PATTERNS, APPROPRIATENESS, AND PREDICTORS OF ANTIMICROBIAL PRESCRIBING FOR ADULTS WITH UPPER RESPIRATORY INFECTIONS IN URBAN SLUM COMMUNITIES OF BANGKOK

Siritree Suttajit[1], Anita K Wagner[2], Ruangthip Tantipidoke[3], Dennis Ross-Degnan[2] and Chitr Sitthi-amorn[4]

[1]College of Public Health, Chulalongkorn University, Bangkok; [2]Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care, Boston, MA, USA; [3]Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok; [4]Institute of Health Research, Chulalongkorn University, Bangkok, Thailand

Abstract. Upper respiratory tract infections (URIs) are the most common infections worldwide. Their frequent inappropriate treatment with antibiotics is likely to increase antibiotic resistance, contribute to morbidity and mortality, and waste scarce resources. Using data from registration books and prescriptions, we measured patterns and assessed appropriateness and predictors of antibiotic prescribing for viral and bacterial URIs treated in health centers located in two slum communities in Bangkok, Thailand. Based on recorded diagnoses and symptoms, 91% of the patients probably had viral URIs; 60% of viral and 89% of bacterial URI patients were prescribed an antibiotic. Compliance with the national treatment guideline was 36.4% for treatment of viral URIs and only 1.7% for treatment of bacterial URIs. Amoxicillin was the most frequently prescribed antibiotic regardless of diagnosis. Among viral URI patients, those who were young, male, and self-paying were more likely to receive antibiotics; part-time physicians were more likely to prescribe antibiotics for these patients. Among patients with bacterial URIs, those who paid for drugs by themselves were more likely to receive antibiotics compared to patients covered by the national health insurance plan. We used these formative results as input to the design of health center and community interventions to encourage more appropriate prescribing for URI among adults.

INTRODUCTION

Upper respiratory tract infections (URIs) are the most common infections worldwide (Bamberger and Jackson, 1995). In Thailand, acute URIs are an important health problem. Nearly half of respondents to the 2000 National Health and Welfare Survey (NSO, 2000) reported having had a respiratory disease during the two preceding weeks, the most frequently reported acute health problem.

Although viruses cause most URIs (Therapeutic Guidelines, 1998), antimicrobial agents are still among the most frequently prescribed drugs for URI. Unnecessary antimicrobial use for URI, both at health facilities and in the community, is one of the most common drug use problems (Grand *et al*, 1999). Adverse consequences of antimicrobial use for viral URIs are particularly unfortunate in developing countries (Kunin, 1993). Since most patients pay out-of-pocket for their medicines, they waste scarce household resources on unnecessary care. Moreover, inappropriate antimicrobial use increases drug resistance in the community, requiring use of more expensive and potentially more toxic alternative drugs when antimicrobial treatment is needed. These more expensive antimicrobials are less likely to be affordable in resource-poor settings. In Thailand, data from the Drug Control Division (2003) showed that antimicrobials are the most frequently used drugs and their use increases every year.

Correspondence: Siritree Suttajit, College of Public Health, Chulalongkorn University, Bangkok 10330, Thailand.
Tel: +66 (0) 2218 8198; Fax: +66 (0) 2255 6046
E-mail: siritree@gmail.com

According to the WHO Strategy for the Containment of Antimicrobial Resistance (WHO, 2001), developing countries play an important role in the emergence of antimicrobial resistance. In developing countries, bacterial resistance to antimicrobial agents is common in isolates from healthy persons (Okeke *et al,* 1999). In urban slum communities with poor sanitation, high incidences of HIV/AIDS, multi-drug resistant tuberculosis (MDRTB), and drug addiction, resistance is likely to spread easily.

Studies in developed countries suggest that both clinical and socio-cultural factors contribute to inappropriate antimicrobial prescribing (Avorn and Solomon, 2000; Murray *et al,* 2000; Pechere, 2001). A recent review by Radyowijati and Haak (2003) highlighted the lack of data to characterize the importance of different determinants of antibiotic use in developing countries. There are few studies of antimicrobial use for URIs in these settings and most report on treatment of URIs in children. Patterns of antimicrobial use in low-income countries differ from those in industrialized countries, and complex relationships exist between antibiotic use and local culture, socioeconomic characteristics, and poor health care infrastructure (Radyowijati and Haak, 2003).

To provide formative data to guide the design of interventions to improve treatment of URI in adults, we assessed patterns of antimicrobial and other drug treatment for adults with URIs treated in health centers in two slum communities in Thailand.

MATERIALS AND METHODS

Setting

We conducted the present study in two of the 61 health centers run by the Bangkok Metropolitan Administration (BMA), which provide care in under-served slum communities in Bangkok, Thailand. More than 125,000 individuals live in 22,063 households in a two square kilometer slum area covered by the two health centers. People in these communities face problems of substandard housing, poor sanitation, unemployment, low income, high incidence of HIV/AIDS, MDRTB, sexually transmitted diseases, and drug addiction.

Data sources

We retrospectively identified in registration books of the two health centers all patients over 18 years of age who were treated for URI in 2001. We included cases with diagnoses of URI, cough and cold symptoms, pharyngitis, tonsillitis, otitis media, or sinusitis. We abstracted the prescriptions these patients had received, which were written by a total of 19 physicians.

Information about patients collected from registration books included age, gender, and diagnoses. Type, amount, and cost of prescribed drugs, type of payment for drugs, and physician name were collected from copies of the prescriptions maintained in the clinic pharmacies. Additional information about physician characteristics (age, gender, full-time or part-time employment status, specialty, and number of years practicing) was gathered directly from the physicians and from health center administrators.

The study was approved by the Human Research Ethical Committee at the Faculty of Medicine of Chulalongkorn University; the Ethical Review Committee for Research in Human Subjects, Ministry of Public Health, Thailand; and the Boston University Medical Center Institutional Review Board.

Definition of 'likely viral' and 'likely bacterial' URIs

We classified patients diagnosed with URI or common cold, unspecified URI, or symptoms like cough, rhinitis or headache as having 'likely viral' URIs. Patients diagnosed with pharyngitis, sore throat, tonsillitis, acute otitis media, or sinusitis were classified as having 'likely bacterial' URIs. Patients with more than one URI diagnosis were classified according to the most severe diagnosis.

Definition of appropriate treatment

We classified treatments according to the National Standard Treatment Guideline for Respiratory Tract Infections (MoPH, 1996). For viral URIs, such as nonspecific URI, acute bronchitis, rhinitis, or influenza, the Guideline emphasizes that antibiotics should not be given unless patients have high fever, severe cough, or abscesses. For bacterial URIs, the Guideline recommends penicillin V, penicillin G, or erythromycin for 7-10 days for pharyngitis and tonsillitis;

amoxycillin (or ampicillin, coamoxycillin), cotri-moxazole or erythromycin for 14 days for otitis media; and the same antimicrobials or doxycy-cline for 14-21 days for sinusitis.

Analysis

We first assessed drug treatment patterns for URIs, cough and cold, pharyngitis/tonsillitis, otitis media, and sinusitis. We calculated the percentage of patients receiving an antimicro-bial prescription; percentage of prescribed treat-ments consistent with the standard treatment guideline; and cost associated with inappropri-ate antimicrobial use. We evaluated differences in antimicrobial prescribing by patient and phy-sician characteristics using chi-square tests or Fisher's exact tests for categorical variables and Student's t-tests for continuous variables. A dif-ference with a two-sided p-value <0.05 was considered statistically significant. Numerical variables were recoded to categorical variables for univariate and logistic regression analyses.

To examine predictors of antimicrobial pre-scribing, we developed generalized linear mixed models (Guo and Zhao, 2000) that adjust for clustering of cases by provider. We looked for factors associated with appropriate treatment using separate logistic regression models for vi-ral and for bacterial URI cases. Variables that were associated with antimicrobial prescribing in univariate analyses (p-value < 0.10) were in-cluded in the initial logistic regression model; variables were removed sequentially if they were non-significant and their removal did not change the odds ratios of remaining predictors by at least 20%. Odds ratios and 95% confidence intervals were calculated from the final models.

We replaced missing age values (n=6, 0.13%) with median age; seven cases (0.16%) with missing payment status were excluded from the logistic regression analyses. Data were man-aged and analyzed using the Statistical Pack-age for the Social Sciences (SPSS) for Windows 12.0.0 (SPSS Inc, 2004) and Statistical Analy-sis Software (SAS) 8.02 (SAS Institute Inc, 1999).

RESULTS

Between January and December 2001, 4,608 adult URI patients visited the study health centers. They accounted for 10.6% of all health center patients, 15.8% of adult patients, and 35.2% of all URI patients. There was no sea-sonal pattern of cases presenting with URI. Al-most all (97.9%) adult URI patients received a prescription, resulting in 4,512 prescriptions for analysis. Patients without a prescription may not have received one or may have filled it at a drug store outside the health center.

Characteristics of patients

Most patients were women and nearly half of the patients were between 18 and 40 years old (Table 1a). More than half of the patients (57.6%) paid for their prescription at the point of service, while the rest received free care or paid a small copay (30 baht, about US$ 0.80) under the national health insurance plan. Nearly all (91.0%) adult URI patients were classified by their diagnoses and symptoms as likely to have viral URIs. Among patients likely to have bacte-rial URIs, more than three-fourths were diag-nosed with pharyngitis. Most (87%) patients did not have other diagnoses at the time of their visit. Those with co-diagnoses mostly had chronic dis-eases, such as hypertension, heart disease, dia-betes, arthritis, gout, and gastrointestinal dis-ease.

Characteristics of physicians

Physicians had an average age of 53 years, half were women, and most had practiced for more than 10 years (Table 1b). Most physicians were general practitioners or trained in public health or family medicine. Only 4 (21%) physi-cians worked full-time at the health centers.

Pattern of drug prescribing for viral and bacte-rial URIs

All patients with bacterial URIs received at least one drug, and only 13 (0.3%) patients with viral URI did not receive a drug. As shown in Table 2, physicians treated viral and bacterial URIs differently. For viral URI patients, analge-sics/antipyretics and antihistamines were the most frequent symptomatic treatments pre-scribed, followed by antimicrobial agents. Phy-sicians prescribed antihistamines and vitamins significantly more frequently for viral URI patients. Bacterial URI patients received significantly greater numbers of drugs, injections, antimicro-

Table 1a
Characteristics of patients receiving prescriptions (n=4,512).

Characteristic	No. (%)
Female	3,173 (70.3)
Age: Year, mean±SD	44.91±17.00
18-40	2,060 (45.7)
41-60	1,352 (29.9)
> 61	1,100 (24.4)
Payment	
Self payment	2,595 (57.6)
Free of charge	1,910 (42.4)
Diagnosis	
Viral URIs	4,107 (91.0)
Bacterial URIs	
Pharyngitis/ Tonsillitis	309 (6.8)
Otitis media	89 (2.0)
Sinusitis	7 (0.2)
Co-morbid illness	586 (13.0)

Table 1b
Characteristics of physicians (n=19).

Characteristic	No. (%)
Female	9 (47.4)
Age: Years, mean±SD	53.0±15.5
Full-time practice	4 (21.1)
General practice	13 (68.4)
Years in practice	
>10	15 (78.9)
≤10	4 (21.1)
URI cases treated/ year	
<100	7 (36.8)
101-500	9 (47.4)
>500	3 (15.8)

bials, analgesics/antipyretics, and cough suppressants than patients with viral illness.

Overall, 62.9% of all URI patients received a prescription for an antimicrobial, 60.3% of viral URI patients and 89.4% of bacterial URI patients (91.6% of patients with pharyngotonsillitis, 83.1% with otitis media, and 71.4% with sinusitis). Antimicrobials made prescriptions more costly. Prescriptions for viral URI patients with an antimicrobial cost 43 baht (about US$1.20) more than those without an antimicrobial.

Appropriateness of antimicrobial prescribing

To assess appropriateness of antimicrobial prescribing, we evaluated the type and duration of antimicrobial treatment among patients with common cold, pharyngitis/tonsillitis, and otitis media, who had no other diagnoses and who received an antimicrobial drug. These patients received 16 different antimicrobials, all of which were on the 1999 National Essential Drugs List. Regardless of diagnosis, amoxicillin was the most frequently prescribed antimicrobial. Macrolides (erythromycin, roxithromycin), chloramphenicol, and lincomycin injection were more frequently prescribed for bacterial than for viral URIs.

Only a small proportion of URI patients were treated according to the National Standard Treatment Guideline for Respiratory Diseases (1996). Shaded boxes in Table 3 show appropriate prescribing based on diagnosis. Only 36.4% (1,287) of viral URI patients were treated correctly without antimicrobials. Among URI patients with likely bacterial diagnoses, 14.2% (52) received appropriate oral antimicrobials, 4.0% (11) of those with pharyngitis/tonsillitis and 54.3% (38) of those with otitis media.

The average duration of prescribed oral antimicrobial treatment was 6.3 days for viral URIs and 6.7 for bacterial URIs. When considering appropriateness of indication and duration of antimicrobial prescribing simultaneously, only 1.7% of bacterial URI patients were treated appropriately, 5 (1.8%) patients with pharyngitis/tonsillitis and 1 (1.4%) patients with otitis media.

Factors associated with antimicrobial prescribing

Adjusted for potential physician clustering and potential confounders, several patient and physician characteristics were associated with greater rates of antimicrobial prescribing in viral URIs (Table 4). Male patients and younger patients (under age 60) were significantly more likely to receive antimicrobials for viral URIs than their respective comparison groups (Table 4). Patients who payed for their medicines out-of pocket or were insured under non-national health plans were somewhat more likely to receive antimicrobials than those insured under the national health

Table 2
Drugs prescribed for URI patients.

Drugs prescribed	No. of prescriptions (%)	
	Viral URIs (n=4,107)	Bacterial URIs (n=405)
Antimicrobial	2,477 (60.3)	362 (89.4)[b]
Analgesic/antipyretic	2,983 (72.6)	328 (81.0)[b]
Antihistamine	2,805 (68.3)	135 (33.3)[b]
Mucolytic	1,842 (44.9)	198 (48.9)
Cough suppressant	1,350 (32.9)	175 (43.2)[b]
Vitamin	836 (20.4)	46 (11.4)[b]
Other symptomatic drug[a]	454 (11.1)	70 (17.3)
Mean no. of drugs per prescription	3.20±1.07	3.67±1.26[b]
Injection	63 (1.5)	27 (9.0)[b]
Median cost per prescription (baht)	44.0	76.0
With antimicrobial	59.0	78.0
With no antimicrobial	16.0	16.0

[a]bronchodilators, anti-inflammatory enzymes, (antiseptic) mouth preparations, topical antiseptics.
[b]p-value <0.05

Table 3
Antimicrobials prescribed among antimicrobial recipients[a].

Antimicrobials prescribed	No. of prescriptions (%)[b]		
	Common cold (n=2,247)	Pharyngitis/ tonsillitis (n=275)	Otitis media (n=70)
Penicillin V	54 (2.4)	8 (2.9)	3 (4.3)
Erythromycin	67 (3.0)	3 (1.1)	2 (2.9)
Amoxicillin±clavulanic acid[c]	1,581 (70.4)	196 (71.3)	31 (44.3)
Ampicillin	6 (0.3)	- -	- -
Co-trimoxazole	70 (3.1)	9 (3.3)	5 (7.1)
Dicloxacillin/ Cloxacillin[c]	217 (9.7)	14 (5.1)	23 (32.9)
Roxithromycin[c]	141 (6.3)	37 (13.5)	4 (5.7)
Chloramphenicol ear drop[c]	10 (0.4)	2 (0.7)	25 (35.7)
Doxycycline	17 (0.8)	2 (0.7)	- -
Tetracycline	87 (3.9)	5 (1.8)	- -
Cephalexin	5 (0.2)	1 (0.4)	- -

[a]patients with co-morbid diagnosis excluded.
[b]totals may sum to more than 100% because some patients received >1 antimicrobial.
[c]p-value <0.05 for differences in prescribing across disease categories.
Note: shading indicates guideline-recommended therapy.

plan. Part-time physicians tended to prescribe more antimicrobials but this association was also not statistically significant.

There was little variability in antimicrobial prescribing for bacterial URI patients. Only payment status was a significant predictor of antimicrobial prescribing for bacterial URIs, after adjusting for the health center. Patients paying out of pocket or insured under non-national health plans were more likely to receive antimicrobials than those insured under the national health plan (OR, 2.17, 95% CI, 1.15 – 4.09).

Cost of URI treatment

The average cost of treating bacterial URI

Table 4
Factors associated with antimicrobial prescribing for viral URI patients (n=4,107).

Characteristics	Antimicrobial prescribed (%)	Crude OR (95% CI)	Adjusted OR [a] (95% CI)
Gender			
Male	779 (64.9)	1.41 (1.20 - 1.64)	1.47 (1.26 - 1.72)
Female	1,698 (58.4)	Referent	Referent
Age			
18-40 yr	1,255 (68.9)	3.95 (3.28 - 4.77)	3.62 (2.92 - 4.50)
41-60 yr	734 (59.4)	2.29 (1.89 - 2.78)	2.17 (1.76 - 2.68)
>60 yr	488 (46.5)	Referent	Referent
Payment type[b]			
Self-payment	1,518 (65.5)	1.96 (1.70 - 2.27)	1.19 (1.00 - 1.40)
Free of charge	954 (53.5)	Referent	Referent
Physician employment status			
Part-time	2,041 (62.8)	2.32 (0.84 - 6.41)	2.58 (0.85 - 7.85)
Full-time	436 (51.0)	Referent	Referent

[a]adjusted for gender, age, payment type, and physician employment status; OR denotes odds ratio, CI denotes confidence interval.
[b]patients paying out-of-pocket or patients insured under health plans other than the national health plan are classified as self-pay patients; patients insured under the national health plan are classified as free-of-charge.

was greater than the cost of treating viral URI (80 baht *versus* 46 baht per case, a difference of approximately US$0.85). Patients who received antimicrobials paid 44-53 baht more per prescription than patients who did not receive antimicrobial treatment.

DISCUSSION

Pattern of prescribing for URIs

The vast majority (90%) of URI patients who visited health centers in these two slum areas in Bangkok in 2001 most likely had viral URIs. High rates of prescribing of symptomatic drugs, such as antipyretics/analgesics and antihistamines, for these viral URI patients would be appropriate according to the National Standard Treatment Guideline (1996). However, 60.3% of patients with viral URIs received antimicrobials. In bacterial URIs, antimicrobials were prescribed more frequently than symptomatic drugs to 89% of patients. Antimicrobial prescribing rates for bacterial URIs in these slum communities were similar to those reported from developed countries (Dosh *et al,* 2000; Linder and Singer, 2003). For viral URIs, however, antimicrobial prescribing

rates were much higher than those observed in developed countries (9 - 46%) (Dosh *et al,* 2000; Linder and Singer, 2003; Steinman *et al,* 2003).

Appropriateness of antimicrobial prescribing

Based on estimates from the National Standard Treatment Guideline (1999), about 0.5-2.0% of viral URI patients who had high fever, severe cough, and/or abscesses would need antimicrobials. High-risk patients, such as those with HIV/AIDS and intravenous drug users, may also need empirical antimicrobial treatment. Proportions of these high-risk patients may have been underestimated in this study due to underreporting of these co-morbidities. Nevertheless, 60.3% of patients with likely viral URI received antimicrobials, a proportion far higher than expected, implying substantial overuse of antimicrobials for most URI patients treated at these health centers.

Among patients with bacterial URIs who received antimicrobials, selection and duration of antimicrobial treatment were problematic. Antimicrobials that were not recommended by the treatment guideline (amoxycillin-clavulanic acid, cefalexin, ciprofloxacin, chloramphenicol,

tetracycline) were prescribed for 85.1% of these patients. About 4% of URI patients received tetracycline or ciprofloxacin, antibiotics which should be very carefully prescribed in women of childbearing age.

The average duration of antimicrobial treatment among bacterial URI patients was 6.7 days and only 18% of patients received antimicrobial treatment for 7-14 days. We cannot assess the appropriateness of failing to prescribe an antimicrobial for 42 patients (10.7%) with bacterial URIs.

Predictors of antimicrobials prescribing

We found different predictors of antimicrobial prescribing for viral and bacterial URI patients. Younger, male patients with viral URIs were more likely to receive antimicrobials than others with viral URIs. This finding agrees with results from some (Linder and Stafford 2001) but not all previous studies (Dosh, 2000; De Sutter *et al*, 2001; Steinman *et al*, 2003). Younger patients are more likely to be infected with Group A β-hemolytic streptococci (GABHS), and some treatment algorithms recommend antimicrobial treatment for younger patients with sore throat (McIsaac *et al*, 1998). It may also be possible that physicians tend to prescribe antimicrobials more frequently because of concern about effects of illness on work loss in this population (Linder and Singer, 2003). Physician age and gender did not influence prescribing patterns, but employment status possibly did. Part-time physicians at the health centers include retired physicians and young medical doctors from other health settings. Because they practice in the community only half a day, 1-3 days per week, they may perceive different prescribing needs than full-time physicians.

Ability to pay may contribute to the decision to prescribe antimicrobials for viral and bacteria URI patients. The recent health system reform in Thailand introduced capitated payment for patients in the national health plan. Physicians may tend to prescribe more drugs for patients who pay out of pocket or are insured in the fee-for-service civil servant medical benefit scheme in order to to compensate for lost health center revenue due to care for patients under

the national health plan. This may also represent greater willingness to conform to patient demand for antibiotics when cost is not an issue. Dong and colleagues (1999) also showed that patients with URI in China who paid out-of-pocket received antimicrobials more frequently, although they hypothesized that this might be due to these patients presenting later at health facilities with more advanced illness.

Cost of unnecessary antimicrobial use

Unnecessary prescribing of antimicrobials for viral URIs is a serious and costly problem. It may increase antimicrobial resistance in the community, rendering common antimicrobials ineffective and causing a need for more expensive new antimicrobials. For individuals with viral URIs, the added cost of unnecessary antimicrobial treatment was 43 baht per case. Based on average monthly total income and expenditures per household in the year 2001 from the National Statistical Office (2003), this accounted for 10.8% of daily household income or 13.2% of total daily household expenditures and a total of 106,511 baht expended per year for unnecessary antimicrobial treatment of viral URI patients at the two study health centers.

Study limitations

We need to acknowledge the following limitations of the study. Some cases may be misclassified as viral or bacterial. Physicians note only broad diagnoses in health center registration books, and detailed information such as clinical signs, duration of symptoms, and other clinical information, such as HIV infection and pregnancy, is limited. We may have overestimated the prevalence of viral URI and thus of inappropriate antimicrobial use. Nevertheless, viral URIs are estimated to account for 65-90% of URIs in adults (MoPH, 1996; Therapeutic Guidelines 1998; Dolin 1998; Heikkinen and Jarvinen, 2003), which is consistent with the 91% estimate of viral cases presenting for treatment in our setting.

Our ability to generalize the present findings from health centers in slum areas to other settings in Thailand or elsewhere may be limited. Patterns of prescribing and the factors that influence prescribing in private health care set-

tings or public hospitals may be quite different, due to institutional policies, pharmaceutical company marketing, and access to laboratory facilities. In addition, the high risk nature of our population may influence the propensity to prescribe antibiotics as preventive therapies.

Future research should explore other possible determinants of antimicrobial use, including patients' expectations (Britten and Ukoumunne, 1997), their attitudes towards antimicrobials (Walker *et al,* 2003), and the impact of existing health care policies and regulations.

Conclusion

Patients with viral URIs treated in health centers in these slum communities frequently receive unnecessary antimicrobials and patients with bacterial URIs frequently receive inappropriate antimicrobial treatments. These patterns are likely to accelerate rates of growth of antimicrobial resistance to commonly used antibiotics. From the perspective of patients, this means wasting money for unnecessary and potentially harmful medicines and from the perspective of society this means risking loss of potent antimicrobials through misuse. Interventions to promote more rational use of antimicrobials in these settings are urgently needed. Incorporating findings from the present study, we are currently developing multi-sectoral interventions to improve treatment of URI among adults in these slum communities (Suttajit *et al,* 2003).

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