first-line agents in overall volume, qualitative prescribing appropriateness remained suboptimal. Gyssen's evaluation revealed a high prevalence of Category IIA errors (33.94%), highlighting widespread dosing inaccuracies, and Category IVA errors (29.36%), indicating the selection of less effective antibiotics when superior alternatives were available. Additionally, 27.52% of evaluated cases were classified as Category V, indicating that no antibiotics were prescribed. This mixed prescribing pattern must be interpreted with caution; it may reflect the appropriate withholding of antibiotics for viral or unspecified pneumonia, or it may signify potential under-prescribing due to diagnostic uncertainty. These findings underscore critical challenges in primary care antimicrobial stewardship, specifically pediatric weight-based dosing errors, suboptimal empirical drug selection, and diagnostic limitations. Addressing these vulnerabilities requires actionable strategies, including routine prescription audits with active clinician feedback, structured training on guideline-concordant dosing, and improved access to current clinical pathways. Furthermore, strengthening diagnostic infrastructure through standardized clinical algorithms or point-of-care tools is essential. While limited by a retrospective, single-center design that constrains broad generalizability, this study provides a valuable empirical baseline. Future multicenter investigations incorporating enhanced diagnostic support are recommended to comprehensively evaluate and optimize antibiotic prescribing practices across primary care networks.

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AUTHORS' CONTRIBUTION

Conceptualization: Hesti Rima Hariyani, Rina Widiyawati, Fauna Herawati

Data curation: Hesti Rima Hariyani
Formal analysis: Hesti Rima Hariyani, Rina Widiyawati, Fauna Herawati
Funding acquisition: -
Investigation: Hesti Rima Hariyani
Methodology: Rina Widiyawati, Fauna Herawati, Nurul Chusna
Project administration: Hesti Rima Hariyani
Resources: Hesti Rima Hariyani
Software: -
Supervision: Rina Widiyawati, Fauna Herawati
Validation: Rina Widiyawati, Fauna Herawati, Nurul Chusna
Visualization: -
Writing - original draft: Hesti Rima Hariyani
Writing - review & editing: Hesti Rima Hariyani, Rina Widiyawati, Fauna Herawati, Nurul Chusna

DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declare no financial, personal, or institutional conflicts of interest that could inappropriately influence the design, execution, or reported outcomes of this study. This research was conducted entirely independently, without commercial sponsorship, pharmaceutical industry support, or external grant funding. The study was fully self-funded by the authors, ensuring complete independence from third-party intervention during research design, data collection, statistical analysis, interpretation, and manuscript drafting. The authors maintained sole access to all primary research data and confirm that no external sponsors or institutions were involved in data interpretation, the formulation of conclusions, or the decision to submit this paper for publication. Consequently, all findings, interpretations, and conclusions presented in this manuscript represent the result of independent scientific analysis free from external bias.

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