Article

Evaluation of Rational Drug Use for Acute Pharyngitis Associated with the Incidence and Prevalence of the Disease at Two Community Health Centers in Indonesia

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Abstract: According to Indonesia's result of Basic Health Research of 2013, prevalence of acute respiratory infection in 2007 and 2013 were not different (25.5% and 25.0%, respectively). Identifying the cause of acute pharyngitis is a key point in determining the optimal treatment. The main purpose is to evaluate the rational use of drugs and its irrational impact as well as the correlation of the drug use with the incidence and prevalence of acute pharyngitis. This study was a descriptive and observational study, carried out retrospectively and concurrently at two community health centers located in Bandung and Cimahi, Indonesia. There were 80.01% over prescription of antibiotics, with a total of 8.98% is non-treatment option, and 62.43% irrational used of corticosteroids. The incidence and prevalence of acute pharyngitis at one health center in Bandung were 2.45% and 2.31%, respectively, with irrationality rate of 83.82%. Those recorded at one health center in Cimahi were 2.11% of incidence and 2.00% of prevalence with irrational rate of 91.29%. It can be concluded that there were still irrational use of medicines in the treatment of acute pharyngitis in community health center. The higher incidence and prevalence might indicate the declining health services quality.

Keywords: acute pharyngitis; rational use of drugs; incidence; prevalence

1. Introduction

Acute respiratory infection (ARI) is one of the most common diseases, accounting as one of the main causes of patients visit to community health centers (40-60%) and hospitals (15-30%). There were 156 million new episodes per year in the world, of which 151 million episodes (96.7%) occur in developing countries. Indonesia is one of the top five countries with the highest ARI cases, as many as 6 million episodes per year [1]. Result of National Basic Health Research showed that the prevalence of ARI in 2007 and 2013 were not different (25.5% and 25.0%, respectively), indicating that the control and management of ARI is still not optimal [2]. Acute pharyngitis, which is part of ARI, estimated to account for 2-5% of patient visits to health facilities [3-5]. In Indonesia (2004), acute pharyngitis wasthe top ten diseases on outpatient visit, *i.e.*, by 1.5% or as many as 214,781 patientsand about 40 million people visited to health facilities each year [6,7].

Acute pharyngitis is an acute infection or inflammation in the mucosa of pharynx and generally extends into the surrounding tissue. Viruses are the most common causes (40-60%) and only about 5-40% are caused by bacteria, which *Streptococcus pyogenes* is the most common pathogen found in patient of acute pharyngitis due to bacteria [3,7]. Thus, antibiotic therapy is generally not recommended and this disease can be cured by itself even without intervention. Identifying the cause of acute pharyngitis is a key point in determining the optimal treatment for the patient.

World Health Organization (WHO) stated that rational use of medicines requires that "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"

[8]. The Ministry of Health of Indonesia determined that use of drug is said to be rational if it meets the "appropriate diagnosis, indications, drug selection, dosage, route, interval, and duration of administration, wary of side effects, precise assessment of the conditions, right of information, proper follow-up and delivery of drugs, allowing to comply to the regimens, as well as the guaranteed of its safety, efficacy, quality and available at any time at an affordable price" [9]. WHO estimated that more than 50% of drugs were prescribed, given, and sold in a way that was inappropriate, ineffective, and inefficient, and also estimated that 50% of drug used inappropriately [10].

Estimating the incidence and prevalence of a disease iscrucial for evaluating the current and projected future unmetmedical need for drugs. Epidemiologic studies are useful for identifying patterns of health care utilization. They can provide estimates of the magnitude of risk related to a particular level of dose and so can be used in the evaluation of appropriate microbiological quality guideline levels or standards. Epidemiological methods can quantify the probability that observed relationships occurred by chance factors and they also have the potential to control for other risk factors and/or confounders of the outcome illness being studied [11,12]. This study was aimed to evaluate the rational use of drugs and its irrational impact as well as the correlation of the drug use with the incidence and prevalence of acute pharyngitis.

2. Materials and Methods

Descriptive and observational study involving incidence and prevalence of the disease was conducted to evaluate the rational use of drugs. This study was carried out retrospectively and concurrently on October 2014 to May 2015 at two community health centers in Bandung and Cimahi, Indonesia. The participants were patients with acute pharyngitis aged ≥3 years. Patients who were lost to follow-up or have comorbid with other infectious disease that required antibiotic therapy were excluded. Patients were grouped based on the etiology of acute pharyngitis, which is determined by Centor score.

Data were obtained from medical records, interviews, and the results of follow-up visit. Data from medical records include patient's identity, diagnosis, history and treatment of acute pharyngitis. Interview was conducted to determine the initial condition of the patient. Follow-up was performed seven days later to evaluate the outcome of therapy, compliance, and impact of the treatment. Population data as well as the incidence and prevalence of acute pharyngitis for comparison was obtained through the report from the Ministry of Health of Indonesia and related institutions.

The rationality of drugs use is defined by prescribing indicators that consist of appropriate indication, drug selection, dosage, route, intervals, duration of administration, assessment of the patient's condition, and patient compliance. Outcome of therapy was assessed by the patient's condition compared to initial condition in the last visit. Data were analyzed descriptively to conclude the event of irrational use of drugs, the proportion of antibiotics prescriptions, the impact of irrationality use of drugs, and correlation of drugs use with the incidence and prevalence of acute pharyngitis.

3. Results

3.1 Causes of Acute Pharyngitis based on Centor criteria

Total of patients with diagnosis of acute pharyngitis in one community health centers in Bandung and Cimahi, respectively were 1083 and 995 patients. As many as 1641 patients met the inclusion criteria; 733 patients (44.67%) were aged 15-44 years, 504 patients (30.71%) aged 3-14 years, and 404 patients (24.62%) were >44 years old. Patients were grouped based on the etiology of acute pharyngitis. In this study, a modified Centor score which also considered the patient's age was conducted on all patients who met the inclusion criteria (Table 1).

Table 1. Modified Centor score of acute pharyngitis patients.

Centor Score	Risk of Streptococcus infection	Health center in Bandung	Health center in Cimahi
		∑patients (%)	∑patients (%)
≤0	1-2.5 %	209 (25.30)	161 (19.68)
1	5-10%	202 (24.46)	268 (32.76)
2	11-17%	437 (52.91)	424 (51.83)
3	28-35%	213 (25.79)	121 (14.79)
≥4	51-53%	19 (2.30)	3 (4.03)
Total patients	**data**	**826**	**818**

Patients with a score of zero or 1 was at very low risk (<10%) and those with a score of 4 or higher were at high risk (>50%) of streptococcal pharyngitis. Patients with a score of 2-3 should be tested using RADT (rapid antigen detection test) or throat culture and positive results would warrant antibiotic therapy. However, this action could not be performed in clinical practice in almost all health centers in Indonesia due to the limited facilities. Thus, patients with score 2-3 were grouped separately. Based on the results, the incidences of the causes of acute pharyngitis in both health centers had similarities (Table 2). As many as 226 patients (13.77%) was expected to have streptococcal pharyngitis, 1179 patients (71.85%) were estimated to be infected by viruses, and causes of acute pharyngitis in 236 patients (14.38%) could not be determined. Respiratory infection contributed 32% of visits at both of health centers, which 9.58% of them were patients with acute pharyngitis. More than 50% of the antibiotics used in health centers given on the respiratory infection patients, and 28.96% of them were given to acute pharyngitis patients.

Table 2. The causes of acute pharyngitis in patients

Etiology	One health center in Bandung	One health center in Cimahi
	∑patients (%)	∑patients (%)
Bacteria	136 (16.52)	90 (11.00)
Virus	564 (68.53)	615 (75.18)
Can nott be determined	123 (14.95)	113 (13.81)
Total patients	**826**	**818**

3.2 Drug Use Evaluation

The goal therapy of acute pharyngitis is to improve the signs and symptoms, minimizingside effects, preventing transmission and complications. Antibiotics were only indicated in patients with disease caused by bacteria. This study found that there was irrational use of antibiotics in the treatment of acute pharyngitis (Table 3) which included inappropriate indication (87.43%), inappropriate drug selection (0.09%), inappropriate duration of administration was found in almost all patients who received antibiotic, and there was no antibiotic prescribed at 2.97% of patients suspected of being infected by bacteria.

As much as 88.24% acute pharyngitis patients received antibiotic (Figure 3), but only 8.23% of patients had appropriate indication. It can be concluded there was 80.01% overprescribing antibiotics in the treatment of acute pharyngitis in two health centers. Amoxicillin, one of the first-line antibiotics for acute pharyngitis caused by bacteria, was the most common antibiotic prescribed (Figure 1a). A total of 8.98% antibiotics was non-treatment option (ciprofloxacin: 6.28%, cotrimoxazole: 2.26%, and thiamphenicol: 0.44%). The duration of antibiotic administration for acute pharyngitis is 6-10 days for adults and 10 days for children. In this study, the appropriate duration of treatment was found only in 0.57% of patients (Figure 1b). Most of the patients (50%) received antibiotics for 5 days.

Table 3. Irrational use of drugs in the treatment of acute pharyngitis

Criteria	Antibiotic therapy (∑patients ,%)		Corticosteroid therapy* (∑patients ,%)
	Health center in Bandung	Health center in Cimahi	
Inappropriate indication	627 (83.82)	639 (91.29)	x
Inappropriate drug selection	10 (1.34)	3 (0.43)	x
Inappropriate dosage	x	x	55 (15.19)
Inappropriate route of administration	x	x	x
Inappropriate intervals of administration	x	x	134 (37.02)
Inappropriate duration of administration	109 (90.08)	54 (88.52)	37 (10.22)
Inappropriate assessment of the patient's condition	x	x	x

Note: *) only in health center in Bandung

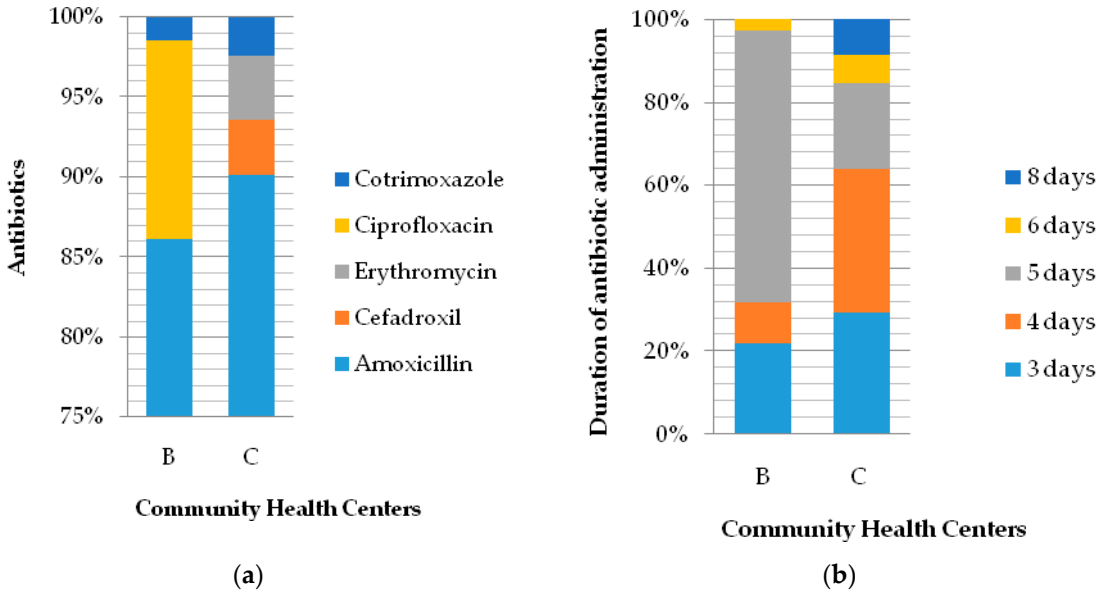

Figure 1. Used of antibiotic in the treatmentof acute pharyngitis patients: (**a**) Antibiotic that prescribed; (**b**) Duration of antibiotic administration; B: health center in Bandung; C: health center in Cimahi

In this study, corticosteroids were prescribed to about 20-30% of patients. There were found irrational use of corticosteroids which includes inappropriate dosage, inappropriate interval of administration, and inappropriate duration of administration. The majority of pediatric patients received corticosteroids overdose. Ibrahim Adjie health center tended to give dexamethasone with prolonged interval (12 hours). South Cimahi health center tended to give dexamethasone with a shorter duration of administration (2 days).

The interview was conducted concurrently in 108 patients of acute pharyngitis and follow-up taken seven days later (Table 4). As many as 31 patients (28.70%) were lost to follow-up. A total of 41 patients (56.94%) whom received antibiotics improved, 28 patients (38.89%) still had complaints, and 3 patients (4.17%) worsen. In the meantime, 2 patients (40%) whom did not receive antibiotics improved, 2 patients (40%) still had complaints, and 1 patient (20%)worsen.Overall, 38.96% (30 patients) recovered in ≤3 days, 14.29% (11 patients) recovered within 4-6 days, and 2.60% (2 patients) recovered in more than 6 days. Result of follow-up also showed that 58.06% patients adhered to the regimen of antibiotics prescribed by doctors and 41.94% of patients did not comply. Non-compliance including forgotten or stopped to take antibiotics due to side effects (6.54%: dizziness, headache,

weakness, stiffness), discomfort in the drug form, or the patient's ignorance. Adverse effects in therapy were reported in 5 patients who received an antibiotic. The majority of patients experienced side-effects in the form of headaches (37.5%), and subsequently in the form of dizziness, headaches, weakness, stiffness, shoulder pain, and heartburn.

Table 4. Outcome therapy of acute pharyngitis patients.

Score Centor	Outcome therapy				
	Improved			Unimproved	
	≤3 days	4-6 days	≥7 days	Persistent	Worsen
Antibiotic	29	10	2	28	3
Without Antibiotic	1	1	0	2	1
Total	30	11	2	30	4

Table 5. Adverse effect of therapy in patients received antibiotic

Adverse effect	Incidence (%)
Dizziness	1 (12.5)
Headache	3 (37.5)
Weakness	1 (12.5)
Stiffness	1 (12.5)
Shoulder pain	1 (12.5)
Heartburn	1 (12.5)

Health centers in Bandung and Cimahi had the same prescribing pattern. At least 50% of acute pharyngitis patient treated with a combination of antibiotics, analgesic-antipyretic, expectorant-mucolytic, and antihistamines (Figure 2). Symptomatic drug that prescribed include corticosteroids (dexamethasone:24.92%, prednisone), analgesic-antipyretics (paracetamol:82.55%, antalgin), expectorants-mucolytics (glyceryl guaiacolate:37.19%, ambroxol, black cough syrup), antihistamine (chlorpheniramine maleate:54.55% loratadine), NSAIDs (diclofenac: 3.22%, ibuprofen, mefenamic acid, piroxicam), antacid-antiemetics (antacid: 10.24%, domperidone, metoclopramide), vitamins (B complex: 10.31%, C, B1, B6, B12, multivitamin).

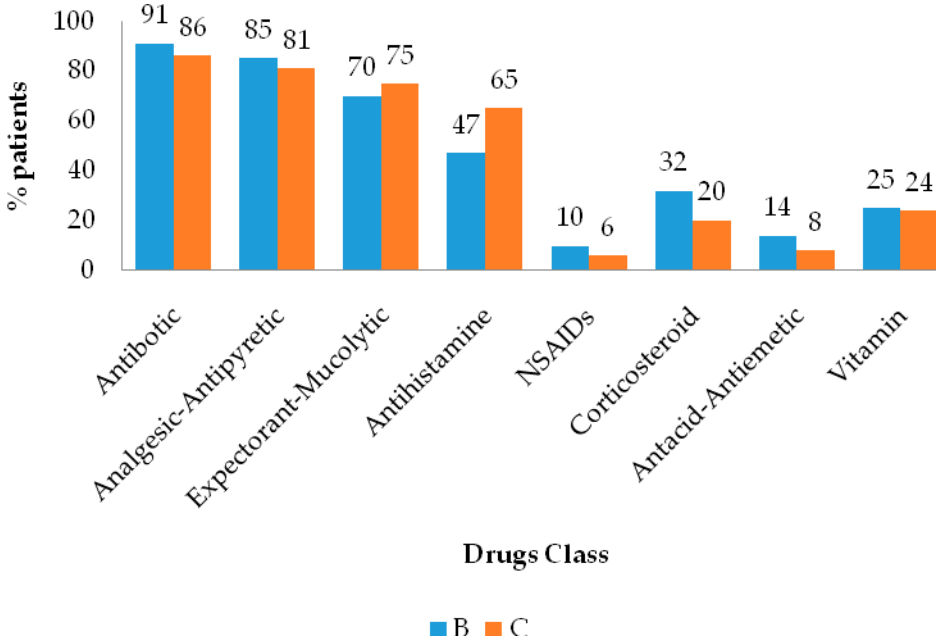

Figure 2. Drugs that prescribed to acute pharyngitis patients.

3.3 Insidence and Prevalence Calculation

The incidence and prevalence of acute pharyngitis was calculated based on the patient's visit. Total population in Bandung health center area was 44608 people. There were 1069 new cases of acute pharyngitis with a total of 1032 patients. The total population in Cimahi health center area was 35833 people. There were 979 new cases of acute pharyngitis with a total of 945 patients. The incidence and prevalence of acute pharyngitis at Bandung health center were 2.45% and 2.31% respectively. Those recorded at Cimahi health center were 2.11% of incidence and 2.00% of prevalence.

4. Discussion

Indonesia Ministry of Health (2014) stipulated that one of the indicators of the rational use of drug on handling of ARI non-pneumonia, including acute pharyngitis, *i.e.,* the tolerance limit of antibiotic prescribing by as much as 20% of the total patient [9]. However, as much as 88.24% of acute pharyngitis patients received antibiotic with a total of 8.98% of antibiotics which was non-treatment option. So it can be said that the use of antibiotics in the treatment of acute pharyngitis was not rational. Irrational used of antibiotics include inappropriate indication, inappropriate drug selection, inappropriate duration of administration and there was also found that some patient did not received antibiotic but actually suspected of being infected by bacteria.

Signs and symptoms of acute pharyngitis caused by bacteria, viruses, and other microbes are generally overlapping and difficult to distinguish. Identifying the cause of acute pharyngitis is a key point in determining the optimal treatment. Although the diagnosis of the etiology of acute pharyngitis depends on the results of laboratory tests such as RADT or throat culture, a scoring system based on the clinical manifestations has been developed to predict the risk of infection of *S. pyogenes* in acute pharyngitis patients [13]. Centor score are a scoring method that can be used to estimate the risk of *S. pyogenes* as the cause of acute pharyngitis based on clinical sign and symptoms [14], especially in developing country such as Indonesia, where laboratory test in clinical practice in almost all health centers was not done due to the limited facilities. The original Centor score using four sign and symptoms to estimate the probability of streptococcal pharyngitis in adults with sore throat [15]. Sign and symptoms include the absence of cough (1 point), swollen and tender anterior cervical nodes (1 point), temperature >38° C (1 point), and tonsillar exudates or swelling (1 point). The score was later modified by adding age and validated in adult and children patients (age 3-14 years: 1 point, age 15-44 years: 0 point, age >44 years: -1 point) [16]. This scoring system has been validated in 206.870 patient age >3 years with a sore throat. The cumulative score specifies the likelihood of streptococcal pharyngitis and the need for antibiotics [17].

Antibiotics are only indicated for patients with disease caused by bacteria. Empirical antibiotic therapy may be considered in patients with Centor score of 4 or higher who were at high risk (>50%) of streptococcal pharyngitis. Selection of antibiotic requires consideration of effectiveness, spectrum of activity, safety, dosing schedule, cost, and compliance issues. Penicillin, penicillin congeners (ampicillin or amoxicillin), clindamycin, and certain cephalosporins and macrolides are effective against streptococcal pharyngitis. Based on cost, narrow spectrum of activity, safety, and effectiveness, penicillin is recommended by the American Academy of Family Physicians (AAFP) [18], the American Academy of Pediatrics (AAP) [19], the American Heart Association (AHA) [20], the Infectious Diseases Society of America (IDSA) [21], and WHO for the treatment of streptococcal pharyngitis [22]. Amoxicillin oral suspension is often substituted by penicillin because it tastes better. Five of the eight studies proved that amoxicillin can eradicate >85% *S. pyogenes*, equivalent to penicillin that can eradicate >92% of these microbes [14]. Erythromycin or first-generation oral cephalosporins such as cephalexin are second-line antibiotics that can be used if the patient is allergic to penicillin or symptoms persist after first-line antibiotics. Quinolone, tetracycline and sulfonamides are not recommended for treatment of streptococcal pharyngitis. Tetracycline has a high prevalence for development of resistance. Sulfonamides and trimethoprim-cotrimoxazole can't eradicate the pathogen in a streptococcal pharyngitis. Old generation fluoroquinolones such as ciprofloxacin has limited activity against *S. pyogenes* [23].

Despite the low incidence of acute pharyngitis caused by bacteria, antibiotics prescribing was exceptionally high. Study in America (2005) reported that 53% of children with acute pharyngitis received antibiotic, far exceeded the prevalence of streptococcal pharyngitis. In Brazil (2014) found 73% of adult patients with acute pharyngitis received antibiotics [24]. In Indonesia, through this study, it can be concluded that respiratory infection contributed 32% of visits at the health centers. More than 50% of the antibiotic in health centers used for this treatment, where about 30% of those given to acute pharyngitis patients. About 80% of acute pharyngitis patients received antibiotics along with the inappropriate duration of administration. Acute pharyngitis is expected to be the main cause of inappropriate use of antibiotics in clinical practice. Antibiotics used in the treatment of respiratory infection, including acute pharyngitis, thought to be the biggest contributor to the development of resistance.

The standard duration of antibiotic administration for acute pharyngitis is 6-10 days for adults and 10 days for children, but the patient compliance was generally not high [7]. This study found that 41.94% of the patients did not comply to the prescribed antibiotic regimens. Study of antibiotic therapy with a shorter duration (3-6 days) for acute pharyngitis has been done, but the effectiveness and clinical application of this strategy was still debated [25-27]. Administering antibiotics with the proper duration for acute pharyngitis was rare even almost did not occur in clinical practice in Indonesia. The appropriateness of the duration of administration only occured on 0.57% of patients, most patients (50%) were given antibiotics for 5 days.

Use corticosteroids in acute pharyngitis patients remained controversial [7,14,28,29]. Sore throat which is the main complaint in most cases of acute pharyngitis patients usually occur due to inflammation of the pharynx. The administration of anti-inflammatory such as corticosteroid to treat the inflammation thought to relieve pain quickly and accelerate clinical improvement. Corticosteroids can be given in the form of dexamethasone with regimen 3 x 0.5 mg dose for 3 days in adults and 0.01 mg/kg divided into 3 doses for 3 days in children [7].

Based on these results, it can be predicted that one of the possible effects of irrational use of antibiotics was potential increasing of noncompliance that may lead to the emergence of bacterial resistance. Overprescribing of antibiotics could increase the risk of side effects in patients, which was seen at 6.45% of patients who taking antibiotics. Irrational use of antibiotics by physicians may have an impact on the quality of medicine and health services, increasing the problem of resistance, waste costs, increasing the risk of side effects, as well as the psychosocial impact.

Health centers in Bandung and Cimahi had not differ on incidence and prevalence values, so that it can be concluded that they had the same quality of health care in the treatment of acute pharyngitis. The calculation showed the increased incidence and prevalence of acute pharyngitis by 0.5-1% within ten years, that might indicate the declining quality of health services. But please note that treatment is only one of the factors that can affect the quality of health services, including the values of incidence and prevalence. The incidence and prevalence of disease can be affected by various factors, such as mortality rate, number of healing, treatment setting, the success of prevention, and others.

Rational use of drugs aimed to facilitate the access of public to obtain drugs at affordable price, preventing the impact of inappropriate use of drugs that may be harmful, and improve compliance. Wise in prescribing antibiotic for acute pharyngitis in health centers is also expected to improve the effectiveness and efficiency of drug expenditures. Each of physicians has the right to determine the type of drug that is most appropriate for their patients. However, if it is not controlled or not based on acceptable scientific then it would risk incurring the irrational use of drugs. To improve the rational use of drugs requires the involvement all elements of health professional, especially pharmacist as a co-physician in prescribing medication.

5. Conclusions

It can be concluded that there were still irrational use of drugs in the treatment of acute pharyngitis. Irrational use of drugs mostly occured on the use of antibiotics and corticosteroids. The increase in disease incidence and prevalence might indicate the declining health services quality.

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References

1. Bratasena, A.; Sitorus, M.; Riana, D.A.; Widiawati; Simbolon, O.E.; Wignjadiputro; et al for Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan. Pedoman pengendalian infeksi saluran nafas akut; Kementrian Kesehatan Republik Indonesia: Jakarta, Indonesia, 2012.
2. Badan Penelitian dan Pengembangan Kesehatan. Riset Kesehatan Dasar 2013. Kementrian Kesehatan Republik Indonesia: Jakarta, Indonesia, 2013.
3. Shaikh, N.; Leonard, E.; Martin, J.M. Prevalence of streptococcal pharyngitis and streptococcal carriage in children: A meta-analysis. *Pediatrics* **2010**, *126*, e557–e564.
4. Vincent, M.T.; Celestin, N.; Hussain, A.N. Pharyngitis. *Am Fam Physician* **2004**, *69*, 1465-70.
5. Snow, V.; Mottur-Pilson, C.; Cooper, R.J.; Hoffman, J.R. Principles of appropriate antibiotic use for acute pharyngitis in adults. *Ann Intern Med* **2001**,*134*, 506–508.
6. Ahmad, S.; Indrasanto, D.; Brahim, R.; Susilo, B.; Hardhana, B.; Sulistiyowati, D.; et al for Pusat Data Kesehatan. Profil kesehatan Indonesia 2004: Menuju Indonesia sehat 2010. Departemen Kesehatan Republik Indonesia: Jakarta, Indonesia, 2006.
7. Kementrian Kesehatan Republik Indonesia. Peraturan Menteri Kesehatan RI No. 5 tahun 2014 tentang panduan praktik klinik bagi dokter di fasilitas pelayanan kesehatan primer. Departenen Kesehatan Republik Indonesia: Jakarta, Indonesia, 2014.
8. The Pursuit of Responsible Use of Medicines: Sharing and Learning from Country Experiences. Available online: http://www.who.int/medicines/areas/rational_use/en/ (accessed on 26 November 2015).
9. Direktorat Bina Pelayanan Kefarmasian. Kegiatan subdit penggunaan obat rasional tahun 2014. Direktorat Jenderal Bina Kefarmasian dan Alat Kesehatan: Jakarta, Indonesia, 2014.
10. Bahaudin N. Implementasi kebijakan penggunaan obat rasional di Indonesia. Jakarta: Departemen Kesehatan Republik Indonesia: Jakarta, Indonesia, 2011.
11. Text book of pharmacoepidemiology; Strom, B.L., Kimmel, S.E. John Wiley & Sons, Ltd: The Atrium, Southern Gate, Chichester,West Sussex, England, 2006, pp. 71-74.
12. Epidemiology: a tool for the assessment risk. Available online: http://www.who.int/water_sanitation_health/dwq/iwachap7.pdf (accessed on 26 November 2016).
13. Orofino, D.H.; Passos, S.R.; Andrade, C.A.; Nigri, D.; Santos; Werneck; et al. Accuracy and interobserver variation of three clinical decision rules for the diagnosis of streptococcal pharyngitis. *Pediatr Infect Dis J* **2011**, *32*, 686-687.
14. Pelluchi, C.; Grigoryan, L.; Galeone, C.; Esposito, S.; Huovinen, P.; Littlem P. Guideline for the management of acute sore throat; ESCMID Sore Throat Guideline Group. *ClinMicrobiol Infect* **2012**, *18*, 1-28.
15. Centor, R.M.; Witherspoon, J.M.; Dalton, H.P.; Brody, C.E.; Link, K. The diagnosis of strep throat in adults in the emergency room. *Med Decis Making* **1981**, *1*,239–246.
16. McIsaac, W.J.;Goel, V.; To, T.; Low, D.E. The validity of a sore throat score in family practice. *CMAJ* **2000,** *163*, 811–815.
17. Fine, A.M.; Nizet, V.; Mandl, K.D. Large-scale validation of the Centor and McIsaac scores to predict group A streptococcal pharyngitis. *Arch Intern Med* **2012**, *172*, 847-852.
18. Cooper, R.J.; Hoffman, J.R.; Bartlett, J.G.; Besser, R.E.; Gonzales, R.; Hickner, J.M.; Sande, M.A.; American Academy of Family Physicians; American College of Physicians; American Society of Internal Medicine; Centers for Disease Control and Prevention. Principles of appropriate antibiotic use for acute pharyngitis in adults: background. *Ann Intern Med* **2001**, *134*, 509–517.
19. American Academy of Pediatrics; Committee on Infectious Diseases. Red Book. 26th ed. American Academy of Pediatrics: Elk Grove Village Ill;America; 2003; pp. 578–580.

20. Dajani, A.; Taubert, K.; Ferrieri, P.; Peter, G.; Shulman, S. Treatment of acute streptococcal pharyngitis and prevention of rheumatic fever: a statement for health professionals. Committee on Rheumatic Fever; Endocarditis; and Kawasaki Disease of the Council on Cardiovascular Disease in the Young; the American Heart Association. *Pediatrics* **1995**, *96*, 758–764.
21. Bisno, A.L.; Gerber, M.A.; Gwaltney, J.M. Jr; Kaplan, E.L.; Schwartz, R.H.; for the Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis. *Clin Infect Dis* **2002**, *35*,113–125.
22. Rimoin, A.W.; Hamza, H.S.; Vince, A. Evaluation of the WHO clinical decision rule for streptococcal pharyngitis. *Arch Dis Child***2005**,*90(10)*,1066–1070.
23. Gerber, M.A.; Baltimor, R.S.; Eaton, C.B.; Gewitz, M.; Rowley, A.H.; Shulman, S.T.; et al. Prevention of rheumatic fever and diagnosis and treatment of acute streptococcal pharyngitis: A scientific statement from the American Heart Association Rheumatic Fever; Endocarditis; and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young; the Interdisciplinary Council on Functional Genomics and Translational Biology; and the Interdisciplinary Council on Quality of Care and Outcomes Research: Endorsed by the American Academy of Pediatrics. *Circulation* **2009**, *119*, 1541–1551
24. Anjos, L.M.M.; Marcondes, M.B.; Lima, M.F. Review article: Streptococcal acute pharyngitis. *Revista da SociedadeBrasileira de Medicina Tropical* **2014**, *47*, 409-413.
25. Altamimi, S.; Khalil, A.; Khalaiwi, K.A. Short versus standard duration antibiotic therapy for acute streptococcal pharyngitis in children. *Cochrane Database Syst Rev* **2009**, *1*, CD004872.
26. Falagas, M.E.; Vouloumanou, E.K.; Matthaiou, D.K. Effectiveness and safety of short-course vs long-course antibiotic therapy for group A β-hemolytic streptococcal tonsillopharyngitis: A meta-analysis of randomized trials. *Mayo Clinic Proceedings* **2008**, *83*,880-889.
27. Casey, J.R.; Pichichero, M.E. Metaanalysis of short course antibiotic treatment for group A streptococcal tonsillopharyngitis. *Pediatr Infect Dis J* **2005**,*24*, 909–917.
28. Bergeson, K.; Rogers, N.; Shailendra, P. Corticosteroids for a sore throat? One dose of a steroid can alleviate the pain—and has the potential to decrease unnecessary use of antibiotics. *The Journal of Family Practice* **2013**, *62*, 372-374.
29. Shulman, S.T.; Bisno, A.L.; Clegg, H.W. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by The Infectious Diseases Aociety of America. *Clinical Infectious Diseases* **2012**, 1-17.