ORIGINAL ARTICLE　　　　JPS. 2025 8(2), 837-846

Antibiotic Use and Prescribing Patterns for Respiratory Tract Infections (ICD-10: J00-J99) in Indonesia During the COVID-19 Pandemic

Tingkat Penggunaan Antibiotik dan Pola Peresepannya Pada Infeksi Saluran Pernapasan (ICD-10: J00-J99) di Indonesia Selama Pandemi COVID-19

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Abstract

Introduction: Respiratory tract infections (RTIs) contribute substantially to global antibiotic consumption, raising concerns about antimicrobial resistance (AMR). This study aimed to analyze antibiotic prescribing patterns for respiratory disorders in an Indonesian teaching hospital during the COVID-19 pandemic. **Methods**: This retrospective, cross-sectional study examined systemic antibiotic prescriptions based on the Anatomical Therapeutic Classification (ATC: J01) for respiratory diseases (ICD-10: J00-J99) at Cilacap Government Teaching Hospital between January and December 2021. Data were extracted from electronic medical records (e-MR), including patient demographics (i.e. age and sex), ICD codes and name of antibiotics. We analyzed WHO AWaRe classifications, administration routes, and seasonal patterns based on patient's entry and antibiotic use. **Results**: The study included 2,395 patients with antibiotic prescriptions for respiratory disorders. The Watch group antibiotics accounted for 85.6% of prescriptions, with the highest use among adults (86.2%). Parenteral administration (71.5%) was more common than oral administration (28.5%). Pneumonia (38.2%) and chronic obstructive pulmonary disease (27%) were the most common indications. Antibiotic use peaked in December (n=529) and was lowest in July (n=84). Ceftriaxone (n=838), azithromycin (n=270), cefixime (n=262), levofloxacin (n=216), and meropenem (n=56) were among the top prescribed antibiotics. **Conclusion**: The study highlights the predominant use of broad-spectrum and parenteral antibiotics for respiratory disorders, raising concerns about AMR. Factors such as seasonality, disease patterns, and diagnostic challenges may have influenced prescribing practices. Implementing antimicrobial stewardship programs, promoting evidence-based guidelines, and addressing modifiable risk factors are crucial to combat AMR and optimize patient outcomes during and beyond the COVID-19 pandemic.

Keywords: *Antibiotic; COVID-19; drug utilization; Indonesia; respiratory tract infections.*

Abstrak

Pendahuluan: Infeksi saluran pernapasan (ISPA) berkontribusi signifikan terhadap konsumsi antibiotik global, menimbulkan kekhawatiran akan resistensi antimikroba (AMR). Studi ini bertujuan untuk menganalisis pola peresepan antibiotik untuk gangguan pernapasan di sebuah rumah sakit pendidikan di Indonesia selama pandemi COVID-19. **Metode:** Studi retrospektif dan cross-sectional ini mengkaji resep antibiotik sistemik berdasarkan Klasifikasi Anatomi Terapeutik (ATC: J01) untuk penyakit pernapasan (ICD-10: J00-J99) di Rumah Sakit Pendidikan Pemerintah Cilacap antara Januari dan Desember 2021. Data diambil dari rekam medis elektronik (e-MR), mencakup demografi pasien (usia dan jenis kelamin), kode ICD, dan nama antibiotik. Kami menganalisis klasifikasi WHO AWaRe, rute pemberian, dan pola musiman

berdasarkan waktu masuk pasien dan penggunaan antibiotik. **Hasil:** Studi ini melibatkan 2.395 pasien dengan resep antibiotik untuk gangguan pernapasan. Antibiotik golongan Watch mendominasi (85,6%), dengan penggunaan tertinggi pada dewasa (86,2%). Pemberian parenteral (71,5%) lebih umum dibandingkan oral (28,5%). Pneumonia (38,2%) dan penyakit paru obstruktif kronis (27%) menjadi indikasi paling umum. Penggunaan antibiotik mencapai puncak pada Desember (n=529) dan terendah pada Juli (n=84). Ceftriaxone (n=838), azitromisin (n=270), sefiksim (n=262), levofloksasin (n=216), dan meropenem (n=56) termasuk antibiotik yang paling sering diresepkan. **Kesimpulan:** Studi ini mengungkap dominasi penggunaan antibiotik spektrum luas dan parenteral untuk gangguan pernapasan, memperkuat kekhawatiran akan AMR. Faktor seperti musim, pola penyakit, dan tantangan diagnostik mungkin memengaruhi praktik peresepan. Penerapan program pengendalian antimikroba, promosi pedoman berbasis bukti, dan penanganan faktor risiko yang dapat dimodifikasi sangat penting untuk memerangi AMR dan mengoptimalkan hasil perawatan pasien selama dan pasca pandemi COVID-19.

Kata Kunci: Antibiotik, COVID-19, Utilisasi Obat, Indonesia, Infeksi Saluran Pernapasan.

https://doi.org/10.36490/journal-jps.com.v8i2.849

Introduction

Respiratory infectious diseases, including upper respiratory infections (URIs) and bacterial respiratory tract infections (RTIs), play a significant role in driving global antibiotic usage. In long-term care facilities (LTCFs), respiratory tract infections are prevalent and commonly treated with antibiotics [1]. These infections can progress to more severe conditions like pneumonia, affecting various parts of the respiratory system. While antibiotics are crucial in treating these infections, concerns arise regarding their appropriateness and effectiveness, as inappropriate use contributes to antimicrobial resistance [2].

A systematic review of 26 articles found peak incidence and prevalence rates of RTIs to be 85.2% and 55.8%, respectively [3]. Since 2020, during the COVID-19 pandemic, antibiotic use for respiratory illnesses has risen [4]. Specifically, consumption of azithromycin and ceftriaxone increased by 46% and 18% in 2020 compared to 2019 [4]. Alarmingly, around 90% of antibiotics prescribed for RTIs were deemed inappropriate, contributing to antimicrobial resistance [5].

Antibiotic surveillance is essential where the frequency of prescriptions for RTIs is notable, particularly during health crises like COVID-19 [6]. Diagnostic challenges arise in COVID-19 due to non-specific symptoms, potentially leading to misdiagnosis or inappropriate prescribing practices [7,8]. However, surveillance of antibiotic consumption for RTIs in Indonesia remains limited, with recent data focusing only on specific antibiotic groups [9,10] or diagnoses [11].

While previous studies have explored antibiotic utilization in respiratory disorders, a comprehensive comparison across various factors such as patient demographics, disease codes, WHO AWaRe classifications, administration routes, and seasonality does not exist. Therefore, this study aims to analyze antibiotic prescription trends among patients with respiratory disorders, considering variables like age, sex, disease

codes, WHO AWaRe classifications, administration routes, and seasonal patterns at Cilacap Government Teaching Hospital, Central Java, Indonesia.

Method

Study design and setting

This retrospective cross-sectional study aimed to explore the patterns of prescribing systemic antibiotics in the inpatient department of an Indonesian teaching hospital during the COVID-19 outbreak from January to December 2021. Cilacap Government Teaching Hospital, located in Cilacap Regency, is one of the largest hospitals in Central Java, serving a population of approximately 2 million people. The hospital treats nearly 60,000 patients annually, with 47,696 inpatient admissions in 2021, including those who received antibiotics. The pulmonary clinic recorded approximately 7,074 patient visits in 2021, making it one of the top 5 departments in terms of patient entries.

Data Source

This study presents data on systemic antibiotics prescribed under the Anatomical Therapeutic Classification (ATC: J01) at Cilacap Government Teaching Hospital from January to December 2021. The data were sourced from the hospital's electronic medical records (e-MR) system, which provided comprehensive patient demographic data, including age, sex, admission date, month, department of admission, and diagnostic information classified according to the International Classification of Diseases (ICD). Antibiotic details such as name, formulation, route of administration, and prescriber identification were also extracted from the pharmacy installation records. Data cleaning involved correcting errors, removing inconsistencies (such as missing ICD-10 codes), and eliminating duplicate entries. Only patients admitted to the inpatient department with respiratory diseases (ICD-10 codes J00-J99) who were prescribed antibiotics (ATC code J01) were included in the study. Patients with incomplete e-MR records were excluded.

Study variables

The main study variables include the total number of prescriptions issued at Cilacap government teaching hospital in 2021, specifically focusing on prescriptions containing antibiotics. We examined the type, formulation, administration route, and specific diagnoses based on ICD-10 Chapter X codes (J00-J99) for respiratory diseases for which antibiotics were prescribed. Our analysis also explored trends in antibiotic prescribing, comparing prescriptions across patient age groups (children: 0-14 years, active adults: 19-65 years, elderly: 65+ years) and sexes (male and female). Additionally, we detailed data on respiratory diseases using WHO's ICD-10 Chapter X codes (J00-J99). Antibiotics were classified according to the WHO AWaRE categorization: 'Access' antibiotics are primary therapies for common infections, 'Watch' antibiotics are used judiciously for specific syndromes, and 'Reserve' antibiotics are reserved for confirmed multi-drug resistant infections or when alternative treatments fail [12]. The seasonality was analysed by the months of patient's entry and antibiotic use.

Statistical analysis

Descriptive statistical analyses were conducted to summarize the sociodemographic characteristics, antibiotic prescribing patterns based on the WHO AWaRe classification, administration routes, and disease distribution according to ICD-10 subgroups. Data processing and analysis were performed using Microsoft Excel 2021, utilizing pivot tables to calculate frequency distributions and percentages. The results were stratified by age group into children (0–14 years), active adults (15–64 years), and elderly (≥65 years). Further visualization and statistical representation were conducted using R Studio version 4.4.2.

Ethical Approval

Ethical approval was obtained from the Health Research Ethics Committee of Universitas Harapan Bangsa (No. B.LPPM-UHB/578/06/2024). Respondents provided written informed consent for participation in the survey. This research was conducted in accordance with the World Medical Association Declaration of Helsinki.

Results and Discussion

Results

The study encompassed a total of 47,696 patients who use antibiotic admitted to the inpatient department in 2021. The final study population focused on 2,395 patients with systemic antibiotic use classified under ATC code J01, specifically addressing ICD-10 respiratory system disorders indications (J00-J99) (see Figure 1).
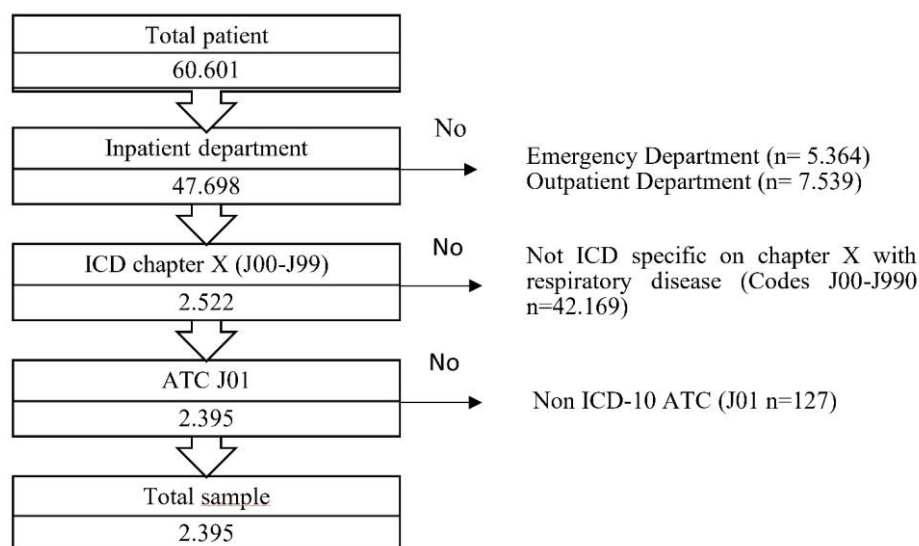

Figure 1. Flowchart Sample Size

Half of patients were males (54.9% n=1,314) and approximately (52.8% n=1,265) of the patient population comprised active adults (see Table 1).

Table 1. Patient Characteristics and Antibiotic Prescribing Patterns

		Children	Active Adults	Elderly	Total
		0-14	15-64	65+	-
Characteristics	N	340 (14.2%)	1265 (52.8%)	790 (33%)	2.395 (100%)
Sex	Female	144 (42.4%)	628 (49.6%)	309 (39.1%)	1081 (45.1%)
	Male	196 (57.6%)	637 (50.4%)	481 (60.9%)	1314 (54.9%)
Antibiotic AWaRe	Access	36 (10.6%)	161 (12.7%)	115 (14.6%)	312 (13%)
	Watch	288 (84.7%)	1090 (86.2%)	673 (85.2%)	2051 (85.6%)
	Reserved	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Not Listed	16 (4.7%)	14 (1.1%)	2 (0.3%)	32 (1.3%)
Administration	Parenteral	201 (8.4%)	897 (37.5%)	614 (25.6%)	1712 (71.5%)
	Oral	139 (5.8%)	368 (15.4%)	176 (7.3%)	683 (28.5%)
	Liquid Oral	46 (31.7%)	1 (0.1%)	(0%)	47 (2.2%)
	Solid Oral	93 (64.1%)	367 (22.6%)	176 (42.6%)	636 (29.1%)
ICD-10 Subgroups	J18.	Pneumonia. organism unspecified 154 (45.3%)	496 (39.2%)	916 (38.2%)
	J44.	Other chronic obstructive pulmonary disease 0 (0%)	299 (23.6%)	646 (27%)
	J96.	Respiratory failure. not elsewhere classified 0 (0%)	51 (4%)	144 (6%)

J90.	Pleural effusion. not elsewhere classified	0 (0%)	82 (6.5%)	94 (3.9%)
J20.	Acute bronchitis	58 (17.1%)	26 (2.1%)	84 (3,5%)
J02.	Acute pharyngitis	41 (12.1%)	28 (2.2%)	72 (3%)
J46.	Status asthmaticus	0 (0%)	58 (4.6%)	58 (2,4%)
J33.	Nasal polyp	12 (3.5%)	34 (2.7%)	55 (2,3%)
J35.	Chronic diseases of tonsils and adenoids	20 (5.9%)	19 (1.5%)	40 (1,7%)
J98	Other respiratory disorders	0 (0%)	28 (2.2%)	28 (1,2%)
J93.	Pneumothorax	0 (0%)	18 (1.4%)	28 (1,2%)
J15.	Bacterial pneumonia. not elsewhere classified	3 (0.9%)	21 (1.7%)	26 (1,1%)
J81.	Pulmonary oedema	0 (0%)	19 (1.5%)	24 (1%)
J86.	Pyothorax	0 (0%)	12 (0.9%)	23 (1%)
J45.	Asthma	13 (3.8%)	9 (0.7%)	22 (0,9%)
J47.	Bronchiectasis	0 (0%)	11 (0.9%)	22 (0,9%)
J00.	Acute nasopharyngitis [common cold]	21 (6.2%)	(0%)	21 (0,9%)
J06.	Acute upper respiratory infections of multiple and unspecified sites	7 (2.1%)	9 (0.7%)	20 (0,8%)
J94.	Other pleural conditions	0 (0%)	8 (0.6%)	14 (0,6%)
J40.	Bronchitis. not specified as acute or chronic	0 (0%)	12 (0.9%)	13 (0,5%)
J42.	Unspecified chronic bronchitis	0 (0%)	0 (0%)	9 (0,4%)
J21.	Acute bronchiolitis	9 (2.6%)	(0%)	9 (0,4%)
J34.	Other disorders of nose and nasal sinuses	0 (0%)	8 (0.6%)	8 (0,3%)
J36.	Peritonsillar abscess	0 (0%)	7 (0.6%)	7 (0,3%)
J85.	Abscess of lung and mediastinum	0 (0%)	4 (0.3%)	4 (0,2%)
J31.	Chronic rhinitis. nasopharyngitis and pharyngitis	0 (0%)	3 (0.2%)	3 (0,1%)
J84.	Other interstitial pulmonary diseases	0 (0%)	3 (0.2%)	3 (0,1%)
J32.	Chronic sinusitis	2 (0.6%)	0 (0%)	2 (0,1%)

Abbreviations: AWaRe: Acces, Watch and Reserve; ICD-10: International Codes of Diseases 10th Revison

Figure 2 illustrate broad-spectrum antibiotic classes were the most frequently antibiotic use in respiratory diseases. Other Beta Lactam group (J01D) were the most prescribed antibiotics use in respiratory disease with 1,478 patients and the lowest usage is sulphonamides and trimethoprim (J01E) with 1 patient.
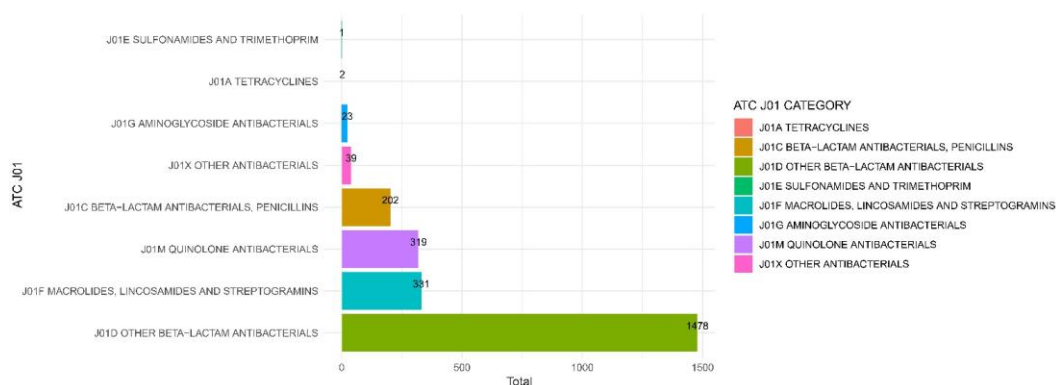
Figure 2. The systemic antibiotic use (ATC: J01) during COVID-19 in 2021

Regarding the seasonality antibiotic use (see **Figure 3**), antibiotic prescription begins to increase again in the rainy season with a sharp increase in December (n=529) and the lowest usage of antibiotics for respiratory tract infections (RTIs) was observed in July (n=84).
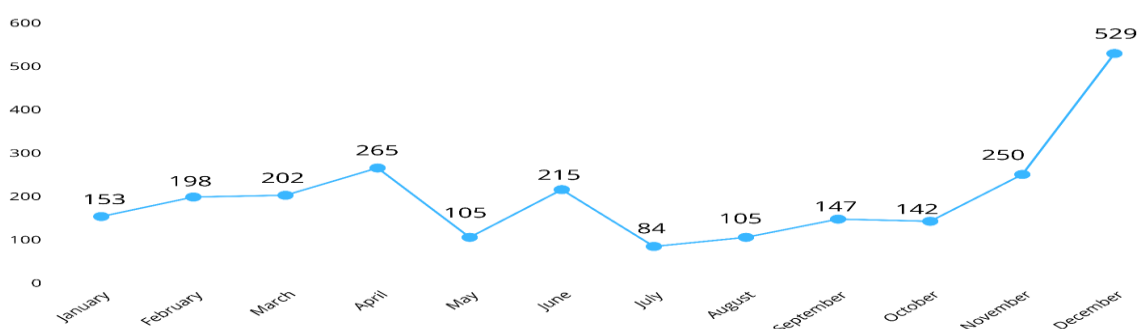

Figure 3. Seasonality Antibiotic Use

The findings in Figure 4 represents a comprehensive overview of the active agents utilized in treating respiratory system diseases (J00-J99). Among the listed agents, ceftriaxone emerges as the most frequently prescribed (n=836), followed by azithromycin (n= 270), cefixime (n=262) and levofloxacin (n=216). The top 10 antibiotics used are generally broad-spectrum, including the cephalosporin group (i.e., ceftriaxone, cefixime, ceftazidime and cefotaxime), the fluoroquinolone group (i.e., levofloxacin and ciprofloxacin), and combinations of penicillins, with beta-lactamase inhibitors (i.e., ampicillin- beta-lactamase inhibitors and amoxicillin-beta-lactamase inhibitors). Interestingly, meropenem, a broad-spectrum carbapenem antibiotic, is also among the top 10 most frequently used antibiotics.
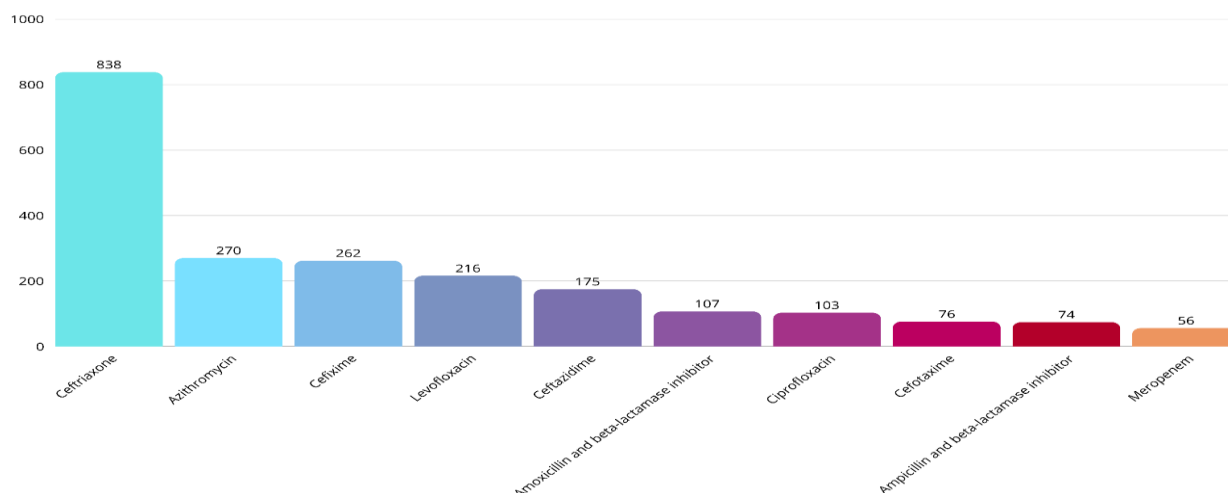

Figure 4. Top 10 antibiotics use in Chapter X Disease of the Respiratory system (J00-J99).

Discussion

To our knowledge, this is the first comprehensive analysis of antibiotic prescribing trends and patterns at a government teaching hospital in Cilacap, Central Java, Indonesia, specifically during the COVID-19 pandemic in the inpatient department. The findings offer several noteworthy insights and implications

Based on prescribing data from electronic medical records system. This study, divide population into 3 age groups: Children (0-14 years), Adults (15-64 years) and the elderly (65+ years) with the higher incidence in adults (n=1.265). Active adults are more affected by respiratory infections due to various factor such as outdoor activity especially during pandemic [13], exposure to air pollution [14] , smoking [15] and psychological stress [16], which can lead to respiratory disease.

Our research indicates that men in Indonesia are more commonly affected by respiratory tract infections (RTIs) and are prescribed more antibiotics. While this study did not collect data on smoking or environmental exposure, external evidence suggests that air pollution may be a contributing factor. Reports from the Indonesian Ministry of Health highlight that chronic obstructive pulmonary disease (COPD) and pneumonia are among the most prevalent respiratory diseases in the country, both of which are strongly associated with air pollution exposure [17]. The higher proportion of RTI cases in men (60.1%) compared to women (39.1%) may reflect differences in environmental exposure, though further investigation is needed to confirm this link. These findings emphasize the need for comprehensive public health strategies aimed at reducing air pollution and its impact on respiratory health.

Our findings indicate that Watch-group antibiotics, particularly third-generation cephalosporins (e.g., ceftriaxone) and macrolides (e.g., azithromycin), accounted for 85.6% of all inpatient antibiotic prescriptions, with the highest use among adults (86.2%). This proportion exceeds that reported in a rural Vietnamese study (40%) based on WHO's AWaRe classification [20]. The Watch group includes antibiotics with a higher risk of contributing to antimicrobial resistance and should be reserved for specific indications [21]. Their widespread use, especially for respiratory tract infections, reflects evolving resistance patterns and raises concerns over potential overuse [22]. The Watch group consists of antibiotics crucial for treating specific infections but requires careful management to prevent misuse and resistance emergence, highlighting the importance of prudent antibiotic prescribing practices [23]. This trend is reflected globally, with substantial variations in AWaRe prescribing observed, especially in lower- and upper-middle-income countries, followed by high-income countries [24]. This high utilization suggests a need for stricter adherence to antibiotic stewardship programs and guidelines to optimize prescribing practices and minimize the risk of emerging resistance. Our findings also show that the higher administration of antibiotics through the parenteral route compared to the oral route is notable (71,5% vs 28,5%). Research has shown that the use of parenteral antibiotics in children is lower compared to adults (8,4% vs 37,4%), potentially due to a lower incidence of severe infections or a preference for oral formulations. Parenteral administration provides a faster onset of action and higher bioavailability than oral administration. Intravenous antibiotics are preferred for patients who cannot tolerate oral medications due to nausea, vomiting, or impaired gastrointestinal function [18].

Respiratory tract infections (RTIs), particularly pneumonia and chronic obstructive pulmonary disease (COPD) (see table 1), were among the most common indications for antibiotic use is consistent with global trends. Additionally, SARS-CoV-2 triggers the release of pro-inflammatory cytokines such as IL-6, IL-1β, and TNF-α, leading to local and systemic hyperinflammation, this may lead to immune suppression, increasing susceptibility to bacterial pathogens such as *Streptococcus pneumoniae* and *Haemophilus influenzae*, which can subsequently cause secondary bacterial pneumonia [19,20]. The high prevalence of COPD among antibiotic users may be linked to the high smoking rates in the study population, as smoking is a well-known risk factor for COPD exacerbations, which frequently require antibiotic treatment [21].

The observed seasonality in antibiotic use, with the highest utilization in December (n=529), suggests a correlation between increased antibiotic demand and the surge in covid -19 cases in Indonesia during that month. Conversely, our data show a significant decline in antibiotic use during July (n=84), which aligns with Indonesia's peak dry season. The rainy season's high humidity and lower temperatures enhance SARS-CoV-2 stability in air and surfaces, increasing transmission risk. Simultaneously, elevated humidity promotes bacterial growth in the environment, heightening human exposure to pathogens. SARS-CoV-2 damages the respiratory epithelium by interacting with ACE2 (Angiotensin-Converting Enzyme 2) receptors, which are abundant on epithelial cells [22]. The combined effects of respiratory epithelial damage from COVID-19,

immune suppression, and increased bacterial exposure during the rainy season explain the surge in antibiotic use in December.

These findings highlight the prevalent use of wide-spectrum antimicrobials, such as ceftriaxone, cefixime, and levofloxacin, in treating Respiratory Tract Infections (RTIs). Ceftriaxone, a cephalosporin, is often recommended as the primary choice for specific RTIs, consistent with previous studies in countries like Qatar, China and Japan [23–25]. However, the overuse of fluoroquinolones like ciprofloxacin and levofloxacin in RTI treatment has been linked to the development of antimicrobial resistance [26]. The increased use of ceftriaxone, often chosen as a first-line treatment for community-acquired pneumonia due to its convenient dosing and affordability, extended to COVID-related pneumonia in cases of suspected bacterial co- or superinfection. Ceftriaxone injection is commonly used in respiratory tract infection patients due to its broad spectrum of activity, availability, and low toxicity [27]. A Spanish study noted a rise in third-generation cephalosporin usage, particularly ceftriaxone, though the increase was not statistically significant and was confined to a single hospital [28]. During the pandemic, ceftriaxone became the most frequently used antibiotic in Indonesia, overtaking co-amoxiclav, which had been the leading antibiotic for many years. Additionally, there was a significant increase in hospital use of macrolides (ATC code: J01FA), with azithromycin ranking second among the top 10 antibiotics in 2021. Early in the COVID-19 pandemic, international and national clinical guidelines recommended azithromycin for its immunomodulatory and antiviral properties, but only for bacterial co-infections [29]. Azithromycin, a macrolide antibiotic that inhibits bacterial protein synthesis, has been extensively prescribed alongside antiviral medications for COVID-19 patients. Its immunomodulatory effects on interleukin 6 (IL-6), IL-1 beta, and ability to regulate extracellular signalling kinases make it beneficial in treating chronic lung diseases and sinopulmonary infections [29]. Azithromycin inhibits bacterial protein synthesis and has been widely prescribed alongside antiviral medications for COVID-19 patients. However, evidence regarding its impact on pro-inflammatory cytokines in COVID-19 patients is limited, and concerns about cardiotoxicity when co-administered with hydroxychloroquine have been raised [30]. The WHO later advised against its use for COVID-19 treatment due to concerns about cardiotoxicity and the risk of developing antibacterial resistance [31]. The high utilization of meropenem, a broad-spectrum carbapenem antibiotic, suggests a potential overuse, particularly for non-severe infections [32]. This raises concerns about the judicious use of meropenem, as its overuse could contribute to the emergence of multidrug-resistant organisms.

Limitations and Implication

This study has several limitations, including potential inaccuracies or incomplete data due to reliance on electronic medical and pharmacy records. Additionally, its focus on a single teaching hospital limits generalizability, and the lack of exploration into diagnostic criteria distinguishing respiratory infections from COVID-19 may have influenced antibiotic prescribing patterns. Despite these limitations, the findings underscore the urgent need for strengthened antimicrobial stewardship programs in Indonesia. Future research should incorporate multicenter data and detailed diagnostic assessments to enhance the accuracy and applicability of prescribing pattern analyses.

Conclusion

The study highlights the most frequently use of broad-spectrum antibiotics like cephalosporins and fluoroquinolones, and parenteral antibiotics for respiratory disorders, raising concerns about AMR. Factors such as seasonality, disease patterns, and diagnostic challenges may have influenced prescribing practices. Implementing antimicrobial stewardship programs, promoting evidence-based guidelines, and addressing modifiable risk factors are crucial to combat AMR and optimize patient outcomes during and beyond the COVID-19 pandemic.

Conflict of interest

This study was conducted with principles of independence and fact-based objectivity, free from external influence or conflicts of interest. From the planning phase to report preparation, all activities were managed

with unwavering commitment to academic integrity and without any form of intervention or pressure. Employing a transparent approach grounded in research ethics, the findings possess robust scientific validity and contribute meaningfully to knowledge advancement and societal well-being.

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