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Survey of antibiotic use of individuals visiting public healthcare facilities in Indonesia

Usman Hadi [a,1,*], D. Offra Duerink [b,1], Endang Sri Lestari [c,1], Nico J. Nagelkerke [d,1], Susanne Werter [e,1], Monique Keuter [e,1], Eddy Suwandojo [a,1], Eddy Rahardjo [f,1], Peterhans van den Broek [b,1], Inge C. Gyssens [g,h,i,1]

[a] *Department of Internal Medicine, Dr. Soetomo Hospital — School of Medicine, Airlangga University, Jl. Manyar Tirtomoyo II/21, Surabaya 60118, Indonesia*
[b] *Department of Infectious Diseases, Leiden University Medical Centre, Leiden, The Netherlands*
[c] *Department of Clinical Microbiology, Dr. Kariadi Hospital — School of Medicine, Diponegoro University, Semarang, Indonesia*
[d] *Department of Community Medicine, United Arab Emirates University, Al Ain, United Arab Emirates*
[e] *Department of Internal Medicine, Nijmegen University Centre for Infectious Diseases International Health (NUCI-IH), Radboud University Medical Centre, Nijmegen, The Netherlands*
[f] *Department of Anaesthesiology, Dr. Soetomo Hospital — School of Medicine, Airlangga University, Surabaya, Indonesia*
[g] *Department of Medical Microbiology and Infectious Diseases and Department of Internal Medicine, Erasmus University Medical Centre, Rotterdam, The Netherlands*
[h] *Department of Medical Microbiology and Infectious Diseases, Canisius-Wilhelmina Hospital, Nijmegen, The Netherlands*
[i] *Department of Internal Medicine, Nijmegen University Centre for Infectious Diseases (NUCI), Radboud University Medical Centre, Nijmegen, The Netherlands*

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Summary
Objectives: To estimate the antibiotic use of individuals visiting public healthcare facilities in Indonesia and to identify determinants of use against a background of high resistance rates.
Methods: Patients on admission to hospital (group A), visiting a primary health center (group B), and healthy relatives (group C) were included in the study. A questionnaire on demographic, socioeconomic, and healthcare-related items including health complaints and consumption of antibiotics was used. Logistic regression was performed to determine the co-variables of antibiotic use.
Results: Of 2996 individuals interviewed, 486 (16%) had taken an antibiotic. Compared to group C (7% consumption), groups B and A exhibited a three-fold and four-fold higher use of antibiotics, respectively. Respiratory (80%) and gastrointestinal (13%) symptoms were most frequent. Ami-

* Corresponding author. Tel.: +62 31 5501617; fax: +62 31 5018434.
E-mail address: i.gyssens@aig.umcn.nl (U. Hadi).
[1] on behalf of the Antimicrobial Resistance in Indonesia 'Prevalence and Prevention' study group (AMRIN).

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nopenicillins and tetracyclines accounted for 80% of the prescribed antibiotics. Similar antibiotics were self-medicated (17% of users). Age less than 18 years and health insurance were independent determinants of antibiotic use. Urban provenance, being adult, male, and having no health insurance were independent determinants of self-medication.
Conclusions: In addition to health complaints, other factors determined antibiotic consumption. In view of the likely viral origin of respiratory complaints and the resistance of intestinal pathogens, most antibiotic use was probably unnecessary or ineffective. Future interventions should be directed towards healthcare providers.

Introduction

Non-industrialized countries, home to the majority of the world's population, have an important role in the emergence of global resistance of bacteria to antimicrobial drugs.[1] Antibiotic use contributes to the selection of resistant micro-organisms.[2,3] This problem has become so widespread that bacterial resistance to antibiotics is threatening health improvements achieved in the tropics in the past decades.[4] Despite the potential impact of this problem, only limited information on resistance of bacteria and antibiotic consumption is available in Indonesia. Most research has been done on diarrheal[5–8] and sexually transmitted diseases.[9] Resistance against penicillins and tetracyclines of diarrheal pathogens and *Neisseria gonorrhoeae* has approached 100% in some areas.[8,9] High resistance rates for enterotoxigenic *Escherichia coli* have been found against amoxicillin, trimethoprim–sulfamethoxazole, chloramphenicol, and tetracycline.[7] Ten years ago in a small survey, 70% of patients with diarrhea and about 80% of patients with respiratory tract symptoms were treated with antibiotics.[10] Doctors in Jakarta prescribed antibiotics for 94% of young children although they believed that the infection was usually of viral origin.[5]

The 1997–1998 East-Asian economic crisis had a major impact on health and healthcare in Indonesia.[11,12] Health insurance schemes are mandatory for government employees (Askes, Asuransi Kesehatan) and private employees (Jamsostek, Jaminan Sosial Tenaga Kerja).[13] A social safety net program including health subsidies (JPS, Jaring Pengaman Sosial) was developed.[12] However, up to 86% of the population is not covered by any form of health insurance scheme, and drugs have to be paid for in cash upon delivery.[13] Antibiotics can be obtained from public and private providers: at primary health centers, government or private hospitals, private doctor or midwife practices, public pharmacies, but also in drug stores and roadside stalls ('kiosks').[14] In the health centers a limited number of antibiotics can be prescribed according to standard practice guidelines for the treatment of infectious syndromes.[15] In public pharmacies, many generic as well as branded products can be purchased.[16] Antibiotics without prescription can be obtained over the counter (OTC) in pharmacies and drug stores, although this has been prohibited by law since 1949.[17]

The Antimicrobial Resistance in Indonesia 'Prevalence and Prevention' (AMRIN) study was set up to investigate antibiotic resistance and antibiotic use inside and outside hospitals in two different areas on Java. AMRIN is a two-phased study whose objective is first to survey the present situation in Indonesia regarding antimicrobial resistance, antibiotic use, and infection control in healthcare facilities, and next to perform interventions in those facilities based on the results of the first phase. We hypothesized that antibiotic use and carriage of resistant bacteria would differ depending on the individual's health and that antibiotic use, and as well as being driven by morbidity would also be determined by demographic, socioeconomic, and healthcare-related variables. Here, we report on the level, diversity, and determinants of antibiotics taken by individuals in the extramural healthcare setting.

Patients and methods

This study was conducted in Surabaya (SBY) in east Java and in Semarang (SMG) in central Java. In SBY a governmental teaching hospital and two urban health centers participated, in SMG a teaching hospital and one rural health center. The aim was to include 3000 individuals, equally divided over three groups. Patients upon admission to hospital in the departments of Internal Medicine, Surgery, Obstetrics and Gynecology, or Pediatrics (group A), patients visiting a health center for consultation or vaccination (group B), and healthy relatives who accompanied group A patients to hospital (group C) were eligible.

The medical ethics committees of the hospitals approved the study protocol (ethical clearance No/Panke.KKE/2001 (Surabaya) and 11/EC/FK/RSDK/2001 (Semarang)). On enrolment, eligible individuals received oral and written information about the study, and informed consent was obtained from all adults and carers of children.

Inclusion procedure and criteria for inclusion and exclusion

Patients in group A were included within the first 24 hours of admission. Individuals in group C were included on admission of group A patients at a rate of one contact per patient. Contacts had to be able to answer the questions properly and to be over 12 years old. Patients in group B were included on specific study days twice weekly in SBY and once weekly in SMG. Individuals were excluded from the study if they had been transferred from another hospital, if they were not accompanied by a relative (group A), or if they had been admitted to a hospital in the previous three months (groups A, B, and C).

Demographic and socioeconomic data and data on health complaints and consumption of antibiotics in the month

preceding the study were collected by interviews, performed by pairs of trained Indonesian and Dutch data collectors (researchers, residents, medical students). For children (<17 years), a carer (usually the mother) was interviewed.

Demographic and socioeconomic factors

Origin (SBY or SMG), sex, age, residence (urban or rural), and ethnicity were recorded. Family income level, employment, highest educational level, health insurance, and the number of individuals sharing a household were chosen as socioeconomic characteristics. Employment was defined as paid work for an employer on a regular basis or having a regular income from a profession (e.g. farmer). Housewives and students were not considered as unemployed.

Antibiotic use survey

A semi-structured questionnaire was used. Interviewees were asked to state their health complaints during the preceding month spontaneously. Subsequently, the interviewers cited complaints from the list on the form. Irrespective of having been ill or not, participants were asked whether they had consumed any drugs in the past month. If the answer was no, the interview was ended; otherwise it was continued. To ascertain whether the drug was an antibiotic, individuals were asked to show the drugs, the package, or the prescriptions. If these were not available, open questions using the names of antibiotics were asked or samples of capsules and tablets of antibiotics were shown. When it was certain that the drug was an antibiotic, the number of units taken and duration of treatment were recorded. When in doubt, the drug was labeled as 'possibly an antibiotic'. Individuals who had (possibly) taken an antibiotic were asked where it was obtained.

Statistical analysis

Individuals with antibiotic use were compared to individuals without antibiotic use. Proportions were analyzed by Chi-square testing, using $p < 0.05$ as the level of significance. The mean duration of treatment was assessed by ANOVA, using $p < 0.05$ as the level of significance. Univariate analysis was performed to determine the risk factors for antibiotic use. Employment and education were analyzed for the population ≥18 years old. The variables age (adult versus child <18 years), education (primary school completed vs. not completed), and family income (below or above poverty line, <300 000 Rupiah or 30 Euro per month)[12] were analyzed as binary variables. Variables for which significance at the 0.05 level or higher was found in univariate analysis were forced into a multivariate model. Forward stepwise logistic regression was used. Odds ratios (OR), significance, and 95% confidence intervals (95% CI) were calculated. SPSS for Windows version 11.5 was used for all analyses. The analysis was done for the outcome 'antibiotic use' versus 'no antibiotic use' and repeated for the outcome 'antibiotic use including possible use' versus 'no antibiotic use'. The analysis was repeated for the outcome 'self-medication' versus 'prescribed by healthcare providers'.

Table 1 Demographic characteristics of the patients and relatives presenting at healthcare facilities in Surabaya (SBY) and Semarang (SMG)

Characteristic	Group A Hospital on admission		Group B Health centre		Group C Healthy relatives		Totals per city		Total
	SBY	SMG	SBY	SMG	SBY	SMG	SBY	SMG	
No. of individuals	498	500	500	500	498	500	1496	1500	2996
Male, *n* (%)	200 (40)	211 (42)	168 (34)	179 (36)	209 (42)	180 (36)	577 (39)	570 (39)	1147 (38)
Age (years), median (range)	28 (0–80)	23 (0–83)	41 (0–87)	23 (0–81)	34 (13–86)	34 (13–82)	34 (0–87)	28 (0–83)	31 (0–87)
Adults ≥18 years, *n* (%)	338 (68)	318 (64)	447 (89)	288 (57)	490 (98)	491 (98)	1275 (85)	1097 (73)	2372 (79)
Residence urban, *n* (%)	366 (74)	331 (66)	497 (99)	51 (10)	368 (74)	331 (66)	1231 (82)	713 (48)	1944 (65)
Ethnic Javanese, *n* (%)	433 (87)	499 (99)	481 (96)	495 (99)	439 (88)	500 (100)	1353 (91)	1494 (99.6)	2847 (95)
Low income, *n* (%)	239 (48)	177 (35)	287 (57)	194 (39)	238 (48)	175 (35)	764 (51)	546 (36)	1310 (44)
No health insurance, *n* (%)	370 (74)	311 (62)	391 (78)	386 (77)	384 (77)	340 (68)	1145 (77)	1037 (69)	2182 (73)
Unemployed ≥18 years, *n* (%)	118 (24)	74 (15)	179 (36)	97 (19)	150 (30)	96 (19)	447 (30)	267 (18)	714 (24)
Primary school not completed ≥18 years, *n* (%)	27 (5)	28 (7)	79 (16)	45 (9)	26 (5)	31 (6)	132 (9)	104 (7)	236 (8)
No. of individuals sharing a household, median (range)	5 (1–40)	5 (1–32)	5 (1–65)	4 (1–13)	5 (1–22)	5 (0–32)	5 (1–65)	5 (0–32)	5 (0–65)

Results

Demography and socioeconomic factors

A total of 3000 individuals were included in this study; 1500 between July and October 2001 in SBY and 1500 between January and April 2002 in SMG. Four individuals were excluded, two from group A, together with their relatives from group C, because these patients had been hospitalized within the month before inclusion, leaving 2996 individuals for analysis. The demographic characteristics of the population are shown in Table 1. The majority was female (62%). The proportions of adults in SBY and SMG were similar, except in group C ($p < 0.001$). In this group, more children were included from the immunization clinic in SMG. Most individuals were of Javanese descent; Madurese accounted for 9% in SBY. This explains the significant difference in ethnicities between the two areas ($p < 0.001$). In SBY, significantly more individuals were living in an urban area ($p < 0.001$), had a low income ($p < 0.001$), and had no health insurance ($p < 0.001$) compared to SMG. Overall, three quarters of the interviewees received no re-imbursement for the costs of antibiotics. A quarter of the individuals ≥18 years old were unemployed. About half of the individuals aged 18–40 years old had completed secondary school. There was a large variation in the number of individuals belonging to one household.

Antibiotic consumption

Of the 2996 participants, 1843 (62%) reported that they took a drug in the month preceding the interview. This was definitely an antibiotic in 486 cases, 26% of medicine users. In 262 (14%) cases the interviewee was not sure whether the drug was an antibiotic. Thus, depending on whether possible use was taken into account, the antibiotic use of the total population varied between 16% and 25%. Hereafter, the consumption data refer to the 486 individuals who definitely took antimicrobial drugs.

The overall proportion of antibiotic users did not differ between SBY and SMG. Large differences were seen between the groups: 7% for relatives, 19% for patients at the health center, and 22% for patients on admission to hospital. Four hundred and seventeen (86%) individuals could specify name and dosage. This applied to 447 antibiotic courses, with 389 (93%) individuals citing a single antibiotic, 26 individuals two antibiotics, and two individuals three antibiotics. Approximately 92% of the antibiotics were dispensed as tablets, capsules, and syrup for oral use. Injections accounted for only 2%.

Overall 71% of the courses were either amoxicillin or ampicillin, slightly more often prescribed for children (76% of prescriptions for children) than adults (69%; $p = 0.16$) (Tables 2 and 3). Amoxicillin or ampicillin was consumed by 60% of adults in group A and 78% of group C. All but one of the treatments for children of groups B and C consisted of amoxicillin or ampicillin. For adults, 9% of the courses were for tetracyclines, which were only used once by a child. Tetracycline use did not differ between the groups. Among children the second most common antibiotic was trimethoprim–sulfamethoxazole: 12% of courses against 6% among adults. All except one course of trimethoprim–sulfamethoxazole had been taken by children in group A. Chloramphenicol and thiamphenicol were frequently used: 6% of courses taken by adults and 12% by children, who all belonged to group A.

The prescribed daily dose for adults (PDD) of most antibiotics was in the order of magnitude of the defined daily dose (DDD).[18] PDDs were lower than DDDs for chloramphenicol 1.6 g vs. 3 g and ampicillin 1.4 g vs. 2 g, and higher for amoxicillin 1.4 g vs. 1 g.

The median duration of most antibiotic treatments was 3 days. Less than 3% of treatments lasted for more than 10 days. The mean duration of self-medication was significantly

Table 2 Antibiotic use by adults (≥18 years) in one month

ATC code		Group A[a] (*N* = 110)			Group B[b] (*N* = 123)			Group C[c] (*N* = 64)		
		Courses *n* (%)	PDD[d]	Duration[e]	Courses *n* (%)	PDD[d]	Duration[e]	Courses *n* (%)	PDD[d]	Duration[e]
J01AA07	Tetracycline	12 (11)	1.0 (0.53)	3 (1–7)	21 (17)	1.3 (0.4)	3 (1–9)	7 (11)	0.9 (0.4)	3 (1–5)
J01BA01	Chloramphenicol	5 (4.6)	1.6 (0.51)	2 (1–7)	5 (4.1)	1.1 (0.4)	3 (3–7)	5 (7.8)	1.1 (0.4)	3 (3–5)
J01BA02	Thiamphenicol	3 (2.7)	1.5 (0)	3 (2–3)	-	-	-	-	-	-
J01CA01	Ampicillin	20 (19)	1.4 (0.26)	3 (1–21)	30 (24)	1.4 (0.2)	3 (1–9)	13 (20)	1.6 (0.5)	3 (1–7)
J01CA04	Amoxicillin	51 (46)	1.4 (0.23)	3 (1–28)	65 (53)	1.4 (0.2)	3 (1–14)	39 (61)	1.4 (0.7)	3 (1–12)
J01EE01	TMP–SMX[f]	11 (10)	1.5 (0.35)	4 (1–10)	6 (4.9)	1.2 (0.8)	3 (2–4)	2 (3.1)	1.4 (0.7)	2 (2–2)
J01FA01	Erythromycin	6 (5.5)	1.3 (0.39)	2 (1–10)	2 (1.6)	1.5 (0)	5 (3–7)	1 (1.6)	1.5	5
J01GB04	Kanamycin	3 (2.7)	1.5 (0)	2 (2–3)	-	-	-	-	-	-
J01MA02	Ciprofloxacin	4 (3.6)	0.9 (0.13)	2.5 (2–5)	-	-	-	-	-	-
P01AB01	Metronidazole	4 (3.6)	1.4 (0.25)	2.5 (1–4)	1 (0.8)	0.5	3	-	-	-
Total courses		119			130			67		

[a] Group A = patients upon admission to hospital.
[b] Group B = patients visiting a public health centre.
[c] Group C = relatives accompanying patients of group A.
[d] PDD = prescribed daily doses in grams, mean (standard deviation).
[e] Median (range) of duration of treatment in days.
[f] TMP–SMX = trimethoprim–sulfamethoxazole.

Table 3 Antibiotic use by children (<18 years) in one month

ATC code		Group A[a] (*N* = 87)			Group B[b] (*N* = 31)			Group C[c] (*N* = 2)		
		Courses *n* (%)	PDD[d]	Duration[e]	Courses *n* (%)	PDD[d]	Duration[e]	Courses *n* (%)	PDD[d]	Duration[e]
J01AA07	Tetracycline	1 (1.1)	0.3	2	-	-	-	-	-	-
J01BA01	Chloramphenicol	8 (9.2)	0.6 (0.28)	3 (1—9)	-	-	-	-	-	-
J01BA02	Thiamphenicol	4 (4.6)	0.9 (0.47)	1 (1—3)	-	-	-	-	-	-
J01CA01	Ampicillin	17 (20)	0.9 (0.45)	3 (1—14)	14 (45)	0.80 (0.50)	4 (2—7)	1 (23)	0.75	4
J01CA04	Amoxicillin	50 (57)	0.7 (0.42)	3 (1—14)	16 (52)	0.82 (0.51)	3 (2—6)	1 (56)	1.9	4
J01EE01	TMP—SMX[f]	15 (17)	0.6 (0.47)	2 (1—9)	1 (3)	0.72	3	-	-	-
J01FA01	Erythromycin	1 (1.2)	1	3	-	-	-	-	-	-
J01MA01	Ofloxacin	1 (1.2)	0.8	1	-	-	-	-	-	-
P01AB01	Metronidazole	1 (1.5)	0.4	1	-	-	-	-	-	-
Total courses		98			31			2		

[a] Group A = patients upon admission to hospital.
[b] Group B = patients visiting a public health centre.
[c] Group C = relatives accompanying patients of group A.
[d] PDD = prescribed daily doses in grams, mean (standard deviation).
[e] Median (range) of duration of treatment in days.
[f] TMP—SMX = trimethoprim—sulfamethoxazole.

Table 4 Independent determinants[a] of antibiotic use

Determinant	Antibiotic use		OR (95% CI)	
	Yes (*N* = 480) *n* (%)	No (*N* = 2248) *n* (%)	Univariate	Multivariate
Area				
Surabaya	223 (46)	1156 (51)	0.82 (0.67—1.00)	-
Group				
A (Patients on admission to hospital)	218 (45)	614 (27)	4.62 (3.46—6.16)	3.74 (2.77—5.04)
B (Patients at primary health center)	192 (40)	724 (32)	3.45 (2.58—4.61)	2.87 (2.13—3.88)
C (Healthy household contacts)	70 (15)	910 (41)	Reference group	Reference group
Sex				
Male	199 (42)	821 (37)	1.23 (1.01—1.51)	-
Age				
≥18 years old	324 (68)	1929 (86)	0.34 (0.27—0.43)	0.49 (0.38—0.62)
Geographic provenance				
Urban	307 (64)	1464 (65)	0.97 (0.79—1.19)	-
Ethnicity				
Javanese	469 (98)	2126 (95)	2.45 (1.31—4.57)	2.35 (1.24—4.45)
Employment				
None	97 (30)	573 (30)	1.002 (0.78—1.30)	-
Health insurance				
None	331 (69)	1664 (74)	0.78 (0.63—0.97)	0.75 (0.60—0.94)
Education				
None	32 (10)	185 (10)	1.03 (0.70—1.53)	-
Income				
Low	196 (41)	995 (44)	0.87 (0.71—1.06)	-

OR, odds ratio; CI, confidence interval.
[a] Independent determinants were identified by multivariate analyses applied to variables significantly associated with antibiotic use in univariate analysis. Six individuals who reported antibiotic use without complaints and 262 individuals who did not know whether the drug they took was an antibiotic were excluded from the analysis.

lower, i.e., 2.8 (standard deviation (SD) 2.1) days, compared with courses prescribed by a healthcare provider, 3.7 (SD 2.8) days ($p = 0.024$).

Morbidity

Almost all patients (99%) who used antibiotics reported health complaints, compared to 62% of the individuals who did not take antibiotics. The proportion of individuals with complaints who consumed antibiotics was 36% in group A, 23% in group B, and 16% in group C. Complaints indicating involvement of a specific organ system were reported by 954 individuals: respiratory tract symptoms (cough and/or flu and/or fever) 80%, gastrointestinal symptoms (diarrhea with or without fever) 13%, skin symptoms (itching/skin infections) 5%, and urinary tract symptoms 2%. One hundred and two individuals reported fever without other symptoms. The remainder (817 individuals) had symptoms not indicative of a specific localization of disease.

Providers

Of the 486 individuals who definitely took an antibiotic, 472 (97%) could indicate the provider: prescribed by doctors in public hospitals (12%), healthcare center (29%), private practice (36%), nurses and midwives (6%). Self-medication was reported in 17% of cases (8% obtained from a pharmacy without prescription, 5% from drugstores, 2% from friends and relatives, 1% from kiosks, and 1% from other sources).

Determinants

Comparison of non-users with users showed that antibiotic use was higher among children (<18 years), individuals of Javanese ethnicity, and those with health insurance (Table 4). The analysis was repeated with non-users versus users including the individuals who had possibly taken an antibiotic. This did not change the findings significantly. In another analysis, the demographic and socioeconomic characteristics of 398 individuals who used antibiotics on prescription were compared with those of 74 individuals with self-medication (Table 5). Being adult, male, and living in an urban area were the strongest associated factors. No differences were found in the type of complaints between individuals on self-medication and those using antibiotics on prescription. Tetracyclines were the only antibiotics that were significantly more often self-medicated than prescribed (OR 4.15, 95% CI 2.05—8.4).

Discussion

This is the first survey on overall antibiotic use in populations outside hospitals in Indonesia. It shows that antibiotic use

Table 5 Independent determinants[a] of self-medication with antibiotics

Determinant	OTC/SM		OR (95% CI)	
	Yes ($N = 72$) n (%)	No ($N = 394$) n (%)	Univariate	Multivariate
Area				
Surabaya	48 (67)	164 (42)	2.81 (1.65—4.76)	-
Group				
A (Patients on admission to hospital)	20 (28)	192 (49)	0.28 (0.14—0.56)	0.49 (0.23—1.05)
B (Patients at primary health center)	33 (46)	151 (38)	0.59 (0.31—1.12)	1.17 (0.57—2.37)
C (Healthy household contacts)	19 (26)	51 (13)	Reference group	Reference group
Sex				
Male	34 (47)	156 (40)	1.37 (0.82—2.26)	2.34 (1.32—4.15)
Age				
≥18 years old	66 (92)	248 (63)	6.48 (2.74—15.31)	6.79 (2.69—17.18)
Geographic provenance				
Urban	59 (82)	234 (59)	3.10 (1.65—5.85)	4.51 (2.26—8.98)
Ethnicity				
Javanese	72 (100)	385 (98)	-	-
Employment				
None	20 (28)	74 (30)	0.98 (0.54—1.76)	-
Health insurance				
None	57 (77)	265 (67)	1.85 (1.01—3.39)	2.42 (1.26—4.64)
Education				
None	5 (8)	27 (11)	0.67 (0.25—1.82)	-
Income				
Low	30 (41)	162 (41)	1.02 (0.61—1.70)	-

OTC/SM, over the counter or self-medication; OR, odds ratio; CI, confidence interval.

[a] Independent determinants were identified by multivariate analyses applied to variables significantly associated with self-medication in the univariate analysis. Fourteen individuals who used both prescribed and self-medicated antibiotics were excluded from the analysis.

was prevalent in Indonesian patients and their relatives. Compared with the relatives, patients visiting a health center and patients on admission to hospital had a 2.4-fold and 3.3-fold higher risk, respectively, of having used an antibiotic in the month before the interview. The differences are most likely explained by the fact that relatives were healthy, patients visiting health centers had minor illnesses, and patients on admission to hospital were more severely ill. Symptoms of respiratory tract infections were most frequently reported with gastrointestinal symptoms ranking second. Older, low cost antibiotics were mostly used, mainly aminopenicillins. This finding is in line with earlier observations in Asian countries.[19–21]

The use of amphenicols, restricted in most countries, was still surprisingly high in our study. The widespread use of these antibiotics in the extramural setting, mostly for complaints pointing at respiratory tract or gastrointestinal infections, raises questions about their appropriateness. Most respiratory tract infections are considered of viral origin and therefore antibiotics are not useful. The results of a randomized controlled trial in West Java demonstrating that ampicillin plus supportive care offers no benefit over supportive care alone for treatment of mild respiratory tract infections in young Indonesian children, support this point.[22] Although bacterial pathogens can be found in up to 21% of acute diarrhea cases admitted to hospital,[7] most antibiotics consumed by our population were not likely to be effective. Resistance rates of enterotoxigenic *Escherichia coli* (ETEC) heat-labile toxin (LT) and heat-stable toxin (ST), the most frequent bacterial cause of acute diarrhea in children as well as adults in Indonesia, are 67% LT and 83% ST for ampicillin, 48% LT and 70% ST for trimethoprim–sulfamethoxazole, and 95% LT and 85% ST for tetracycline.[7] *Shigella spp* account for 27% of bacterial causes of diarrhea, and *Shigella flexneri* demonstrate resistance to ampicillin and tetracycline in 50% and 83%, respectively.[8]

As expected, having health complaints was the most important determinant of antibiotic use. Another independent determinant of antibiotic use was being less than 18 years old. Worldwide, the barrier to (over)prescribe antibiotics to children is lower than to adults, which may be caused by a greater fear of a poor outcome. The independent determinant 'Javanese ethnicity' is more difficult to explain; cultural factors might play a role. Finally, individuals with health insurance consumed antibiotics more frequently. Free medical care has been described as a determinant of antibiotic use by others; it was associated with the use of more expensive drugs in the community in rural China.[23,24] Inversely, changes in reimbursement have resulted in reducing overuse.[21,25]

An important finding for tailoring future interventions is that authorized healthcare providers prescribed the majority of the antibiotics that were taken by the study population. This was also found in Mexico.[26] Only a limited amount of use, 17%, consisted of self-medication in our population. This figure is comparable to 27% self-medicated antibiotics consumed before a medical consultation in Chinese pediatric respiratory tract infection cases.[23] In contrast, a large proportion (66%) of children arriving for outpatient care had already been self-administering antibiotics in Taiwan.[21] Another interesting finding was that prescribed or self-medicated antibiotics did not differ, except tetracycline that was significantly more often used without prescription. Self-medicating individuals also predominantly used the same affordable antibiotics. Copying behavior of prescribers, providers, and patients is discussed in a review by Radyowijati and Haak.[27] Healthcare professionals also determine the 'health-seeking behavior' of the public. Duration of self-medication courses was shorter than that of courses prescribed by regular healthcare providers. This was also observed in Mexico, where the duration of treatment was four days when the drug was prescribed by a physician, compared to a median of two days when the drug was self-medicated.[26]

Our study has some limitations. The data are not applicable to the general Indonesian population. This was not a community-based survey. Data were collected only in a population visiting healthcare services. Two out of the three groups involved patients and one included relatives of patients. However within our study population, the data on the relatives, mostly adults, probably approximate the situation of the adult population in the community. The prevalence of antibiotic use of 7% in this group was comparable to the 5% reported from Mexico,[26] but higher than the 3.5% prevalence found in Pakistan.[28] However one should be careful when comparing with other countries. Indonesia has many islands, and we only studied two areas in Java (Central and East), the most developed island. Regional disparities of healthcare and health status exist, and were accentuated by the recent economic crisis. We only interviewed individuals at public healthcare institutions. However, the survey showed that these same individuals also consult private providers. Public providers have private practice after office hours,[13] but might have different prescribing behavior in this setting.[13] Finally, these results should be interpreted with some caution as the morbidity and antibiotic use were self-reported and therefore a subjective and imprecise measure. The one-month recall period might be rather long for interviewees to recall specific and reliable information on symptoms and antimicrobial drugs. However, this recall period has been used by others in Indonesia[14] and other Asian countries.[19,28] Adult literacy rates are relatively high in Indonesia, 86% and 83% in Central and East Java, respectively,[12] which was confirmed by our data and should render the information on drugs by our interview more reliable than in some other low-income countries with high illiteracy rates. However, we cannot rule out that we missed antibiotic use and that 'possible antibiotic use' might have been actual use.

In conclusion, knowing that the majority of the complaints leading to antibiotic use were probably of viral origin and that many bacteria that cause diarrhea are resistant to aminopenicillins in Indonesia, a large proportion of antibiotic consumption was either unnecessary or ineffective. Our results should urge healthcare officials to promote the prudent use of antibiotics. Healthcare authorities can stimulate the development of national evidence-based guidelines by scientific societies and support further research on the use of antibiotics; individual doctors can change their prescription behavior by adhering to these guidelines. Primary targets for improved prescribing are the treatment of respiratory tract infections and gastroenteritis. Since most of the antibiotics were prescribed by doctors, any intervention should primarily concentrate on the doctors.

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References

1. World Health Organization. *WHO global strategy for containment of antimicrobial resistance*. Report No. WHO/CDS/CSR/DRS/2001.2. Geneva: WHO; 2001.
2. Tenover FC. Development and spread of bacterial resistance to antimicrobial agents: an overview. *Clin Infect Dis* 2001;**33**(Suppl 3):S108—15.
3. Austin DJ, Kristinsson AG, Anderson RM. The relationship between the volume of antimicrobial consumption in human communities and the frequency of resistance. *Proc Natl Acad Sci* 1999;**96**:1152—6.
4. Shears P. Antibiotic resistance in the tropics. *Trans Royal Soc Trop Med Hyg* 2001;**95**:127—30.
5. Gani L, Arif H, Widjaja SK, Adi R, Prasadja H, Tampubolon LH, et al. Physician's prescribing practice for treatment of acute diarrhoea in young children in Jakarta. *J Diarrhoeal Dis Res* 1991;**9**:194—9.
6. Ismail R, Bakri A, Nazir M, Ryanto, Haridawati. Indicators for antibiotic therapy in invasive bacterial diarrhoea. *J Diarrhoeal Dis Res* 1994;**3**:208—13.
7. Subekti DS, Lesmana M, Tjaniadi P, Machpud N, Sriwati. Sukarma, et al. Prevalence of enterotoxic *Escherichia coli* (ETEC) in hospitalized acute diarrhea patients in Denpasar, Bali, Indonesia. *Diagn Microbiol Infect Dis* 2003;**47**:399—405.
8. Tjaniadi P, Lesmana M, Subekti D, Machpud N, Komalarini S, Santoso W, et al. Antimicrobial resistance of bacterial pathogens associated with diarrheal patients in Indonesia. *Am J Trop Med Hyg* 2003;**68**:666—70.
9. Ieven M, Van Looveren M, Sudigdoadi S, Rosana Y, Goossens W, Lammens C, et al. Antimicrobial susceptibilities of *Neisseria gonorrhoeae* strains isolated in Java, Indonesia. *Sex Transm Dis* 2003;**30**:25—30.
10. Santoso B, Suryawati S, Prawaitasari JE. Small group intervention vs formal seminar for improving appropriate drug use. *Soc Sci Med* 1996;**42**:1163—8.
11. Waters H, Saadah F, Pradhan M. The impact of the 1997—1998 East Asian economic crisis on health and healthcare in Indonesia. *Health Policy Plan* 2003;**18**:172—81.
12. Indonesia Human Development Report 2004. The economics of democracy: financing human development in Indonesia. Indonesia: BPS-Statistics BAPPENAS and UNDP; 2004.
13. Hidayat B, Thabrany H, Dong H, Sauerborn R. The effects of mandatory health insurance on equity in access to outpatient care in Indonesia. *Health Policy Plan* 2004;**19**:322—35.
14. Simanjuntak CH, Punjabi NH, Wangsasaputra F, Nurdin D, Pulungsih SP, Rofiq A, et al. Diarrhoea episodes and treatment-seeking behaviour in a slum area of North Jakarta, Indonesia. *J Health Popul Nutr* 2004;**22**:119—29.
15. Anonymous. *Pedoman kerja Puskesmas*. Jakarta: Departemen Kesahatan RI; 1990.
16. Darmansjah I, Wardhini S. The Indonesian drug advisory committee and the drug approval process. *J Clin Epidemiol* 1991;**44**: 39S—43S.
17. Anonymous. Undang-Undang Obat Keras. *Staatsblad* No. 419; 22 December 1949.
18. Who Collaborating Centre for Drug Statistics Methodology. *Anatomic therapeutical chemical (ATC) classification index with defined daily doses (DDDs)*. Oslo, Norway: WHO; 2003. Available at: www.whocc.no/atcddd/ (accessed February 2007).
19. Larsson M, Kronvall G, Chuc NT, Karlsson I, Lager F, Hanh HD, et al. Antibiotic medication and bacterial resistance to antibiotics: a survey of children in a Vietnamese community. *Trop Med Int Health* 2000;**5**:711—21.
20. Hossain MM, Glass RI, Khan MR. Antibiotic use in a rural community in Bangladesh. *Int J Epidemiol* 1982;**11**:402—5.
21. Ho M, Hsiung CA, Yu HT, Chi CL, Chang HJ. Changes before and after a policy to restrict antimicrobial usage in upper respiratory tract infections in Taiwan. *Int J Antimicrob Agents* 2004;**23**:438—45.
22. Sutrisna B, Frerichs RR, Reingold A. Randomised, controlled trial of effectiveness of ampicillin in mild acute respiratory tract infections in Indonesian children. *Lancet* 1991;**338**:471—4.
23. Hui L, Li XS, Zeng XJ, Dai YH, Foy HM. Patterns and determinants of use of antibiotics for acute respiratory tract infection in children in China. *Pediatr Infect Dis J* 1997;**16**:560—4.
24. Dong H, Bogg L, Rehnberg C, Diwan V. Association between health insurance and antibiotics prescribing in four counties in rural China. *Health Policy* 1999;**48**:29—45.
25. Sorensen TL, Monnet DL. Control of antibiotic use in the community: the Danish experience. *Infect Control Hosp Epidemiol* 2000;**21**:387—9.
26. Calva J, Bojalil R. Antibiotic use in a periurban community in Mexico: a household and drugstore survey. *Soc Sci Med* 1996;**42**:1121—8.
27. Radyowijati A, Haak H. Improving antibiotic use in low-income countries: an overview of evidence on determinants. *Soc Sci Med* 2003;**57**:733—44.
28. Sturm AW, van der Pol R, Smits AJ, van Hellemondt FM, Mouton SW, Jamil B, et al. Over-the counter availability of antimicrobial agents and self-medication and patterns of resistance in Karachi, Pakistan. *J Antimicrob Chemother* 1997;**39**:543—7.