Indonesian Journal of Clinical Pharmacy, June 2020
Vol. 9 Iss. 2, pg 95–104
ISSN: 2252–6218, e-ISSN: 2337-5701
Available online at:
http://ijcp.or.id
DOI: 10.15416/ijcp.2020.9.2.95
Research Article

Quality of Antibiotic Prescribing for Respiratory Tract Disease in Primary Healthcare Centers in Tegal Regency, Central Java, Indonesia

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Abstract
The prescription of antibiotics for diagnosed upper respiratory tract infections (URTIs) is frequently practiced. Furthermore, inappropriate use has been implicated in numerous problems, including the onset of resistance. This study is, therefore, aimed to evaluate the antibiotic prescribing quality for respiratory tract disease diagnosed at the outpatients of primary healthcare centers in Tegal District, Central Java, Indonesia. In addition, cross-sectional evaluation was employed, using data obtained within the period of June–August, 2018 in six locations, and subsequently subjected to qualitative analysis. The prescribing quality was evaluated by comparing the drug selected, dosage, frequency, and duration of administration stated in the prescriptions, with the terms in the Clinical Practice Guidelines for Primary Healthcare Facilities, 2014. A total of 1453 samples were selected through purposive sampling, where 632 were diagnosed with respiratory tract diseases, with common cold as the most frequent diagnosis (87.2%). In addition, exactly 621 (98.3%) failed to fulfill the rational antibiotic prescribing criteria, evidenced by irrational drug selection (22.0%), dosage (9.5%), frequency (1.7%), and duration of administration (65.0%). The physicians tend to comply more with the national treatment guidelines (OR: 1.828, 95%CI: 0.486–6.874, p-value 0.365), and the less experience of prescribers (<12 years of service) was identified as a negative contributing factor (OR: 0.536, 95%CI: 0.143–2.016, p-value 0.349). Furthermore, irrational prescription was observed in a much larger proportion, influenced by the prescribers' qualification and experience. This association is currently not significant, due to deficiency of influencing samples.

Keywords: Antibiotic, appropriateness prescribing, national treatment guidelines, qualification prescribers, rationality

Kualitas Peresepan Antibiotik pada Penyakit Saluran Pernafasan di Beberapa Puskesmas di Kabupaten Tegal, Jawa Tengah, Indonesia

Abstrak
Peresepan antibiotik untuk diagnosis infeksi saluran pernafasan atas sering dilakukan. Peresepan antibiotik yang tidak tepat dapat menyebabkan banyak masalah, salah satunya resistensi antibiotik. Tujuan dari penelitian ini adalah mengevaluasi kualitas peresepan antibiotik pada diagnosis penyakit saluran pernafasan pasien rawat jalan di Puskesmas Kabupaten Tegal, Jawa Tengah, Indonesia. Penelitian potong lintang menggunakan data peresepan pasien rawat jalan periode Juni–Agustus 2018 di enam puskesmas di Kabupaten Tegal. Resep dengan diagnosis penyakit saluran pernafasan digunakan untuk analisis kualitatif. Kualitas peresepan dinilai dengan membandingkan pemilihan obat, dosis pemberian, frekuensi pemberian dan durasi pemberian antara yang tertulis pada resep dengan Panduan Praktik Klinis Fasilitas Kesehatan Primer 2014. Sebanyak 1453 resep diambil secara *purposive sampling*, 632 resep di antaranya dengan diagnosis penyakit saluran pernafasan. Diagnosis yang paling sering yaitu salesma (87,2%). Sebanyak 621 (98,3%) resep tidak memenuhi kriteria peresepan antibiotik yang rasional, meliputi ketidakrasionalan pemilihan antibiotik (22,0%), dosis pemberian (9,5%), frekuensi penggunaan (1,7%), dan durasi pemberian (65,0%). Peresepan antibiotik oleh dokter lebih sesuai dengan panduan pengobatan nasional (OR 1,828, 95% CI: 0,486–6,874, *p-value* 0,365). Pengalaman penulis resep yang lebih singkat (<12 tahun) juga menjadi faktor persepan tidak rasional (OR 0,536, 95% CI: 0,143–2,016, *p-value* 0,349). Sebagian besar peresepan antibiotik pada penyakit saluran pernafasan tidak rasional. Baik kualifikasi maupun pengalaman penulis resep pada penelitian ini memiliki memengaruhi rasionalitas resep, meskipun tidak signifikan karena kurangnya sampel terhadap kerasionalan.

Kata kunci: Antibiotik, kerasionalan, kesesuaian peresepan, kualifikasi penulis resep, panduan pengobatan nasional

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Submitted: 6th September 2019, Accepted: 6th May 2020, Published: 29st June 2020

Introduction

Respiratory tract disease is a type of disease that affects the air passage. Such condition includes acute respiratory infections (ARIs) and chronic respiratory diseases, such as asthma.[1] ARIs are common in Indonesia, leading to hospitalization and even death particularly among children and older adults.[2] ARIs can attack one or more parts of respiratory tracts, starting from the nose (upper part) to alveoli (lower part).[3] Among the lower respiratory tract infections (LRTIs) are acute bronchitis and pneumonia. Pneumonia may result from viruses and bacteria. Secondary bacterial infections are likely to occur because a virus suppresses the antibacterial activity in the lung. Acute bronchitis is usually caused by a virus and can mostly clear up by itself.[4,5] This also works for upper respiratory tract infections (URTIs). URTIs can be triggered by viruses and bacteria, usually from group A streptococcus. Bacterial infections have a lower proportion (0.5–10%).[6] However, antibiotic prescribing for diagnosed URTIs is frequently practiced. Approximately 30–64% antibiotics have been inappropriately prescribed for patients with URTIs, such as for unidentified bacterial infections or viral etiology.[6,7]

Inappropriate and high rates use of antibiotics can increase antibiotic resistance, healthcare cost, adverse events, and also poor treatment outcomes.[7–9] Antibiotic resistance is a growing problem worldwide and now becomes the most serious threat in the field of health.[9,10] Antibiotic consumption is still a concern in Asia-Pacific countries, prescribing at ambulatory care centers reaches 82%.[6] Approximately 70% outpatients with fever in primary healthcare facilities in China were inappropriately administered with antibiotics.[11] In the United States, antibiotic prescribing for respiratory disease reached 72.3% with 23.4% of which was prescribed for ARIs diagnosis without indications.[12]

In 2014, the government of Indonesia via the Ministry of Health published the Clinical Practice Guidelines for Physicians in Primary Healthcare Facilities. Such guideline become a reference for physicians to provide services in public as well as private primary healthcare facilities and to administer appropriate therapy for patients with 144 disease types, including infections.[13] However, many of the healthcare facilities fail to adhere to the guidelines. A study in primary healthcare centers in Depok City found that 220 out of 392 prescriptions did not fulfill the criteria of rational antibiotic use.[14]

Tegal Regency has a population of 1,418,353 in 2017. The number of primary healthcare centers in this area reached 29 units in December 2017. The use of antibiotics, particularly amoxicillin, ranked second after paracetamol, reaching 2.6 million tablets during 1 January–31 December 2017. Meanwhile, the most common diagnosed case in 2017 was acute nasopharyngitis (common cold) with a total of 97,785 cases subsequently followed by other URTIs (49,803 cases).[15] No research data has been fetched in relation to the rationality of antibiotic use in primary healthcare centers in the Tegal Regency. This current study therefore aimed to evaluate the quality of antibiotic prescribing for diagnosed respiratory tract diseases among the outpatients of primary healthcare centers in Tegal Regency.

Methods

A cross-sectional study was conducted in six primary healthcare centers having a pharmacist, general physician, as well as dental and oral clinics at sub-regency level in Tegal Regency, Central Java, Indonesia. This research has been approved by the Ethics Committee of the Faculty of Medicine of Universitas Indonesia (no. 0762/UN2.

F1/ETIK/2018) as well as by the Board of Regional Development Planning and Research and Development (Bappeda and Litbang) of Tegal Regency.

Selected prescriptions were those containing systemic antibiotics for outpatients during June–August 2018. The minimum sample target was set to 214 antibiotic prescriptions.[16] Purposive sampling method was employed to collect the samples, followed by selection of prescriptions for diagnosed respiratory tract diseases to be analyzed qualitatively (Figure 1). Data in the prescriptions consisted of patient's name, age, diagnosis, prescriber, name of drugs, and administered regimen. Diagnosis could also be traced or obtained from the medical record. If the medical record contained no information about the diagnosis, the prescription would be invalid (excluded). Prescribing quality was assessed by comparing the choice of drug and dosage regimen (dosage, frequency, and duration of administration) in the prescriptions with the guidelines from the Ministry of Health, the Clinical Practice Guidelines for Physicians in Primary Healthcare Facilities 2014.[13]

The statistical analysis was performed in Version 18 SPSS Program (SPSS Corp., Chicago, IL, USA). The descriptive analysis involving a Chi-Square test comprised the frequency and percentage of antibiotic use as well as diagnosis of the types of respiratory tract disease.

Results

Of 13362 prescriptions collected from six primary healthcare centers at sub-district level during the research period, 1453 prescriptions for different diagnoses were taken with purposive sampling and 632 prescriptions for diagnosed respiratory tract disease were evaluated. The prescriptions were gathered from the general clinic for patients >5 years old and the mother-child clinic for <5 year-old patients. Of 21 prescribers, most of them were female (90.5%), and these prescribers work as a physician (23.8%), and others (76.2 %) (Table 1). A large majority of antibiotics were prescribed by non physicians (59.2%),

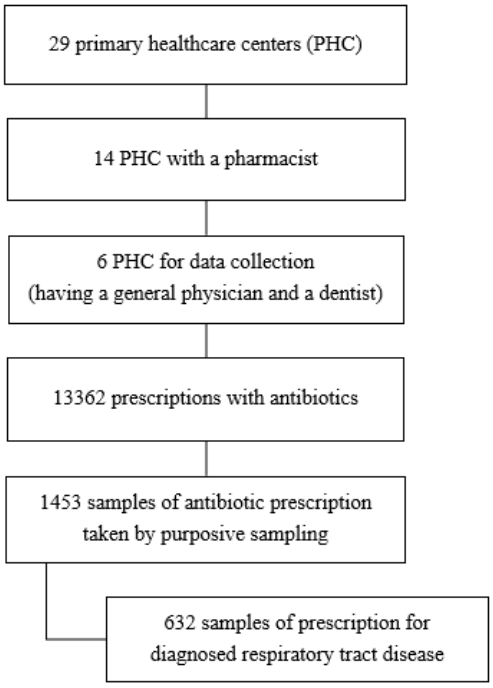

Figure 1 Flowchart of Data Collection

Table 1 Demographic Characteristics of Patients and Prescribers

Characteristic	Quantity (%)
Patients (n=632)	
Sex	
Male	262 (41.5)
Female	370 (58.5)
Age (Years)	
<5	190 (30.1)
6–12	132 (20.9)
13–18	35 (5.5)
19–60	258 (40.8)
>60	17 (2.7)
Number of Prescriptions Written by	
Physician	258 (40.8)
Non-Physician (midwife/nurse)	374 (59.2)
Prescribers (n=21)	
Sex	
Male	2 (9.5)
Female	19 (90.5)
Qualification	
Physician	5 (23.8)
Non-Physician (midwife/nurse)	16 (76.2)
Experience (Years of Service)	
<12.0	8 (38.1)
>12.0	13 (61.9)

administered more to female than to male (58.5% or 370 female patients), and their age ranged >19–60 years old (Table 1).

There were eight diagnoses of respiratory tract disease according to the ICD X code (Table 2). The most frequent diagnosis was acute nasopharyngitis or common cold (87.2%) followed by acute pharyngitis (6.3%) for URTIs as well as pneumonia (1.9%) for LRTIs. Seven types of antibiotics were prescribed

Table 2 Number of Cases and Distribution of Antibiotic Use in Each Diagnosis

ICD X	Diagnosis	Total (%)	Antibiotics (Total, (%))						
			Amx	Cot	Met	Cip	Cef	Ery	Chlo
J00	Acute Nasopharyngitis (common cold)	551 (87.2)	419 (66.3)	67 (10.6)	0 (0)	45 (7.1)	16 (2.5)	2 (0.3)	2 (0.3)
J02	Acute Pharyngitis	40 (6.3)	36 (5.7)	0 (0)	1 (0.2)	2 (0.3)	0 (0)	1 (0.2)	0 (0)
J03	Acute Tonsillitis	8 (1.3)	5 (0.8)	1 (0.2)	0 (0)	1 (0.2)	1 (0.2)	0 (0)	0 (0)
J11	Influenza	2 (0.3)	2 (0.3)	0 (0)	0 (0)	0 (0)	0	0 (0)	0 (0)
J18	Pneumonia	12 (1.9)	10 (1.6)	1 (0.2)	0 (0)	0 (0)	1 (0.2)	0 (0)	0 (0)
J20	Acute Bronchitis	7 (1.1)	5 (0.8)	1 (0.2)	0 (0)	0 (0)	1 (0.2)	0 (0)	0 (0)
J30	Allergic Rhinitis	5 (0.8)	4 (0.6)	0 (0)	0 (0)	1 (0.2)	0	0 (0)	0 (0)
J45	Asthma	7 (1.1)	4 (0.6)	0 (0)	0 (0)	3 (0.5)	0 (0)	0 (0)	0 (0)
	Total	**485 (76.7)**	**70 (11.1)**	**1 (0.2)**	**52 (8.2)**	**19 (3.0)**	**3 (0.5)**	**2 (0.3)**	

Amx=Amoxicillin; Co=Cotrimoxazole; Met=Metronidazole; Cip=Ciprofloxacin; Cef=Cefadroxil; Ery=Erythromycin; Chlo=Chloramphenicol

Table 3 Distribution of Drug Prescribing Irrationality

Diagnosis	Type of Irrationality (n=623)				Total (%)
	Antibiotic Selection	Dose of Administration	Frequency of Administration	Duration of Administration	
Acute Nasopharyngitis (common cold)	114	57	9	364	544 (86.1)
Acute Pharyngitis	3	0	2	35	40 (6.0)
Acute Tonsillitis	3	0	0	5	8 (1.3)
Influenza	2	0	0	0	2 (0.3)
Pneumonia	0	3	0	7	10 (1.6)
Acute Bronchitis	5	0	0	2	7 (1.1)
Allergic Rhinitis	5	0	0	0	5 (0.8)
Asthma	7	0	0	0	7 (1.1)
Total					**623 (98.3)**

for the treatment of respiratory tract disease, among which amoxicillin became the most commonly prescribed (76.7%).

Of 632 prescriptions, 621 (98.3%) failed to match the criteria of rational antibiotic prescribing. Inappropriate prescribing included antibiotic selection (22.0%), dosage of administration (9.5%), frequency of administration (1.7 %), and duration of administration (65.0%). Irrationality occurred in antibiotic therapy for acute nasopharyngitis (common cold) for all types of inappropriateness (Table 3).

There was an overall difference in the level of antibiotic prescribing rationality between physicians and non-physicians. Antibiotic prescribing by physicians was 1,828-fold more appropriate than by non-physicians. The prescribers' shorter experience was also a factor in irrational prescribing with odds ratio (OR): 0.536 (Table 4).

Discussion

This study found 632 in 1453 prescriptions (43.49%) intended for diagnosed respiratory tract disease with 95.1% URTIs, 3.0% LRTIs, and 1.9% other respiratory tract diseases. This finding remains unsurprising due to the high prevalence of acute respiratory tract infections in Indonesia.[2] Our findings are in line with the research by Ab Rahman, *et*

Table 4 Bivariate Correlation between the Characteristics of Prescribers and the Rationality of Antibiotic Prescribing in Six Primary Healthcare Centers

Characteristic of Prescribers	Rationality of Prescribing (n=9)	OR*	95%CI	p-value
Qualification				
Physician	5 (55.5%)	1.828	0.486–6.874	0.365
Non-Physician	4 (45.5%)			
Experience (Years of Service)				
<12.0	4 (45.5%)	0.536	0.143–2.016	0.349
>12.0	5 (55.5%)			

*OR=Odds ratio

al. in primary healthcare centers (PHC) in Malaysia, indicating antibiotic prescribing for diagnosed acute upper respiratory infection that reached 49.2%, followed by 6.0% acute tonsillitis, 1.7 % acute bronchitis, and 1.3% asthma.[17] Study in Switzerland also found the highest percentage of antibiotic prescribing in primary care for a diagnosis of common cold (25.4%) followed by influenza (21.0%) and acute bronchitis (14.2%).[18]

Antibiotic prescribing for URTIs reached 95.1% with prescriptions most frequently given to common cold diagnosis (87.2%). Such diagnosis is a group of disease typically caused by heterogeneous viruses. It is therefore unresponsive to antibiotics and not recommended to be treated with any.[19] Guidelines from the Ministry of Health of the Republic of Indonesia tolerate the administration of antibiotics for common cold if secondary infection is proved to exist.[13] However, a majority of patient medical records have no information on secondary infections or other medical conditions that require antibiotic administration. Therefore, prescribers must be more selective in giving antibiotic therapy to patients with URTIs, and pharmacists must dispense antibiotics more strictly.

Other respiratory tract diseases administered with antibiotics in this study include allergic rhinitis (0.8%) and asthma (1.1%). Allergic rhinitis is clinically defined as a group of nasal symptoms due to allergens or an inflammation of the nasal membranes mediated by IgE.[20] Meanwhile, asthma is a diagnosis associated with chronic inflammation in respiratory organs.[21] Neither of them are infections. Therefore, no recommendation is made for the use of antibiotics for allergic rhinitis and asthma according to both national and international guidelines, including ARIA for allergic rhinitis and GINA for asthma.[13,20,22] A study by Baan, *et al.* in the United Kingdom (UK) also indicated a high frequency of antibiotic prescribing for patients with asthma, including for those with asthma exacerbations alone or with asthma-URTIs combination. In fact, both conditions require no antibiotic therapy.[23] There was limited evidence that antibiotics could be used for asthma attacks, thus leaving it extremely doubtful.[21] Moreover, the use of antibiotics in asthma improves neither the symptoms nor conditions after an asthma attack.[24]

This study focused on the quality of antibiotic prescribing for respiratory tract disease in primary healthcare centers in Tegal District. Antibiotic prescribing rationality is assessed from appropriateness of indications, patients, types, and dosage regimen of antibiotics in following the provided guidelines/policy.[25] In addition, the qualification and experience of prescribers can affect prescribing quality.[26–28]

Irrationality in duration of administration dominates the findings of this study (65.0%). Overall, antibiotic therapy is administered for 3 days, which is obviously shorter than the average minimum 5-day administration recommended by the guidelines.[13] This irrationality of duration of administration would potentially lead to antibiotic resistance. Therefore, policy in PHC which allow to prescribe antibiotic only for 3 days should be reviewed. The Nasional Formulary of 2017 also allowed antibiotic prescribing in primary healthcare centers within a regimen period of 10 – 21 days.[29] The second most irrationality is in terms of antibiotic selection (22.0%), particularly the choice for common cold. The national guidelines suggest administrating antibiotics, which includes Amoxicillin, Cefadroxil, and Erythromycin, to URTIs, one of which is common cold, when they are accompanied by a secondary infection. Meanwhile, Cotrimoxazole, Ciprofloxacin, and Chloramphenicol are not a choice for such indication.[13]

Based on previous research, some of the factors contributing to the pattern of antibiotic

selection are educational attainment and qualification of the prescribers, competitive environment, and antibiotic availability.[30] Our study classified two groups of prescribers, namely physicians and non- physicians. The non- physicians group comprises midwives and nurses who are both representatives of a physicians to provide health services for patients in primary healthcare centers because physicians cannot serve all of the patients. The assignment of nurses and midwives is stipulated in a decree approved by the head of Primary Healthcare Center. This study found that prescribers who work as physicians had 1,828-fold appropriateness in following the national treatment guidelines (95% CI: 0.486–6.874). Shorter term of prescribing experience (<12 years) was also a contributing factor in irrational prescribing (OR: 0.536l, 95% CI: 0.143–2.016). However, both factors were statistically insignificant.

This is different from the findings of a study by Andrajati, *et al.,* in which physicians with shorter term of experience were 3.9-fold more rational in prescribing antibiotics.[14] The difference in the results of our study was highly likely caused by the fact that there were other prescribers than physicians. The number of midwives and nurses was higher and they prescribed more antibiotics. Most of them have not acknowledged nor understood the Clinical Practice Guidelines, especially prescribers' shorter experience. Limited knowledge of prescribing is a contributing factor in antibiotic prescribing.[14] In addition, prescribers with lower educational attainment tend to administer antibiotics more irrationally.[14, 30]

Rational prescribing can be improved by providing educational intervention for prescribers along with auditing and prescribing feedback.[31] In addition, the implementation of Antibiotic Stewardship is essential to reduce antibiotic prescribing.[11,31] In China, the implementation of Antibiotic Stewardship could reduce antibiotic prescribing in children with ARIs by 29%.[11] Reduction of antibiotic prescribing and exposure can decrease the risk of antibiotic resistance.[32,33] Updating and implementing the national treatment guidelines becomes an important step to reduce the use of antibiotics and improve their rational prescribing.[34] Therefore, regular trainings for prescribers and a refresher of national treatment guidelines are required to improve the quality of prescribing.

Conclusion

This cross-sectional study found irrationality in antibiotic prescribing for respiratory tract diseases. Such irrationality was dominated by the duration of administration and antibiotic selection, which would potentially lead to antibiotic resistance. Physicians had 1,828-fold appropriateness in following the national treatment guidelines. Prescribing experience <12 years was also a contributing factor in irrational prescribing. Both the factors affected the rationality of prescription, even though not significant due to lack of sample influenced the rationality.

Acknowledgement

The authors would like to thank all the heads of primary healthcare centers as the research site for the permit as well as to all parties for the support.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article

Funding

The study was not funded by any source of grants.

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