

Research Article

Cost-analysis of antibiotic prescription for upper respiratory infections (URIs) and acute diarrhea (AD) from hospital perspective: A cross sectional study in Noenmaprang district hospital

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ABSTRACT

Ministry of Public Health, Thailand, implemented key performance indicators (KPIs) for rational drug use (RDU) since 2016. The target was limitation of antibiotic prescription for less than 20% among upper respiratory infections (URIs) and acute diarrhea (AD) patients. This cross sectional descriptive study aimed to define the direct cost of antibiotics from a hospital perspective. URI and AD cases, during February to April 2017, were selected by the designated ICD-10 codes. We separated patients into 3 main groups; rational, irrational, and controversial group. In terms of controversial and irrational indications of antibiotic prescription, we investigated 203 and 962 URI visits and 62 and 247 AD visits, respectively. All cost data were presented in Thai baht where 1.00 US dollar = 33.2 baht in 2017. The total cost of antibiotics was 13,621 baht for URI and 1,648 baht for AD. We found 21 AD visits in irrational group that had risk factors and potential to characterize as rational use. This consumed 616 baht, therefore it was 1,032 baht of antibiotics cost for AD visits. The overall cost of OPD service charge and antibiotic cost for URI and AD were 54,216 and 23,775 baht, respectively. The most common prescribed antibiotic was amoxicillin. The result failed the target KPIs. This value revealed to hospital administrator in implementing a much greater use of evidence-based diagnostic and treatment guidelines by health professionals.

1. INTRODUCTION

WHO (1985) defined rational drug use as patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community. Common example of irrational drug use is antimicrobial medicines are prescribed in inadequate doses or duration or antibiotics prescribed for non-bacterial infections, thereby contributing to the growing problem of antimicrobial resistance.

Upper respiratory infections (URIs) and acute diarrhea (AD) are the most common infectious diseases throughout in the world^{1, 2}. Often, etiology of the diseases are non-infectious and viral, e.g. AD from norovirus. Such condition tends to resolve with

supportive care and rest without the use or need for any antibiotics. Nevertheless, there have been several reports of overuse of antibiotics and an associated increase in microbial drug resistance³. In Thailand in 2010, antimicrobial resistance was responsible for direct medical cost of between 84.6 million and 202.8 million US dollars. Especially increased cost of treatment without benefit from antibiotics or even harm from incidence of potential adverse drug reactions in some cases⁴. Kalasin province reported irrational antibiotics used in 1,393 out of 4,705 URI cases and 266 out of 810 AD cases during fiscal year 2011. A total cost of detriment treatment was 75,762 and 7,147 baht, respectively. The total cost of antibiotic overused was estimated as 82,909 baht, accounting for 16% of overall antibiotic cost⁵.

Increasing awareness of antimicrobial resistance and promoting the rational use of antibiotics among prescribers are key to combating the unnecessary use of these drugs. Thailand Food and Drug Administration (FDA) task force launched the 15th National Health Service (NHS) plan for rational drug use (RDU) in 2016. This plan is designed to promote and optimize RDU particularly in government hospitals through the adoption 18 key performance indicators (KPIs). Four indicators are intended to control rational antibiotic prescribing.

In this study, we focus on 2 KPIs which are designed to ensure that antibiotic prescriptions must less than 20% among URI or AD patients⁶. RDU calculation is based on the 10th International Classification of Disease (ICD-10). This study aimed to expand the cost analysis of both 50 ICD-10 codes of URI either 36 ICD-10 codes of AD from the hospital's perspective. Some ICD-10 codes may possibly non-tangible measurement. We also proposed to refine and interpret qualitative information to feedback KPI outcomes for direction of the hospital and NHS plan.

2. MATERIALS AND METHODS

This is a cost analysis of antibiotic prescribing from a hospital's perspective using hospital database. The estimate of incremental cost, interventions, and comparison outcome will be excluded.

2.1. Definition of rationality prescription

The 15th NHS plan defines rationality prescribing of antibiotics in the treatment of URI and AD patients when patient are diagnosed with a specific ICD-10 code and where antibiotics are prescribed, whether administered orally or intravenous antibiotics (ATC code: J01) divided by a total number of URI and AD patients.

Irrational use of medicines (WHO) is too many medicines per patient (polypharmacy), inappropriate use and dosage of antimicrobials for non-bacterial infections, overuse of injections when oral formulations would be more appropriate, failure to prescribe in accordance with clinical guidelines, inappropriate self-medication of prescription-only medicines, non-adherence to dosing regimen.

In this study, we characterized the use of antibiotics for URI and AD patients into 3 groups; rational, irrational, and controversial group. We categorized irrational use of antibiotics as use of antibiotics for non-bacterial infections. For example in URI case, J02.0 (streptococcal pharyngitis) was included to rational group of URI because this disease need to use antibiotic for treatment, but J02.9 (acute pharyngitis unspecified) is possibility to include in both irrational group either controversial group because the most of pathogenic for this disease being virus. In AD case, A043 (enterohaemorrhagic *E. coli*) is an infection diarrhea that antibiotics were recommended as contraindication. Then, prescribing antibiotics for A04.3 is classified as irrational use of drug. In summary, we categorized these groups by reviewing the standard treatment guidelines, e.g. WHO, CDC and Infectious Diseases Society of America (IDSA).

2.2. Population and sample

This was a cross sectional study at Noenmaprang hospital. Subjects data were selected only URI or AD patients from outpatient department during February to April, 2017. Since we included all patients at the time to analysis cost of antibiotic that mean sample size no need for this study. We assigned each study subject to one of three categories of prescribing using the following algorithm;

Table 1. Characteristics of participants who were prescribed antibiotics

Characteristics	Rational group		Controversial group or irrational group		Total visits	
	URIs	AD	URIs	AD	URIs	AD
	N=29	N=0	N=203	N=62	N=232	N=62
Age (years old)	30±4.9	0	30±1.7	33±3.7	30±2.7	33±3.7
Male No. (%)	16 (55.0)	0	85 (42.0)	31 (50.0)	101(44.0)	31 (50.0)

1. RI patient was patients who diagnosed at least one of these 50 ICD-10;

1.1. ICD-10 of controversial or irrational group were J00, J01.0, J01.1, J01.2, J01.3, J01.4, J01.8, J01.9, J02.9, J03.8, J03.9, J04.0, J04.1, J04.2, J05.0, J06.0, J06.8, J06.9, J10.1, J11.1, J20.0, J20.3, J20.4, J20.5, J20.6, J20.7, J20.8, J20.9, J21.0, J21.8, J21.9, H65.1, H65.9, H66.9, H67.1, H67.8, H72.0, H72.1, H72.2, H72.8, H72.9

1.2. ICD-10 of rational group were J02.0, J03.0, J05.1, J20.1, J20.2, H65.0, H66.0, H66.4, H67.0

2. AD patient was patient who diagnosed at least one of these 23 ICD-10;

2.1. ICD-10 of controversial group or irrational group were A08.0, A08.1, A08.2, A08.3, A08.4, A04.3, A04.4, A046, A05.0, A05.4, A05.9, A04.0, A04.1, A04.8, A04.9, A05.3, A08.5, A090, A09.9, A09, K52.1, K52.8, K52.9

2.2. ICD-10 of rational group were A00.0, A00.1, A00.9, A02.0, A03.0, A03.1,

A03.2, A03.3, A03.8, A03.9, A04.2, A04.5, A04.7

2.3. Data collection

We collected patient data from 11 out of 43 national standard folders in Noenmaprang HIS. We used LibreOffice-based database: BC2017 to recruit patients profile at OPD visit. Patients were included when they were diagnosed with specific 50 ICD-10 of URI and 36 ICD-10 of AD during February to April, 2017. The direct cost of service expenditure and drugs price were obtained from actual price at the hospital. This study was ethical approved by IRB of faculty of Pharmacy, Chiangmai University. The approval number was 27/2560.

2.4. Cost-analysis model

This study calculates cost of antibiotics from the hospital's perspective in Thai baht. The equation for calculation is;

$$\text{Overall OPD cost} = [\text{amount of prescribed drug} \times \text{unit cost of drug}] + [\text{service expenditure}]$$

Table 2. Classification of patients by diagnosis (ICD-0)

Code	Diagnosis	Number of patients
URI : ICD-10 of controversial or irrational group		
J00	Acute nasopharyngitis [common cold]	17
J01.9	Acute sinusitis, unspecified	7
J02.9	Acute pharyngitis, unspecified	56
J03.9	Acute tonsillitis, unspecified	61
J20.9	Acute bronchitis, unspecified	30
J21.9	Acute bronchiolitis, unspecified	3
H65.9	Unspecified nonsuppurative otitis media	9
H66.9	Otitis media, unspecified	19
H72.9	Unspecified perforation of tympanic membrane	1
URI : ICD-10 of rational group		
J03.0	Streptococcal tonsillitis	6
H65.0	Acute serous otitis media	9
H66.0	Acute suppurative otitis media	12
H66.4	Suppurative otitis media, unspecified	2
AD : ICD-10 of controversial or irrational group		
A085	Other specified intestinal infections	1
A090	Other and unspecified gastroenteritis and colitis of infectious origin	2
A099	Gastroenteritis and colitis of unspecified origin	59

Table 3. Frequency of antibiotics prescribed for URIs and AD patients

Generic name	Unit of medicine	Total prescription	No. of controversial antibiotic prescription		No. of rationality antibiotic prescription
			AD	URIs	URIs
Amoxicillin					
250 mg, capsule	206				
500 mg, capsule	2,408	170	2	148	20
125 mg/5 mL, dry syrup bottle	136				
Amoxicillin/Clavulanic 1 g, tablet	629	39	0	30	9
Ceftriaxone 1 g, vial for intravenous	36	9	9	0	0
Ciprofloxacin 250 mg, tablet	50	2	0	2	0
Clarithromycin 250 mg, tablet	172	9	0	9	0
Dicloxacillin					
250 mg, capsule	20	2	0	2	0
62.5 mg/5 mL, dry syrup bottle	2				
Norfloxacin 400 mg, tablet	270	33	31	2	0
Roxithromycin 150 mg, tablet	94	9	0	9	0
Trimethoprim/sulfamethoxazole, suspension bottle	22	21	20	1	0
Total	-	284	52	203	29

Overall cost means summation cost of all medicines and service expenditures. Service expenditure is fee of laboratory, nursing, operation, and doctor.

3. RESULTS

Over the 3-months study period, 962 and 247 patients were included in the URI and AD groups, respectively. The characteristics of the study subjects is shown in Table 1. Eligible patients in the controversial or irrational groups represented 203 URIs cases (21.1%) and 62 AD cases (25.1%). We classified patients to a range of specific diagnostic codes as reported in Table 2. The most controversial or irrational antibiotic use for URI patients were for unspecified acute tonsillitis, unspecified acute pharyngitis, and unspecified acute bronchitis. Gastroenteritis and colitis of unspecified origin were the most frequently prescribed antibiotic category in the controversial or irrational AD group. Nevertheless, we investigated 62 AD patients who were prescribed controversial antibiotics, 21 cases (33.9%) had at least one risk factor which possibly a rational prescription. These risk factors were age more than 70 years old in

6 patients and fever more than 38 °C in 15 patients

Table 3 shows frequency of antibiotics used. Amoxicillin and amoxicillin/clavulanic were the highest prescribed drugs for URIs. Dicloxacillin and ciprofloxacin were prescribed for URIs without recommendation from any standard practice. Norfloxacin and trimethoprim/ sulfamethoxazole were frequently prescribed for AD, as well as, amoxicillin was prescribed for AD without recommendation from any standard practice. Interestingly, ceftriaxone intravenous injection was prescribed as a single shot for 9 OPD visits.

Cost of controversial or irrational antibiotics was 13,621 baht for URIs cases (82.9% of overall antibiotic cost) and 1,648 baht for AD cases (100% of overall antibiotic cost). If we refined some possible AD cases that may rationality to prescribe antibiotic, it would be cost 616 baht. From recalculation a total cost by subtract this exclusion AD group, overall accurate controversial or irrational antibiotics cost was 14,653 baht (96.1% of overall antibiotic cost). Moreover, a total cost of OPD service which included costs of antibiotics and service expenditures for URIs and AD were 54,216 and 23,879 baht, respectively (Table 4).

Table 4. Overall OPD Cost and antibiotic cost (Thai Baht) of URIs and AD cases

Patient group	Cost of treatment, baht	
	Overall cost	Antibiotic cost
URIs (n = 962)	213,861	16,427
URIs, antibiotics prescribed (n = 232)	54,216	16,427
URIs, antibiotics rational prescribed (n = 29)	5,676	2,806
URIs, antibiotics controversial or irrational prescribed (n = 203)	48,540	13,621
AD (n = 247)	68,282	1,648
Non-infectious AD cases (n = 1)	104	0
Infectious AD (n = 99)	68,178	0
Infectious AD, controversial or irrational antibiotics prescribed (n = 62)	23,775	1,648
Infectious AD with risk factors*, controversial or irrational antibiotics prescribed (n = 21)	8,852	616

* risk factors; age \geq 70 years old, fever \geq 38 °C, pregnancy, HIV infection, or neutropenia

4. DISCUSSION AND CONCLUSION

This study conducts in a single district hospital. Eligible patients in controversial group or irrational group were 21.1% of URIs cases, even though antibiotics have little or no benefit. This antibiotic prescription rate is nearly in the United States.^{7, 8}

We found 25.1% of all study subjects to be assigned to both controversial either irrational AD cases. Another report in a large hospital in Bangkok showed the rate of overuse of antibiotics as 48.9%⁹. Noticeably, most of AD cases were recorded A099 code in HIS defined as controversial group. This was a weakness of database analysis. We assumed that more than 70-80% AD patients in controversial group should be prescribed antibiotic because of their risk factors. Further information from OPD card assessment was needed to verify validity and reliability of report.

Contrary to AD, we could not exclude potential irrationality cases from HIS because scanty data. For example, we required swap reporting which uncommon practice at OPD. In addition, estimates probability streptococcal pharyngitis by Centor score was involved missing record of exudates or swelling on tonsils, tender/swollen anterior cervical lymph nodes, and cough^{5,7}.

This study showed prescriptions of antibiotic which low susceptible to isolated organism from stool, for example, sulfamethoxazole/trimethoprim was prescribed for 38% of AD cases. Combination of sulfamethoxazole/trimethoprim had high activity against *Vibrio spp.* but low susceptibility for *Shigella spp.* and *E.coli*¹⁰. Third generation cephalosporin, amoxicillin, fluoroquinolone, macrolide and sulfamethoxazole/trimethoprim

were frequently prescribed for both AD and URIs, resulting in the increasing risk of antibiotic resistance in this area. Unnecessary antibiotics prescription may associated with *Clostridium difficile* diarrhea or colitis¹¹.

We reported 14,653 baht of unnecessary or controversial antibiotics valid cost for AD and URIs cases during 3 months. This cost covered 96.1% of overall tangible antibiotics loss during 3 months in this hospital. If we scaled up the cost from 3 months into 1 year, under hypothesis that there was no any condition change during a whole year, it would be reach 58,612 baht. More or less, a cost analysis in another district hospital showed the value of antibiotic overused for both groups was 82,909 baht per year⁵.

Cost-analysis in this study may influenced by sociodemographic and disease related factors. Future studies should consider using multivariate regressions to adjust for potential confounding factors. Another limitation is the accuracy of input ICD-10 codes for URI and AD cases in HIS.

Assuming in macro level, there are roughly 720 district hospitals in Thailand. Assuming the same condition, antibiotic cost would be approximately 60,000 baht per a secondary care unit per year. The nation would be loss over 42 million baht each year for irrational antibiotic prescription. This number was not include unexpected cost of treatment from antibiotic induced adverse drug events, recurrence infection, long term hospitalization, demanding of more expensive alternative antibiotics therapy, and mortality from drug resistance bacterial. Besides antibiotics cost, further study is needed to investigate these affected cost from antibiotics.

This result failed the target, which employed by the 15th health service plan, to control less than 20% of antibiotic prescriptions

among URIs or AD patients. Information on cost and side effects of the antibiotics was influenced to promote rational prescribing by hospital administrators¹². We do cost-analysis from national standard 43 folders in HIS. Thus, Thailand health data center (HDC) is able to analyze a cost-analysis in widely area by the same protocol of this study.

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Conflict of interest

We have no conflict of interest.

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Ethical approval

This study was ethical approved by IRB of faculty of Pharmacy, Chiangmai University. The approval number was 27/2560.

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