

# Drug use study for acute respiratory infection in children under 10 years of age

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## ABSTRACT

Iwan Dwiprahasto - *Drug use study for acute respiratory infection in children under 10 years of age*

**Background:** Acute respiratory infection (ARI) is the commonest illness in children and the leading cause of morbidity and mortality in many developing countries. It comprises approximately 50 % of all illness in children under five years. Even though usually viral in origin and of a self-limiting nature, various study indicate that antibiotic prescribing for ARI is inappropriately high.

**Objective:** This study was aimed to assess general practitioners' (GPs) prescribing pattern for acute respiratory infection in children seen in private practices.

**Method:** This study is carried out in a cross sectional study design. Participants were GPs and pharmacies in Yogyakarta Special Province. Data on patient and measure of respiratory rate were obtained from GPs' office and data on prescribing were searched at all pharmacies in the province.

**Result:** All pharmacies and 92.27% of GPs participated in the study. The average number of drug item prescribed for children with ARI was 3.74. The most widely used drugs for ARI were antibiotics followed by paracetamol, ibuprofen, chlorpheniramine maleate, phenobarbital, vitamin-C, dextromethorphan, glyceryl guaiacolate, dexamethasone, prednisone, vitamin-B6, ephedrine HCl, vitamin B1, and vitamin B2. Medication error was commonly found in the study. More than 60% children with ARI received drugs in either overdose (27.51%) or under dose (41.12%). Wrong preparation were detected in 24.07% prescriptions. It was also found that more than one fifth of children with ARI received drugs in wrong frequency of administration. Risk predictor for prescribing antibiotics were fever, abnormal respiratory rate, and duration of common cold symptom of more than 2 days.

**Conclusion:** ARI in children was often treated unnecessarily. Medication error was also commonly found in the treatment of children with ARI visiting GPs. Physicians must be encouraged to improve their prescribing practices by always catching up with current best research evidence.

**Key words:** acute respiratory infection – inappropriate prescribing – medication error – general practitioners – emergence of resistance

## ABSTRAK

Iwan Dwiprahasto – *Studi penggunaan obat untuk infeksi saluran pernafasan akut pada anak usia kurang dari 10 tahun*

**Latar Belakang:** Infeksi saluran pernafasan akut (ISPA) merupakan penyakit yang paling sering terjadi pada anak dan menjadi penyebab utama angka kesakitan dan kematian pada anak khususnya di Negara-negara sedang berkembang. Penyakit ini diderita oleh hamper 50% Balita. Meskipun umumnya disebabkan oleh virus dan bersifat dapat sembuh sendiri, berbagai studi menemukan bahwa penggunaan antibiotika secara keliru sangat sering terjadi untuk mengatasi penyakit ini..

**Tujuan:** Penelitian ini bertujuan untuk mengetahui pola peresepan untuk ISPA pada anak oleh dokter umum di praktek swasta.

**Metoda:** Rancangan studi ini adalah *cross sectional*. Subyek penelitian adalah dokter praktek umum dan seluruh apotik di wilayah provinsi DIY. Data pasien dan pengukuran kecepatan respirasi dikumpulkan dari tempat praktek swasta sedangkan data mengenai peresepan obat diperoleh dari seluruh apotik yang terdapat di Provinsi DIY.

**Hasil:** Seluruh apotek dan sebagian besar dokter umum praktek swasta ikut serta dalam penelitian ini. Jumlah rata-rata obat yang diberikan kepada anak dengan ISPA mencapai 3,74. Obat yang paling sering diresepkan adalah antibiotika disusul oleh parasetamol, ibuprofen, chlorpheniramine maleate, fenobarbital, vitamin-C, dekstrometorfan, gliseril guaiakolat, deksametason, prednison, vitamin-B6, efedrin HCl, vitamin B1, and vitamin B2. *Medication error* sangat sering terjadi. Lebih dari 60% anak dengan ISPA mendapat obat dalam dosis yang tidak tepat, yaitu berlebih (27.51%) atau kurang (41,12%). Pemberian obat dalam sediaan yang tidak tepat ditemukan pada 24.07% resep. Penelitian ini juga menemukan bahwa lebih dari seperlima penderita ISPA mendapat obat untuk frekuensi pemberian yang keliru. Faktor yang mendorong dokter untuk meresepkan antibiotika pada ISPA antara lain adalah demam, kecepatan respirasi lebih dari normal, dan gejala batuk pilek lebih dari 2 hari.

**Simpulan:** ISPA pada anak sering diterapi secara tidak tepat. *Medication error* juga sering terjadi dalam penatalaksanaan ISPA di praktek swasta. Sudah saatnya dokter umum mulai meningkatkan mutu peresepan dengan senantiasa mendasarkan pada bukti-bukti ilmiah terbaru.

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## BACKGROUND

Acute respiratory infection (ARI) is the commonest illness among children, especially in developing countries. It comprises approximately 50% of all illness in children under five years<sup>1</sup> with mortality rate of 10.23 per 1000 persons in infants and 3.0 per 1000 persons in children one to four years of age.<sup>2</sup>

Managing ARI in general practice is very common. Acute respiratory infections are usually viral in origin and of self-limiting nature. However, various studies indicate that antibiotic prescribing for ARI is inappropriately high, i.e. around 50 per cent of patients who present with ARI to their GP receive antibiotic, a rate of prescribing which has remained virtually unchanged in the last few years.<sup>3-8</sup>

Various attempts have been made to reduce morbidity and mortality due to ARI. However, irrational prescribing is still common for this particular disease. Very often less ill children receive more unnecessary drugs, while the children who really need drug treatment are inappropriately treated.<sup>9</sup>

The objective of this study is to assess general practitioners' (GPs) prescribing pattern for acute respiratory infection in children seen in private practices.

## METHODS

This study was carried out in a cross sectional study design involving all General Practitioners and

pharmacies in Yogyakarta Special Province for one month period (May – June, 1997). Before the study was conducted a pilot study was carried out to test the reliability of study instrument.

Subjects were enrolled in the study if they met the following criteria: children under 10 years of age, presented at GPs' private practices with symptoms of common cold (such as fever, runny nose, cough, and sore throat). Data on ARI patients (include date of patient's visit, name, date of birth, age, address, and respiratory rate) were obtained from GPs' private practice office using ARI structured form. Prescribing data on ARI patients were obtained from all pharmacies at the province during the study period. The following data were collected from pharmacies: (1) date of prescriptions; (2) name and address of prescribers; (3) name, age, and address of patients; (4) drugs and number of drugs prescribed to the patients, dose, drug administration, dosage form, additional information written in the prescription, prescribed drug's cost; and (5) how many of drugs had been dispensed to the patients, and how much money had been spent by patients to get their drugs. The WHO criteria for acute respiratory infections in children were used to classify patients' diagnosis by age and respiratory rate<sup>10</sup>.

Immediately after the diagnosis had been made, subjects were randomly selected and visited by research assistants to check whether appropriate measure of respiratory rate had been done by GPs. This visit was also aimed to check whether patients or their parents had dispensed the drug from

pharmacies. At the end of the study period, patients' data forms were taken from all physicians by research assistants and submitted to the computer centre for data entry. Data were thereafter used to search for matching prescriptions among all prescriptions from pharmacies. All data were validated by the principal investigator and when missing data had been identified, relevant physicians were contacted immediately to get the data completed.

**RESULTS**

**1. Participants and patients characteristics**

Out of 207 GPs 92.27% participated in the study and none of 88 pharmacies (100%) refused

to participate. Total number of under 10 year old patients with ARI visited GP's office during the study period was 698. More than 69% of patients reported by GPs were under five years of age. The mean age of male and female patients seen by GPs were 3.47 and 3.58 year respectively. The mean of respiratory rate of patients recorded by GPs are 23.3 and 22.9 per minute for male and female respectively.

**2. Drug use for ARI patients**

Of the 698 children with ARI, drug use data were obtained either by searching for prescriptions at pharmacies or were available from prescribers. The breakdown of drug use for ARI patients is shown in TABLE 2.

TABLE 1. Patient characteristics

No. of patients	Male	Female	Total number (n=698)
- < 1 year	45	53	98 (14.04)
- 1 year-5 years	177	210	387 (55.44)
- 5 years-10 years	101	112	213 (30.52)
Average age (year)	3.47	3.58	
Average respiratory rate (x/minutes)	25.4	24.2	

TABLE 2. Drugs prescribed by General Practitioners for children with Acute Respiratory Infections (ARI)

No	Drug	No. of drugs prescribed	(%)
1.	Antibiotics	656	93.98
2.	Paracetamol	437	76.27
3.	Ibuprofen	178	25.50
4.	Chlorpheniramine maleate	467	50.60
5.	Phenobarbital	284	30.77
6.	Vitamin C	190	20.59
7.	Dextromethorphan	129	13.98
8.	Glyceryl Guaiacolate	127	13.76
9.	Dexamethazone	97	10.51
10.	Prednisone	88	9.53
11.	Vitamin B6	82	8.88
12.	Ephedrine HCl	79	8.56
13.	Vitamin B 1	56	6.07
14.	Vitamin B 2	50	5.42
15.	Others	321	34.67

The most widely used drugs for ARI were antibiotics followed by paracetamol, ibuprofen, chlorpheniramine maleate, phenobarbital, vitamin-C, dextromethorphan, glyceryl guaiacolate, dexamethasone, prednisone, vitamin-B6, ephedrine HCl, vitamin B1, and vitamin B2.

### 3. Number of drugs prescribed for ARI patients

TABLE 3. Number of drugs prescribed for ARI

No. of drug	No. of patients (%)
1 – 3	256 (36.68)
4 – 6	370 (53.01)
7 – 9	45 (6.45)
10 – 12	15 (2.15)
> 12	12 (1.71)

Average number of drugs prescribed for ARI patients was 3.74. More than 50% of subjects (53.01%) received 4-6 items of drugs. Even though only a few, almost 2% of patients were prescribed more than 12 items of drugs. There was one patient reported by a GP who received 20 drugs.

### 4. The use of antibiotics for ARI patients

More than 90% of patients with ARI treated by GPs were given at least one antibiotics (TABLE 2). In relation to the measure of respiratory rate reported by GPs, only a small number of patients really need antibiotic. None of the patients less than 2 months had a respiratory rate of 60 or more per

minute. Only a few patients between 2 months and 1 year should have been given an antibiotic. Even though the age between 1 and 5 years showed the biggest proportion of patients that need an antibiotic, this number did not exceed 15 % .

### 5. The most frequently used antibiotics for children under 10 years of age with ARI.

In this study, ampicillin was the most often prescribed antibiotics by GPs (44.05%), followed by cotrimoxazole (28.96%), amoxycillin (10.98%), erythromycin (4.73%), and chloramphenicol (3.05%). Surprisingly some antibiotics which are no longer recommended for respiratory infections such as sulfasomydin, tetracycline, and triple-sulfa were still being prescribed by GPs.

Powder preparation was the most often used drug formulation for ARI patients and accounted for more than 50% of all prescriptions, followed by solution/liquid (20.98%). Other formulation e.g. nasal drops and lozenges were also given by GPs (1.64%).

As shown in TABLE 4, most patients with fast breathing were given cotrimoxazole, ampicillin, or amoxycillin and only 5 patients who saw GPs were prescribed cyprofloxacin or cephadroxyl. Average length of antibiotic prescribing is less than 5 days, i.e. 4.21 days for cotrimoxazole, 3.47 days for ampicillin, and 3.23 days for amoxycillin. For those who received antibiotics, the drugs were commonly prescribed in less than recommended dose. For those who were eligible for antibiotics treatment only less than 50% patients received amoxycillin, ampicillin or cotrimoxazol for adequate length/duration.

TABLE 4. Antibiotics use for the suspected pneumonia patients

	Cotrimoxazole	Ampicillin	Amoxycillin	Others
Average length of antibiotic prescribing (days)	4.21	3.47	3.23	2.98
Appropriate (adequate) dosages (%)	12	23.32	18	
Incorrect frequency of antibiotic administration (%)	72.57	89.27	12.93	
Proportion of patients who received antibiotics for adequate length (%)	28.45	37.24	42.15	39.34

\* All the antibiotics were given in powder form.

Except cephadroxyl, all others were given in fixed drug combination (FDC).

TABLE 5. Type of medication error identified during the study

Type of medication error	Frequency (%)
Improper dose	
• Overdose	192 (27.51)
• Underdose	287 (41.12)
Wrong preparation	168 (24.07)
Wrong time (frequency of administration)	147 (21.06)

This study identified various types of medication error. More than 60% children with ARI received drugs in either overdose (27.51%) or under dose (41.12%). Wrong preparation due to prescribing various incompatible drugs into one preparation were detected in 24.07% prescriptions. It is also found that more than one fifth of children with ARI received drugs in wrong frequency of administration.

TABLE 6. Risk predictor for antibiotics prescribing in ARI patients

	Unadjusted OR	Adjusted OR
<b>Fever</b>		
No	1	1
Yes	2.38 (1.75 – 5.24)	1.24 (1.11 – 6.03)
<b>Respiratory rate abnormal</b>		
No	1	1
Yes	1.52 (1.05 – 1.71)	1.37 (1.12 – 1.69)
<b>Sore throat</b>		
No	1	1
Yes	1.42 (1.24 – 1.93)	0.91 (0.64 – 1.23)
<b>Runny nose</b>		
No	1	1
Yes	1.15 (1.03 – 1.52)	0,87 (0.62 – 1.79)
<b>Age of children</b>		
< 2 months	1	1
2 months – 5 years	1.21 (0.94 – 1.55)	1.19 (0.92 – 1.54)
5 years – 10 years	1.32 (1.02 – 1.72)	1.25 (0.94 – 1.66)
<b>Multiple prescribing</b>		
No	1	1
Yes	1.12 (1.03 – 1.53)	1.21 (0.82 – 1.78)
<b>Duration of symptoms</b>		
< 2 days	1	1
2 days and over	1.26 (1.05 – 1.51)	1.36 (1.09 – 1.69)

TABLE 6 shows that children with fever attended GPs and diagnosed as ARI during the study were twice more likely to receive antibiotics (OR=2.38, 95%CI: 1.75-5.24) and this remained significant after adjusting for abnormal respiratory rate, sore throat, runny nose, age of children, multiple prescribing, and duration of symptoms (OR=1.24; 95%CI: 1.11-6.03).

Abnormal respiratory rate which was significantly correlated with prescribing of antibiotics in the univariate analysis was also significantly contribute to the prescription of antibiotics after adjusting for several confounders (OR=0.91; 95%CI: 0.64 – 1.23).

In univariate analysis sore throat was found to be strongly correlated with the prescribing of antibiotics (OR=1.42; 95%CI: 1.24-1.93). After adjusting for several confounders children with sore throat were no longer corelated with prescribing of antibiotics for ARI (OR=0.91; 95%CI: 0.64-1.23).

A univariate analysis showed that children aged 5 – 10 years were strongly correlated with the prescribing of antibiotics (OR=1.32; 95%CI: 1.02-1.72). However, this was not shown to be significantly correlated with the prescribing of antibiotics, after adjusted for several potential confounders. Similarly, a univariate analysis also showed that children who had reported to have

runny nose symptom were more likely to received antibiotics. This correlation, however, was no longer significant after adjusting for other confounding factors.

Duration of symptoms of 2 days or more was shown to be strongly correlated with the prescribing of antibiotics, and this remained significant even after adjusting for the effects of several confounding factors (OR=1.36; 95%CI: 1.09 – 1.69).

## DISCUSSION

This study found a high inappropriateness of drug use for treating ARI patients. Nine out of nine children with ARI visited GPs were most likely received antibiotic unnecessarily. Using WHO criteria for respiratory rates, the data suggest that only 7-14% of children really needed antibiotics according to their respiratory rate. Therefore, majority of children in the study may have taken unnecessary antibiotics during their episode of ARI. This finding is similar to other reports of antibiotic use in children at the primary health care level.<sup>11-16</sup>

The use of ampicillin for ARI in children seen by GPs is common, even though this antibiotics has already been withdrawn from the list of essential drugs by The WHO Expert Committee on the Use of Essential Drugs since November 1989.<sup>17</sup> Surprisingly, tetracycline, sulfasomydin, and chloramphenicol were also prescribed, even though these antibiotics are no longer recommended for ARI.<sup>18</sup>

The widespread use of antimicrobials, whether appropriate or inappropriate, has driven the emergence and spread of resistant organisms. The association of resistance with the use of antibiotics has been documented in outpatient settings. For example, more than five cross-sectional studies have documented that the likelihood of culturing a resistant strain of pneumococcus from the nasopharynx is increased if the patient recently completed a course of antibiotics.<sup>19-23</sup>

Achieving more judicious prescribing of antibiotics requires (a) an understanding of the factors that promote overuse and the barriers to change and (b) the implementation of effective strategies for changing behaviour. Surveys of

primary care doctors show that many have inaccurate knowledge regarding the need for antibiotics in patients with purulent rhinitis,<sup>24,25</sup> and many family practitioners do not follow expert recommendations for diagnosis and management of pharyngitis.<sup>26</sup>

Type of medication error commonly found in the study are wrong dose (either over or under dose), wrong preparation, and wrong time error or wrong frequency of administration. In this study, incorrect prescription of ampicillin occurred in more than 80% of patients seen by GPs. Most children were given ampicillin 3 times a day, and no other instruction were written on the prescription. According to its pharmacokinetic profile, ampicillin should be taken 4 times a day or every six hours due to its short elimination half life, i.e. 0.5 hour. Cotrimoxazole which should be given twice a day (every 12 hours) was commonly given for 3 times a day, which may result in over dose. The use of powder preparation for the treatment of ARI in children in this study is accounted for more than sixty percent. Mixing together antibiotic with other drugs such as analgesic, antihistamine or others is irrational and must be avoided.

A medication error, is defined as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labeling, packaging, nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use. Medication misadventures, a broad categorical group, include adverse drug events (ADEs), adverse drug reactions (ADRs), and medication errors.<sup>27</sup>

In a case-control study covering a four-year period at a single hospital, there was an almost twofold increase in the risk of death associated with ADEs, of which 1% was attributable to medication errors.<sup>28</sup> In the Harvard Medical Practice Study, ADEs accounted for 19.4% of all disabling adverse events, of which 45% were caused by medication errors, and 30% of patients with drug-related

injuries died.<sup>29</sup> In a prospective cohort study, 247 ADEs were evaluated, of which 28% were judged preventable, 1% were fatal (not preventable), 12% were life-threatening, 30% were serious, and 57% were significant.

Prescribing multiple drugs is common for children with ARI seen by GPs. It is likely, therefore, that children who comply with drug treatment and take their medication regularly during their illness are unnecessarily exposed to drugs which might be harmful for them. Various studies showed that the greater the number of drugs given to patients, the greater the probability of adverse drug reactions due to their adverse cumulative effects.<sup>30</sup>

The study shows that the top ten commonly used drugs for the treatment of ARI in children include phenobarbital, prednisone, and dexamethasone which have never been recommended for the treatment of ARI. The use of phenobarbital regularly for children with fever as prophylaxis to prevent seizures is unjustified.

It was found in the study that 10 percent of children with ARI were given prednisone for unknown reasons and no special attention on duration was given or written in the prescriptions. It can be estimated, therefore that at least 10 % of children with ARI would have been unreasonably treated with this unnecessary potentially harmful drug.<sup>31</sup>

This study showed that the risk predictors for prescribing antibiotics in children with ARI included fever, abnormal respiratory rate, and duration of symptom of more than 2 days. Prescribing antibiotics based on clinical findings of fever is misleading and often result in exposing children with unnecessary drugs which in turn increasing the risk of adverse event and emergence of resistance.<sup>18</sup>

In conclusion, using simple method of drug utilization study we could find that ARI is often treated unnecessarily, Medication error is also commonly found in the treatment of children with ARI visiting GPs. Physicians must be encouraged to improve their prescribing practices by always catching up with current best research evidence.

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