JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Antibiotic prescribing for children five years or younger in Indonesian primary care settings

Yosi Irawati Wibowo[1], Niken Firdhausi[2], Nur Rahmah[2], Noviana Setianur[2], Bruce Sunderland[3], Adji Prayitno Setiadi[1]

[1] Centre for Medicine Information and Pharmaceutical Care (CMIPC) and Clinical and Community Pharmacy Department, Faculty of Pharmacy, Universitas Surabaya, Surabaya, Indonesia
[2] Faculty of Pharmacy, Universitas Surabaya, Surabaya, Indonesia
[3] Medical School, Faculty of Health Sciences, Curtin University, Perth, Australia

Abstract

Introduction: Children are at a higher risk of antibiotic overprescribing, while limited surveillance is evident in primary care settings. This study aims to examine patterns of infections and associated antibiotic use in children attending Primary Health Centers (PHCs), including an explanatory analysis of antibiotics for non-pneumonia acute respiratory infections (ARIs), pneumonia, and diarrhea.

Methodology: An observational study used records of all children ≤ 5 years of age prescribed antibiotics from January 2019 to December 2020 in selected PHCs in Surabaya and Banjarmasin, Indonesia. Data on children's characteristics, diagnoses, and antibiotics prescribed, were collected from patient records. The explanatory analysis was based on national guidelines. A descriptive analysis was used to summarize the data.

Results: A total of 1053 and 1463 children's records with antibiotics were located at Surabaya and Banjarmasin PHCs, respectively. ARIs were the most common indications for antibiotic prescribing in both settings, either non-pneumonia ARIs (60.6% versus 33.8%, respectively) or pneumonia (20.2% versus 25.2%, respectively). High conformity with guidelines were evident for antibiotics used for pneumonia (i.e., amoxicillin/cotrimoxazole/erythromycin – 89.3%) or specified upper ARIs (e.g., amoxicillin for pharyngitis – 73.9%), and for diarrhea (i.e., cotrimoxazole – 73.1%). However, some information, such as diagnoses, were not recorded or were unspecific, hence limiting assessment.

Conclusions: This study provided insights into prescribing antibiotics among children in Indonesia. Lack of specific guidelines for children and inadequate documentation for antibiotic prescribing warrants improvement. Larger prospective studies should assess appropriate prescribing at the national level to optimize the use of antibiotics.

Key words: antibiotic; prescribing; children; primary care; Indonesia.

J Infect Dev Ctries 2025; 19(3):409-417. doi:10.3855/jidc.19581

(Received 19 November 2023 – Accepted 29 February 2024)

Copyright © 2025 Wibowo *et al*. This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Antibiotics can be a lifesaving treatment for bacterial infections and are among the most commonly prescribed drugs globally [1]. In younger children, individual exposures to antibiotics are frequently high, especially in low-middle income countries (LMICs) [2], including Indonesia. A small study in Indonesian rural communities (n = 334) reported that 33% of children had received antibiotics within the last 30 days (about 4 courses per child per year) [3]. This figure was similar to the rate of antibiotic courses prescribed for children less than 2 years (4.9 courses per child per year) in a cohort study conducted in eight LMICs across Asia, Africa and Latin America [4].

Excessive use of antibiotics can cause more adverse events, drug toxicity and detrimental effects on the gut microbiota and enteric immune system [4]. At both the individual and population levels, antibiotic overuse drives the development and transmission of antimicrobial resistance (AMR), which is one of the leading causes of death in the world [15]. To tackle the global issue of AMR, the World Health Organisation (WHO) initiated a "Global Action Plan on Antimicrobial Resistance" in May 2015 [6], which was followed by The Indonesian Government issuing regulations establishing a 'National Action Plan for Controlling AMR 2020-2024' [7]. This action has focused on pre- and post-marketing surveillance, which included, but not limited to, increasing public awareness as well as monitoring and optimizing the use of antibiotics in health facilities [7].

International studies have reported high levels of antibiotic prescribing in primary health facilities [8]. A previous study in rural communities in Indonesia (n =

203) reported that 49.3% children under 5 years of age received antibiotics, with 98% originating from primary health facilities [3]. It has been suggested that antibiotics are often prescribed for mild illnesses in children, where little evidence exists of any benefits from antibiotics [2,4,9]. While children are at a higher risk of antibiotic overprescribing, a considerable investment in surveillance of antibiotic use patterns among neonates and children would be of importance [10].

Primary Health Centres (PHCs, *Puskesmas*) are technical units of the regional health offices at the district (*kecamatan*) level [11]. In 2019, a ratio of 1.4 PHCs per district was reported [12], thus PHCs are considered as frontline primary care providers in Indonesia. To evaluate quality use of medications in PHCs, the Ministry of Health established quality indicators according to WHO, which included the use of antibiotics in non-pneumonia acute respiratory infections (ARIs) and non-specific diarrhea [13]; the evaluation, however, was conducted using general patients and not all PHCs were analyzed or provided a complete data set [13]. Studies involving children in PHCs have generally been small and limited when evaluating the use of antibiotics for specific illnesses, such as pneumonia, ARIs, or diarrhea [14-16]. Hence, this study aimed to describe patterns of illnesses as well as antibiotic use in children (≤5 years of age) attending Indonesian PHCs. This was followed with an explanatory analysis evaluating the choice of antibiotics for common illnesses in children, including non-pneumonia ARIs, pneumonia, and diarrhea. Diarrhea and ARIs are common illnesses among children in Indonesia [3], where pneumonia and diarrhea have been reported as the leading causes of death in children under five years of age [17].

Methodology

This study obtained permission from Regional Health Office (number 072/17297/436.7.2/2022), and was approved by the Research Ethics Committee at Universitas Surabaya (number 89/KE/VI/2022).

Study setting and design

An observational study was conducted in May-July 2022 in Surabaya and Banjarmasin, Indonesia. Surabaya is the capital city of East Java Province (western part of Indonesia) with a very high Human Development Index - HDI (82.31 in 2021); while Banjarmasin is the capital city of South Kalimantan (central part of Indonesia) with a lower HDI (77.97 in 2022) [18,19]. Surabaya covers 31 districts, and has 63 PHCs with a ratio of 0.22 per 1,000 population [20]. Two districts (RK and SU) were selected by the regional health office staff to include a range of socioeconomic levels; all PHCs in the districts were included, i.e., two PHCs in RK District and three PHCs in SU District. Banjarmasin is divided into five districts with a total of 26 PHCs [19]. Two districts (NB and CB) were selected by the regional health office staff to include a range of socioeconomic levels; all five PHCs in CB District were included, and only two of four PHCs in NB District were involved due to limitations in their records system. All children ≤ 5 years of age prescribed antibiotics from January 2019 to December 2020 in the selected PHCs were included. The children were identified based on antibiotic prescriptions received at the pharmacy unit in the PHCs; their records were then retrieved to obtain data on the characteristics, diagnosis, and antibiotic therapy.

Table 1. Antibiotics recommended by the national guidelines.

Indication	Guidance of Clinical Practice for General Practitioners in Primary Care Settings	Integrated Management of Childhood Illnesses
Pneumonia	First-line (ambulatory settings): amoxicillin oral or co-trimoxazole oral	First line: amoxicillin oral - if not responded: erythromycin
Non-pneumonia ARIs		
A. Upper ARIs	When recommended (bacterial aetiology suspected):	N/A
-Pharyngitis	amoxicillin	
-Laryngitis	penicillins	
-Tonsilitis	amoxicillin or erythromycin	
-Rhinitis	amoxicillin or erythromycin or cefadroxil*	
-Sinusitis	amoxicillin or co-trimoxazole or erythromycin	
B. Influenza	No antibiotics	
Diarrhea	When recommended [diarrhea with blood (mainly caused by shigellosis) or suspect cholera] - Dysentery (shigellosis): ciprofloxacin (caution in children) or azithromycin* or cefixime*; Cholera: ciprofloxacin (caution in children) or co-trimoxazole	When recommended [diarrhea with blood (dysentery) or suspect cholera] - Dysentery (shigellosis): first-line: co-trimoxazole, second line: cefixime*; Cholera: first-line: tetracycline, second-line: co-trimoxazole

*the agents were not included in the 2019 National Formulary for primary care settings.

Data analysis

Data were analyzed using IBM SPSS version 25. Descriptive analysis summarized the data. This was followed with an explanatory analysis evaluating the antibiotics prescribed for non-pneumonia ARIs, pneumonia, and diarrhea; being the most common illnesses among children in Indonesia [3]. While formal or specific prescribing guidelines for children in PHCs are not available, the antibiotic prescribing was compared to those recommended by Guidance of Clinical Practice for General Practitioners in Primary Care Settings and/or Integrated Management of Childhood Illnesses (*Manajemen Terpadu Balita Sakit*, MTBS) (Table 1) [21-23]. MTBS is an integrated approach where different sectors – healthcare professionals, health system, and family/community – work together to manage childhood illnesses [22]. The recommended antibiotics would also be checked for their compatibility with 2019 National Formulary, which is a list of medications that should be provided and used in Indonesian health facilities under national health coverage (*Jaminan Kesehatan Nasional*, JKN) [23]. The proportions of children prescribed the recommended antibiotics were then calculated.

Results

A total of 1053 and 1463 records of children (≤ 5 years) prescribed antibiotics were identified in the selected PHCs in Surabaya and Banjarmasin, respectively. Table 2 shows a summary of the children's characteristics. Most children were between 1 to 2 years in Surabaya PHCs, and 2 to 3 years in Banjarmasin PHCs (38.6% and 37.3%, respectively). The proportions of males were slightly higher than females in both regions. Children's bodyweights in Banjarmasin PHCs were generally lower than those in Surabaya PHCs for all age groups.

The majority of children prescribed antibiotics in Surabaya and Banjarmasin PHCs had diagnoses of non-pneumonia ARIs (60.6% versus 33.8%, respectively) or pneumonia (20.2% versus 25.2%, respectively); of those with non-pneumonia ARIs, the majority were not recorded with a specific diagnosis (560 and 284 cases, respectively) (Table 3). Furthermore, a small proportion of children prescribed antibiotics had a diagnosis of diarrhea in both Surabaya PHCs and Banjarmasin PHCs (6.4% and 3.6%, respectively). In addition, of those prescribed antibiotics, tuberculosis and skin infection cases were reported to be higher in Banjarmasin compared to those in Surabaya. It should be noted that 12.2% of children in Banjarmasin PHCs had no information of their diagnoses.

The most frequently prescribed antibiotics for children in Surabaya and Banjarmasin PHCs were amoxicillin (70.5% versus 48.8%, respectively) and co-trimoxazole (22.3% versus 23.0%, respectively). Cefadroxil was prescribed for 14.9% of children in Banjarmasin PHCs, but none in Surabaya PHCs. Details on antibiotics prescribed in children at these PHCs are reported in Table 4.

The explanatory analysis findings can be seen in Table 5. The analysis was limited to antibiotics prescribed for non-pneumonia ARIs, pneumonia, and diarrhea (n = 1811); while most cases of non-pneumonia ARIs were not specified (560 cases for Surabaya PHCs, and 284 cases for Banjarmasin PHCs), an appropriate prescribing analysis was performed only for 967 cases or antibiotic prescriptions. Overall, the choice of antibiotics conformed to the national guidelines (808/967; 83.6%). In terms of pneumonia

Table 2. Characteristics of children prescribed antibiotics in Primary Health Centers (PHCs).

Characteristics	PHC Surabaya Region			PHC Banjarmasin Region		
	PHCs RK District N = 434, n (%)	PHCs SU District N = 619, n (%)	Total N = 1053, N (%)	PHCs NB District N = 719, n (%)	PHCs CB District N = 744, n (%)	Total N = 1463, N (%)
Age						
0-12 months	45 (10.4)	53 (8.6)	98 (9.3)	28 (3.9)	53 (7.1)	81 (5.5)
> 12-24 months	113 (26.0)	142 (22.9)	255 (24.2)	251 (34.9)	295 (39.6)	546 (37.3)
> 24-36 months	150 (34.6)	256 (41.4)	406 (38.6)	172 (23.9)	186 (25.0)	358 (24.5)
> 36-48 months	108 (24.9)	158 (25.5)	266 (25.3)	146 (20.3)	138 (18.5)	284 (19.4)
49-60 months	18 (4.1)	10 (1.6)	28 (2.7)	122 (17.0)	73 (9.8)	195 (13.3)
Gender						
Male	251 (57.8)	335 (54.1)	586 (55.7)	368 (51.2)	443 (59.5)[a]	811 (55.4)[a]
Female	183 (42.2)	284 (45.9)	467 (44.3)	348 (48.4)	300 (40.3)	651 (44.5)
Body weight (Mean ± SD, kg)						
0-12 months	10.4 ± 1.46	11.2 ± 1.21	10.9 ± 1.38	8.2 ± 1.15[b]	8.5 ± 1.36	8.3 ± 1.16
> 12-24 months	13.1 ± 1.98	13.5 ± 1.70	13.3 ± 1.84	9.2 ± 1.88[b]	9.5 ± 1.56	9.2 ± 1.85
> 24-36 months	14.9 ± 2.06	15.2 ± 2.06	15.1 ± 2.06	11.5 ± 2.17[b]	11.9 ± 2.34	11.5 ± 2.19
> 36-48 months	18.2 ± 2.31	18.7 ± 2.41	18.5 ± 2.38	13.1 ± 2.37[b]	13.3 ± 4.04	13.4 ± 2.81
49-60 months	20.2 ± 2.9	24.2 ± 1.14	21.7 ± 3.11	15.6 ± 2.71[b]	15.1 ± 0.74	15.0 ± 2.61

PHC: Primary Health Centre; kg: kilogram; SD: standard deviation; RK, SU, NB, CB: codes for the district; [a]1 missing data; [b]no weight data available from one PHC in NB District (N = 581).

Table 3. Distribution of diagnoses for which antibiotics were prescribed for children in Public Health Centers (PHCs).

Disease name	PHC Surabaya Region			PHC Banjarmasin Region		
	PHC RK District N = 434, n (%)[b]	PHCs SU District N = 619, n (%)[b]	Total N = 1053, N (%)[b]	PHC NB District N = 719, n (%)[b]	PHCs CB District N = 744, n (%)[b]	Total N = 1463, N (%)[b]
Specific infectious and parasitic diseases						
Tuberculosis	-	-	-	42 (5.8)	8 (1.1)	50 (3.4)
Intestinal infectious diseases (e.g., typhoid, dysentery)	11 (2.5)	11 (1.8)	22 (2.1)	19 (2.6)	20 (2.7)	39 (2.7)
Viral infections (e.g., HFMD, varicella, measles)	-	-	-	15 (2.1)	8 (1.1)	23 (1.6)
Others (e.g., scabies)	-	-	-	8 (1.1)	5 (0.7)	13 (0.9)
Diseases of skin and subcutaneous tissue						
Infections of the skin and subcutaneous tissue (e.g., abscess, furuncle and carbuncle)	10 (2.3)	3 (0.5)	13 (1.2)	33 (4.6)	31 (4.2)	64 (4.4)
Dermatitis	31 (7.1)	23 (3.7)	54 (5.1)	51 (7.1)	18 (2.4)	69 (4.7)
Others (e.g., miliaria)	-	-	-	3 (0.4)	9 (1.2)	12 (0.8)
Diseases of respiratory system						
Non-pneumonia ARIs:						
A. Non-pneumonia ARIs (unspecified)	229 (52.8)	331 (53.5)	560 (53.2)	21 (2.9)	263 (35.5)	284 (19.4)
B. Upper ARIs						
- Pharyngitis	23 (5.3)	55 (8.9)	78 (7.4)	33 (4.6)	111 (14.9)	144 (9.8)
- Tonsilitis	-	-	-	8 (1.1)	14 (1.9)	22 (1.5)
- Laryngitis	-	-	-	-	6 (0.8)	6 (0.4)
- Rhinitis	-	-	-	13 (1.8)	4 (0.5)	17 (1.2)
- Sinusitis	-	-	-	1 (0.4)	-	1 (0.1)
C. Influenza	-	-	-	12 (1.7)	9 (1.2)	21 (1.4)
Pneumonia	78 (18.0)	133 (21.9)	211 (20.0)	248 (34.5)	121 (16.3)	369 (25.2)
Chronic respiratory diseases (e.g., asthma, bronchitis)	-	-	-	2 (0.3)	5 (0.7)	7 (0.4)
Diseases of eye, ear or oral cavity						
Diseases of eye						
- conjunctivitis	11 (2.5)	5 (0.8)	16 (1.5)	21 (2.9)	26 (3.5)	47 (3.2)
- others (e.g., hordeolum)	-	-	-	14 (1.9)	9 (1.2)	23 (1.6)
Diseases of the ear (e.g., otitis)	-	-	-	8 (1.1)	7 (0.9)	15 (1.0)
Diseases of oral cavity (e.g., gingivitis)	14 (3.2)	13 (2.1)	27 (2.6)	6 (0.8)	3 (0.4)	9 (0.6)
Diseases of genitourinary system						
Urinary tract infection	1 (0.2)	-	1 (0.1)	-	3 (0.4)	3 (0.2)
Symptoms, signs or abnormal clinical/laboratory findings						
Fever	-	-	-	9 (1.3)	16 (2.2)	25 (1.7)
Diarrhea	25 (5.8)	42 (6.8)	67 (6.4)	31 (4.3)	21 (2.8)	52 (3.6)
Allergy	4 (0.9)	5 (0.8)	9 (0.9)	-	-	-
Cough	2 (0.5)	2 (0.3)	4 (0.4)	-	20 (2.7)	20 (1.4)
Not available[a]				142 (19.7)	37 (5.0)	179 (12.2)

PHC: Primary Health Centre; ARIs: acute respiratory infections; HFMD; hand, foot, and mouth disease; RK, SU, NB, CB: codes for the district; [a]no information about the diagnosis; [b]n=number of cases/diagnoses where an antibiotic was prescribed (note: one child might have more than one diagnoses or antibiotic).

Table 4. Antibiotics prescribed for children in Primary Health Centers (PHCs).

Prescribed antibiotic	PHC Surabaya Region			PHC Banjarmasin Region		
	PHC RK District N = 434, n (%)[a]	PHCs SU District N = 619, n (%)[a]	Total N = 1053, N (%)[a]	PHC NB District N = 719, n (%)[a]	PHC CB District N = 744, n (%)[a]	Total N = 1463, N (%)[a]
Oral antibiotic						
Amoxicillin	319 (73.5)	423 (68.3)	742 (70.5)	345 (48.0)	372 (50.0)	717 (49.0)
Azithromycin	1 (0.2)	-	1 (0.1)	-	1 (0.1)	1 (0.1)
Erythromycin	12 (2.8)	20 (3.2)	32 (2.9)	1 (0.1)	7 (0.9)	8 (0.5)
Cefadroxil	-	-	-	101 (14.0)	117 (15.7)	218 (14.9)
Cefixime	-	11 (1.8)	11 (1.0)	18 (2.5)	109 (13.6)	127 (8.6)
Chloramphenicol	1 (0.2)	-	1 (0.1)	6 (0.8)	13 (1.7)	19 (1.3)
Cotrimoxazole	83 (19.1)	152 (24.6)	235 (22.3)	95 (13.2)	81 (10.9)	176 (12.0)
Isoniazid	-	-	-	42 (5.8)	6 (0.8)	48 (3.3)
Metronidazole	-	-	-	-	1 (0.1)	1 (0.1)
External antibiotic						
Bacitracin	-	-	-	23 (3.2)	20 (2.7)	43 (2.9)
Chloramphenicol	22 (5.1)	13 (2.1)	35 (3.3)	20 (2.8)	7 (0.9)	27 (1.8)
Fusidic Acid	-	-	0 (0.0)	24 (3.3)	-	24 (1.5)
Gentamicin	-	-	0 (0.0)	42 (5.8)	60 (8.1)	102 (7.0)
Oxytetracycline	17 (3.9)	14 (2.2)	31 (2.9)	50 (7.0)	6 (0.8)	56 (3.8)
Neomycin/Polymyxin SO_4	-	-	-	-	1 (0.1)	1 (0.1)

PHC: Primary Health Centre; RK: SU, NB, CB: codes for the district; [a]n = number of cases/diagnoses where an antibiotic was prescribed (note: one child might have more than one diagnoses or antibiotic).

choice of antibiotics in Surabaya and Banjarmasin PHCs was amoxicillin [105/211 (49.7%) versus 271/369 (73.4%), respectively] and co-trimoxazole [93/211 (44.1%) versus 36/369 (9.8%), respectively]. Low percentages of other antibiotics prescribed were not recommended, such as cefixime. Regarding specified non-pneumonia ARIs with antibiotic prescriptions (n = 268), 74.6% were according to the guidelines. The most common antibiotics for specified non-pneumonia ARIs included: amoxicillin for pharyngitis (75/78 cases in Surabaya PHCs and 86/144 cases in Banjarmasin PHCs; 73.9%), amoxicillin for tonsillitis (18/20 cases in Banjarmasin PHCs), amoxicillin for laryngitis (6/6 cases in Banjarmasin PHCs), amoxicillin and cefadroxil for rhinitis (5/18 and 4/18 cases in Banjarmasin PHCs, respectively), and amoxicillin for sinusitis (1/1 case in Banjarmasin PHC). However, there were 21 cases of prescribed antibiotics for influenza in Banjarmasin PHCs, which were not according to the guideline recommendations.

Low case numbers involved diarrhea being treated with antibiotics (n = 119); these were reported in both Surabaya and Banjarmasin PHCs (67 and 52 cases, respectively). Co-trimoxazole was the most common

Table 5. Antibiotic prescribed for Acute Respiratory Infections (ARIs), Pneumonia and Diarrhea in Public Health Centers.

Diagnoses	Prescribed antibiotic	PHC Surabaya Region			PHC Banjarmasin Region			Conformity with the guideline*, Case/total case (%)
		PHC RK District (n)	PHCs SU District (n)	Total (N)	PHC NB District (n)	PHC CB District (n)	Total (N)	
Non-pneumonia ARIs:								
A. Non-pneumonia ARIs (unspecified)	Amoxicillin	184	257	441	15	96	111	N/A
	Cefixime	-	51	51	5	84	89	
	Cefadroxil	-	-	-	-	55	55	
	Cotrimoxazole	39	12	51	1	23	24	
	Erythromycin	6	11	17	-	1	1	
	Chloramphenicol	-	-	-	-	4	4	
				N = 560			**N = 284**	
B. Upper ARIs								
Pharyngitis	Amoxicillin*	22	53	75	8	81	89	164/222 (73.9)
	Cefadroxil	-	-	-	8	16	24	
	Cefixime	-	-	-	1	3	4	
	Cotrimoxazole	1	2	3	16	10	26	
	Erythromycin	-	-	-	-	1	1	
				N = 78			**N = 144**	
Tonsillitis	Amoxycillin*	-	-	-	7	11	18	20/22 (90.9)
	Cefadroxil	-	-	-	1	1	2	
	Erythromycin*	-	-	-	-	2	2	
				N = 0			**N = 22**	
Laryngitis	Amoxicillin*	-	-	-	-	6	6	6/6 (100)
				N = 0			**N = 6**	
Rhinitis	Amoxicillin*	-	-	-	2	3	5	9/17 (52.9)
	Cefadroxil*	-	-	-	3	1	4	
	Cotrimoxazole	-	-	-	8	-	8	
				N = 0			**N = 17**	
Sinusitis	Amoxicillin*	-	-	-	1	-	1	1/1 (100.0)
				N = 0			**N = 1**	
				N = 78			**N = 190**	
C. Influenza	Amoxicillin	-	-	-	7	5	12	0/0 (0.0)
	Cefadroxil	-	-	-	3	1	4	
	Cotrimoxazole	-	-	-	2	2	4	
	Chloramphenicol	-	-	-	-	1	1	
				N = 0			**N = 21**	
Pneumonia	Amoxicillin*	48	57	105	172	99	271	518/580 (89.3)
	Cefadroxil	-	-	-	42	13	55	
	Cefixime	-	-	-	5	-	5	
	Cotrimoxazole*	25	68	93	27	9	36	
	Chloramphenicol	-	-	-	2	-	2	
	Erythromycin*	5	8	13	-	-	-	
				N = 211			**N = 369**	
Diarrhea	Amoxicillin	8	10	18	1	8	9	87/119 (73.1)
	Cefadroxil	-	-	-	-	1	1	
	Cefixime	-	-	-	-	3	3	
	Cotrimoxazole*	16	32	48	30	9	39	
	Erythromycin	1	-	1	-	-	-	
				N = 67			**N = 52**	

ARIs: Acute Respiratory Infections; *recommended by the national guidelines (Table 1); n: number of cases/diagnoses where an antibiotic was prescribed (note: one child might have more than one diagnoses or antibiotics.

antibiotic used, of which 87/119 (73.1%) of prescriptions were compliant with the guidelines when shigella dysentery or cholera were suspected (Table 5).

Discussion

This study has provided data on the prescribing of, and appropriate choice of antibiotics among children five years or younger, in Indonesian primary care settings. Most children prescribed antibiotics had diagnoses of ARIs – pneumonia and non-pneumonia – in both Surabaya and Banjarmasin PHCs in Indonesia. Globally, ARIs are very common and are the leading cause of death in young children. WHO reported that pneumonia was responsible for 740,180 deaths among children under five years in 2019, representing 14% of all deaths in this age group [24]. In parallel, the Indonesian health profile data in 2021 reported the prevalence of pneumonia was 3.55% in children under five years of age, and pneumonia accounted for 14.4% and 9.4% of the total deaths in children aged under 1 year and 1-5 years, respectively [17].

Most of the antibiotics prescribed for young children in this study were within the Access group (e.g., amoxicillin and co-trimoxazole) according to the 2019 WHO AwaRe (Access, Watch, and Reserve) classification [25]; the Access group contains antibiotics with narrow-spectrum activity and a lower risk of AMR, classifying them as first-line treatments for most infections [26]. However, this study also indicated a lower percentage of antibiotics within the Watch group (e.g., cefixime and erythromycin) [25]. Watch antibiotics generally have a higher potential for AMR and are more often used in hospitalized patients [26], thus the use of such antibiotics in primary care settings as reported in this study warrants careful monitoring to avoid overuse. A review of the limited data available from Indonesian primary care settings reported a different profile of antibiotic prescribing with amoxicillin and cefadroxil (both Access), and ciprofloxacin (Watch) as the most prescribed antibiotics [27]; however, this data was obtained from the general population which might have different profiles of infections compared with children. Hence, this study has provided valuable insight on the use of antibiotics specifically for younger children.

In terms of the appropriateness of prescribing, this study found that antibiotics used for pneumonia were mainly amoxicillin or co-trimoxazole, which conformed with the available guidelines [21,22]. In parallel, a prior study in a single PHC (n = 70 children) in Semarang, Central Java, Indonesia, reported that all children with pneumonia were treated either with amoxicillin or co-trimoxazole [28]. Pneumonia in children younger than 5 years is often related to bacterial pathogens, particularly *Streptococcus pneumoniae* (30% to 50%) and *Haemophilus influenzae* (10% to 30%) [29]. Hence, empirical treatment with antibiotics in countries with high case fatalities due to pneumonia, including Indonesia, has been recommended by the WHO [30].

On the contrary, the use of antibiotics for non-pneumonia ARIs warrants further consideration. Most cases of upper ARIs prescribed antibiotics in this study were not specified (844 cases out of 2516 children prescribed antibiotics; 33.5%). While most upper ARIs have a viral etiology [21,31], this 33.5% cases requires adequate justification for the presence of bacterial infections, or otherwise, these cases can be considered as overprescribing. Likewise, the use of antibiotics for some children with diagnoses of influenza in Banjarmasin PHCs warrants special attention. It was suggested that antibiotics have no role in influenza treatment, unless a secondary bacterial infection is confirmed [21,31]. In addition to non-pneumonia ARIs, this study reported low case numbers of diarrhea treated with antibiotics in both Surabaya and Banjarmasin PHCs (67 and 52 cases, respectively); while 70–90% of cases of diarrhea in children are caused by viruses [32], a specific diagnosis is required to justify the use of antibiotics in these cases. Based on the guidelines, antibiotics are only recommended for diarrhea specifically caused by bacterial pathogens (e.g. cholera, or dysentery) [21,22].

The potential risk of overprescribing or inappropriate antibiotic prescribing among children in outpatient settings has also been reported in previous international studies [33,34]. Overuse of antibiotics is a primary factor for AMR, which is responsible for less treatable infections. Over the last 20 years, there has been an alarming increase in the number of pathogenic bacteria that have developed resistance to common antibiotics, particularly in LMICs [35]. It was reported that AMR is associated with a substantial disease and economic burden in LMICs [36]. In addition, inappropriate antibiotic prescribing has been reported to cause negative impacts on human health. A cohort study of more than 2.8 million children indicated that inappropriate antibiotic prescriptions have been associated with increased risk of adverse drug events (e.g., *Clostridioides difficile* infection, severe allergic reaction) [33]. Potential longer-term risks of pediatric antibiotic exposure, such as increased risks of asthma and autoimmune disorders have also been reported [34].

To address the problem of inappropriate use of antibiotics, previous evidence has shown that multiple interventions should be carried out and developed based on a careful assessment of the context-specific barriers and facilitators [27]. In Indonesia, the implementation of Antimicrobial Stewardship (AMS), an organizational or health system wide-approach to optimize the use of antibiotics, has mainly focused on the hospital setting and are typically in an early stage; challenges reported were lack of basic infrastructure, hospital antibiotic guidelines, AMS staff training and education, human resources (including infectious disease specialists), and information technology support [37,38]. While antibiotics are highly prescribed in primary care settings [3], the role of the primary care sector needs to be strengthened. This study has highlighted the importance for PHCs to develop specific guidelines for the use of antibiotics for children, and for clinicians to provide a specific diagnosis to enable antibiotic prescribing. It was reported that the use of electronic clinical pathways integrated with point of care tests to assist clinicians to detect a bacterial infection (such as C-reactive protein, hemoglobin) has the potential to reduce antibiotic use in children in LMICs [39,40]. This should be supported with an adequate surveillance system to monitor the use of antibiotics and AMR on a regular basis. Further, post-prescription review and feedback efforts on the use of antibiotics can be considered; previous evidence has shown their potential in reducing antibiotic consumption and duration [41].

Although the generalizability of the findings in this study might be limited, the two regions investigated, are major cities in Indonesia which cover a range of different socioeconomic areas. In addition, as a retrospective study, this study depended on data entered into a clinical database; hence, lack of information on patients records, such as diagnoses (either not available or not specific, e.g., only stated upper ARIs) and justification of the use of antibiotics (bacterial infections suspected or any special conditions, such as parents having difficulty returning as living far away from health facilities), has limited further assessment of the quality of antibiotic prescribing.

Conclusions

This is the first large study that has provided data on illnesses and the associated antibiotic prescribing among children in PHCs as frontline healthcare providers in Indonesia. Appropriate antibiotic usage in these facilities can be strengthened by the implementation of AMS and the development of specific guidelines (or clinical pathways) on the use of antibiotics in children. This should be supported with diagnostic tests in primary care settings to justify the presence of bacterial infections. Larger prospective studies are required to characterize antibiotic prescribing at the national level to assist the development of context-specific strategies to optimize the use of antibiotics and reduce AMR.

Acknowledgements

We would like to thank all staff of Surabaya and Banjarmasin PHCs who provided technical assistance and support in collecting the data. We also would like to thank I Gusti Agung Ari Kusuma Yana and Gusti Ayu Putu Laksmi Puspa for assisting with the data management.

Authors' contribution

YIW: methodology, data curation, formal analysis, writing-original draft preparation. APS, BS: conceptualisation, data curation, writing-reviewing and editing. NF, NR, NW: investigation, formal analysis.

Corresponding author

Yosi Irawati Wibowo, PhD
Senior Lecturer, University of Surabaya
Jl. Raya Kalirungkut, Surabaya 60293, Indonesia
Tel: +62 31 2981170
Fax: +62 31 2981170
Email: yosi_wibowo@staff.ubaya.ac.id

Conflict of interests

No conflict of interests is declared.

References

1. Nicolini G, Sperotto F, Esposito S (2014) Combating the rise of antibiotic resistance in children. Minerva Pediatr 66: 31-39.
2. Fink G, D'Acremont V, Leslie H, Cohen J (2020) Antibiotic exposure among children younger than 5 years in low-income and middle-income countries: a cross-sectional study of nationally representative facility-based and household-based surveys. Lancet Infect Dis 20: 179-187. doi: 10.1016/S1473-3099(19)30572-9.
3. Alkaff R, Kamigaki T, Saito M, Ariyani F, Iriani D, Oshitani H (2019) Use of antibiotics for common illnesses among children aged under 5 years in a rural community in Indonesia: a cross-sectional study. Trop Med Health 47: 45. doi: doi: 10.1186/s41182-019-0173-6.
4. Rogawski E, Platts-Mills J, Seidman J, John S, Mahfuz M, Ulak M, Shrestha SK, Soofi SB, Yori PP, Mduma E, Svensen E, Ahmed T, Lima AA, Bhutta ZA, Kosek MN, Lang DR, Gottlieb M, Zaidi AK, Kang G, Bessong PO, Houpt ER, Guerrant RL (2017) Use of antibiotics in children younger than two years in eight countries: a prospective cohort study. Bull World Health Organ 95: 49-61. doi: 10.2471/BLT.16.176123.
5. Bebell L, Muiru A (2014) Antibiotic use and emerging resistance: how can resource-limited countries turn the tide? Glob Heart 9: 347-358. doi: 10.1016/j.gheart.2014.08.009.
6. World Health Organisation (2015) Global action plan on antimicrobial resistance. Available:

https://www.who.int/publications/i/item/9789241509763. Accessed: 15 November 2022.
7. Coordinating Ministry of Human Development and Cultural Affairs, Republic of Indonesia (2021) Coordinating ministry of human development and cultural affairs republic of Indonesia regulation In 2021: National action plan in tackling antimicrobial resistance for 2020-2024. Available: https://jdih.kemenkopmk.go.id/sites/default/files/2021-11/Permenko%207%202021%20RAN%20PRA.pdf. 2021. Accessed: 8 December 2022. [Article in Indonesian].
8. Williams M, Greene G, Naik G, Hughes K, Butler C, Hay A (2018) Antibiotic prescribing quality for children in primary care: an observational study. Br J Gen Pract 68: e90-e96. doi: 10.3399/bjgp18X694409.
9. Holstiege J, Schink T, Molokhia M, Mazzaglia G, Innocenti F, Oteri A, Bezemer I, Poluzzi E, Puccini A, Ulrichsen SP, Sturkenboom MC, Trifirò G, Garbe E (2014) Systemic antibiotic prescribing to paediatric outpatients in 5 European countries: a population-based cohort study. BMC Ped 14: 174. doi: 10.1186/1471-2431-14-174.
10. Bielicki J, Musiime V (2022) Global antibiotic use patterns in children. Available: https://revivegardporg/global-antibiotic-use-patterns-in-children/. Accessed: 10 December 2022.
11. Ministry of Health Republic of Indonesia (MoH-RI) (2014) Indonesia: sample registration system 2014. Available: https://perpustakaan.badankebijakan.kemkes.go.id/index.php?p = show_detail&id = 36293. Accessed" 16 November 2022. [Available in Indonesian].
12. Ministry of Health Republic of Indonesia (2020) Indonesia health profile in 2019. Available: https://www.kemkes.go.id/id/profil-kesehatan-indonesia-2019. Accessed: 10 November 2022. [Available in Indonesian]
13. Ministry of Health Republic of Indonesia (MoH-RI) (2019) Work report from Directorate General of Pharmaceutical Care in 2018. Available: https://farmalkes.kemkes.go.id/2019/02/laporan-kinerja-direktorat-pelayanan-kefarmasian-tahun-2018/. Accessed: 15 November 2022. [Available in Indonesian].
14. Dewi M, Sari IP, Probosuseno P (2015) The effect of counseling on adherence and hypertension control among hypertension patients Prolanis at Husada Mitra Clinic Kendal. J Far Klin 4: 242-249. [Article in Indonesian].
15. Agtini M, Puspandari N (2017) The use of antibiotics among children younger than 5 years with acute diarrhoea at 5 Indonesian provinces in 2009-2012. Biotek Med Ind 6: 1-8. [Article in Indonesian].
16. Dewi R, Sutrisno D, Purnamasari R (2020) Evaluation on the use of antibiotics among children younger than 5 years with upper respiratory tract infections at Puskesmas Koni Kota Jambi. J Sains Kes 2: 385-390.
17. Ministry of Health Republic of Indonesia (MoH-RI) (2022) Indonesian health profile in 2021. Available: https://www.kemkes.go.id/id/profil-kesehatan-indonesia-2021. Accessed: 15 November 2022. [Available in Indonesian].
18. Badan Pusat Statistik (BPS) Kota Surabaya (2022) Human Development Index of Surabaya City in 2022. Available: https://surabayakota.bps.go.id/publication/2022/05/13/fca0333697dd4bbd492ce3ad/indeks-pembangunan-manusia-kota-surabaya-2021.html. Accessed 10 March 2023. [Available in Indonesian].
19. Badan Pusat Statistik (BPS) Kota Banjarmasin (2022) (New method) Human Development Index of Banjarmasin City in 2020-2022. Available: https://banjarmasinkota.bps.go.id/indicator/26/84/1/-metode-baru-indeks-pembangunan-manusia.html. Accessed: 10 March 2023. [Available in Indonesian]
20. Surabaya Regional Health Office (Dinkes Surabaya) (2019) Surabaya health profile in 2019. Available https://dinkes.surabaya.go.id/portalv2/dokumen/Profil%20Kesehatan%20Kota%20Surabaya%202019.pdf. Accessed: 1 November 2022. [Available in Indonesian].
21. Ministry of Health Republic of Indonesia (MoH-RI) (2022) Ministry of Health Republic of Indonesia Decree Number H.K.01.07/MENKES/1186/2022: Clinical practice guidelines for physicians in primary health care facilities. Available: https://drive.google.com/file/d/1K7QeczeDwQ9dLoLQamokfTJz9JmL6bfg/view. Accessed: 10 November 2022. [Available in Indonesian].
22. Ministry of Health Republic of Indonesia (MoH-RI) (2015) Integrated management of childhood illnesses (*Manajemen Terpadu Balita Sehat*, MTBS). Available: https://dinkes.jatimprov.go.id/userimage/dokumen/BAGAN%20MTBS_05.04.2016(1).pdf. Accessed: 10 November 2022. [Available in Indonesian].
23. Ministry of Health Republic of Indonesia (MoH-RI) (2019) Ministry of Health Republic of Indonesia Decree Nomor HK.01.07/MENKES/813/2019: National formulary. Available: https://pafi.or.id/media/upload/20200309042447_466.pdf. Accessed: 2 December 2022. [Available in Indonesian].
24. World Health Organization (WHO) (2022) Pneumonia in children. Available: https://www.who.int/news-room/fact-sheets/detail/pneumonia. Accessed: 18 February 2023.
25. World Health Organization (WHO) (2019) WHO releases the 2019 AWaRe classification antibiotics. Available: https://www.who.int/news/item/01-10-2019-who-releases-the-2019-aware-classification-antibiotics. Accessed: 18 February 2023.
26. Zanichelli V, Sharland M, Cappello B, Moja L, Getahun H, Pessoa-Silva C, Sati H, van Weezenbeek C, Balkhy H, Simão M, Gandra S, Huttner B (2023) The WHO AWaRe (Access, Watch, Reserve) antibiotic book and prevention of antimicrobial resistance. Bull World Health Organ 101: 290-296. doi: 10.2471/BLT.22.288614.
27. Limato R, Lazarus G, Dernison P, Mudia M, Alamanda M, Nelwan E, Sinto R, Karuniawati A, Rogier van Doorn H, Hamers RL (2022) Optimizing antibiotic use in Indonesia: a systematic review and evidence synthesis to inform opportunities for intervention. Lancet Reg Health - Southeast Asia 2: 100013. doi: 10.1016/j.lansea.2022.05.002.
28. Prasetyaningrum E (2018) Profiles of antibiotics use among patients with pneumonia at Puskesmas Ngesrep Semarang in 2017. Media Informasi Ind 13: 1362-1366. [Article in Indonesian].
29. Falade A, Ayede A (2011) Epidemiology, aetiology and management of childhood acute community-acquired pneumonia in developing countries - a review. Afr J Med Sci 40: 293-308.
30. Lodha R, Kabra S, Pandey R (2013) Antibiotics for community-acquired pneumonia in children. Cochrane Database Syst Rev Issue 6. Art. No: CD004874. doi: 10.1002/14651858.CD004874.pub4.
31. Sur D, Plesa M (2022) Antibiotic use in acute upper respiratory tract infections. Am Fam Physician 106: 628-636.

32. Bányai K, Estes M, Martella V, Parashar U (2018) Viral gastroenteritis. Lancet 392: 175-186.
33. Butler AM, Brown DS, Durkin MJ, Sahrmann JM, Nickel K, O'Neil CA, Olsen MA, Hyun DY, Zetts RM, Newland JG (2022) Association of inappropriate outpatient pediatric antibiotic prescriptions with adverse drug events and health care expenditures. JAMA Netw Open 5: e2214153. doi: 10.1001/jamanetworkopen.2022.14153.
34. Ardillon A, Ramblière L, Kermorvant-Duchemin E, Sok T, Zo A, Diouf J, Long P, Lach S, Sarr FD, Borand L, Cheysson F, Collard JM, Herindrainy P, de Lauzanne A, Vray M, Delarocque-Astagneau E, Guillemot D, Huynh BT (BIRDY study group) (2023) Inappropriate antibiotic prescribing and its determinants among outpatient children in 3 low- and middle-income countries: a multicentric community-based cohort study. Plos Med 20: e1004211. doi: 10.1371/journal.pmed.1004211.
35. Poddighe D (2019) Macrolide resistance and longer-term assessment of azithromycin in MORDOR I. New England J Med 381: 2184-2185. doi: 101056/nejmc1910014.
36. Allel K, Stone J, Undurraga E, Day L, Moore C, Lin L, Furuya-Kanamori L, Yakob L (2023) The impact of inpatient bloodstream infections caused by antibiotic-resistant bacteria in low- and middle-income countries: a systematic review and meta-analysis. Plos Med 20: e1004199. doi: 10.1371/journal.pmed.1004199.
37. Lee TH, Lye DC, Chung DR, Thamlikitkul V, Lu M, Wong AT, Hsueh PR, Wang H, Cooper C, Wong JG, Shimono N, Pham VH, Perera J, Yang YH, Shibl AM, Kim SH, Hsu LY, Song JH (2021) Antimicrobial stewardship capacity and manpower needs in the Asia Pacific. J Glob Antimicrob Resist 24: 387-394. doi: 10.1016/j.jgar.2021.01.013.
38. Ministry of Health Republic of Indonesia (MoH-RI) (2015) Peraturan Menteri Kesehatan Republik Indonesia nomor 8 tahun 2015 tentang program pengendalian resistensi antimikroba di rumah sakit. Available: https://peraturan.bpk.go.id/Home/Details/114886/permenkes-no-8-tahun-2015. Accessed: 20 January 2023. [Available in Indonesian].
39. Sayood S, Bielicki J, Gandra S (2024) Tackling inappropriate antibiotic use in low-and middle-income countries. Nat Med 30: 33-34. doi: 10.1038/s41591-023-02725-6.
40. Tan R, Kavishe G, Luwanda LB, Kulinkina AV, Renggli S, Mangu C, Ashery G, Jorram M, Mtebene IE, Agrea P, Mhagama H, Vonlanthen A, Faivre V, Thabard J, Levine G, Le Pogam MA, Keitel K, Taffé P, Ntinginya N, Masanja H, D'Acremont V (2024) A digital health algorithm to guide antibiotic prescription in pediatric outpatient care: a cluster randomized controlled trial. Nat Med 30: 76-84. doi: 10.1038/s41591-023-02633-9.
41. Van Dijck C, Vlieghe E, Cox J. Van Dijck C, Vlieghe E, Cox JA (2018) Antibiotic stewardship interventions in hospitals in low-and middle-income countries: a systematic review. Bull World Health Organ 96: 266-280. doi: 10.2471/BLT.17.203448.