

Clinical predictors of childhood streptococcal pharyngitis

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Abstract

Background Antibiotic prescription for the management of all acute pharyngitis seems to be increasing recently. Streptococcal pharyngitis is the one that has strong indication for antibiotic prescription. It is quiet hard to distinguish the clinical features of streptococcal pharyngitis from non-streptococcal one.

Objective To determine specifically clinical features of streptococcal pharyngitis and distinguish them from non-streptococcal one.

Methods We conducted a cross-sectional study on children with acute pharyngitis at Pediatric Outpatient Department Dr. M. Djamil Hospital, Padang from November 2006 until March 2007. Data on clinical features and pharyngeal swab culture results were analyzed using chi-square test for clinical predictors. All were then reanalyzed using multivariate logistic regression.

Results Ninety-five children aged 3-13 years were enrolled and pharyngeal swab culture was performed. Group A β -haemolytic streptococcus was found in 13 children (14%). Absence of cough, sore throat, tonsillar exudates and tender anterior cervical adenopathy were the clinical predictors for streptococcal pharyngitis and the last two shared highest risk (OR 55.05; 31.82). Combination of tonsillar exudates, tender anterior cervical adenopathy and absence of cough contributed 99,3% probability.

Conclusions Streptococcal pharyngitis includes a small part of all childhood with acute pharyngitis. High grade fever, sore throat, absence of cough, tonsillar exudates and tender anterior cervical adenopathy were considered as clinical predictors for childhood streptococcal pharyngitis. Combination of some clinical predictors will strengthen the probability of streptococcal pharyngitis.

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Keywords: acute pharyngitis, GABHS, pharyngeal swab culture, clinical predictors

Acute pharyngitis in children is one of the most frequent illness consulted to primary care clinicians. Evidence show that most are viral, self limiting, easily self managed and do not require antibiotics.¹⁻³ Qualitative studies in the worldwide recently show the widespread use of antibiotics for all childhood's acute pharyngitis.^{2,4,5} A big part of these problems is due to the fact that clinicians are overprescribing, they have uncomfortable sense of not prescribing or they want to maintain a clinician-patient relationship.⁴⁻⁷

Group A β -haemolytic streptococcus (GABHS) is the most common bacterial cause of acute pharyngitis, accounting for approximately 15-30 percents of cases in children and 5-10 percents of cases in adults.^{3,8,9} Only streptococcal pharyngitis that needs antibiotics.⁶⁻⁹ However, only a small percentage of childhood acute pharyngitis is caused by GABHS.^{10,11}

Unfortunately, the clinical features of streptococcal pharyngitis are non-specific for GABHS

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infection.^{1,8} If a diagnosis is based on clinical impression alone, clinicians generally overestimate that the patients have GABHS infection.^{10,12} Clinical features of streptococcal pharyngitis often overlap with pharyngitis of other etiologies and hard to distinguish.^{11,13,14}

Since it is not rational to treat all childhood's acute pharyngitis with antibiotics while laboratory facilities for culture and serology test are generally not available in pediatric ambulatory settings, it is necessary to have guidelines specifically for clinical identification of streptococcal pharyngitis.¹⁵⁻¹⁸ The aim of this study was to formulate new several clinical predictors that could specifically determine streptococcal pharyngitis and distinguish them from non-streptococcal pharyngitis.

Methods

This was a cross-sectional study conducted on patients aged 3-13 years with acute pharyngitis at the Pediatric Outpatient Departments of Dr. M. Djamil Hospital Padang, Indonesia, from November 2006 until March 2007. The study protocol was approved by The Committee of Medical Research Ethics of Dr. M. Djamil Hospital/ Medical School, Andalas University, Padang. Written informed consent was obtained from parents or guardians.

Children who got oral antibiotic within three days or intramuscular antibiotics within 28 days prior to clinic visit, or those who suffered from rheumatic fever/ rheumatic heart disease, malnutrition, tuberculosis or diseases requiring hospitalization were excluded from this study. After enrollment, demographic information was recorded and a physical examination was performed. Data on specific signs and symptoms associated with pharyngitis were collected using a standard form. Specimen obtained from pharyngeal swab using sterile cotton swab was cultured for bacteria with a reference standard method.

The swab was applied to any area appeared either very red or discharging pus and removed gently without touching the teeth, gums or tongue. The swab was then placed in a sterile tube for immediate delivery and culture in the laboratory. Sore throat for younger children, aged less than six years was clearly noted by oral hypersalivation and painful expression in swallowing.

Children participating in this study were categorized as having acute streptococcal or non-streptococcal pharyngitis based on culture results.

A chi-square statistic (15) was calculated to assess whether signs and symptoms were significantly or not associated with streptococcal pharyngitis. Variables statistically significant for streptococcal pharyngitis ($P < 0,05$) were termed as clinical predictors and selected for the next stage of analysis. Multivariate logistic regression was used to model the probability of streptococcal pharyngitis in terms of these variables.

Results

Ninety-five patients who met the criteria were selected for this study. Forty-nine patients (51%) were well-nourished. Out of all, female and less than six years old patients were more common (55% and 58%). Their ages ranged from 3.1-11.8 years, with mean age of 6.1 (SD 2.3) years. Mean age of positive and negative culture for GABHS were 6.1 (SD 1.8) years and 6.1 (SD 2.4) years, respectively. The baseline characteristics of patients are shown in **Table 1**.

Data on clinical signs or symptoms and pharyngeal swabs culture results were successfully obtained from 95 subjects. Positive culture for GABHS was found in 13 cases (14%). Culture results from all specimens showed 11 different bacteria including GABHS. There were two or more bacterial growths in one specimen, covering single normal pharyngeal flora and bacterial pathogen or combination of both. Compared to normal floras, bacterial pathogens were only found in a small quantity (<15%). Group A *β-haemolyticus streptococcus* (GABHS) alone took

Table 1. Baseline characteristics of patients

	n (%)
Age	
<6 years	55 (58)
6-13 years	40 (42)
Nutritional stage	
wellnourished	49 (52)
undernourished	46 (48)
Sex	
male	42 (44)
female	53 (56)

the highest number among bacterial pathogens in all specimens followed subsequently by *Klebsiella* sp., *Enterobacter* sp. and *E. coli* (2 case each). **Figure 1** showed the distribution of bacterial microorganisms found on culture.

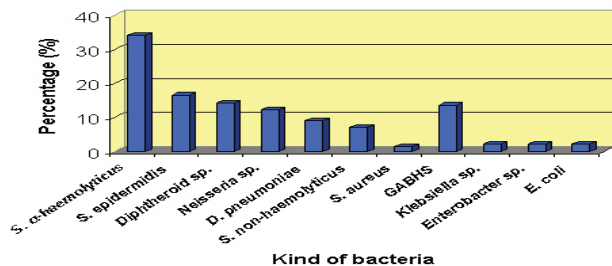


Figure 1. Distribution of bacterial microorganisms found on pharyngeal swab cultures

Out of all variables (baseline characteristics and clinical features), it seemed tonsillar/pharyngeal erythema and tonsillar enlargement couldn't be included, due to their absolute presence in either streptococcal or non-streptococcal pharyngitis patients. There were only 13 variables testable and selected for this study.

The study result showed that high grade fever, sore throat, absence of cough, tonsillar exudates and tender anterior cervical adenopathy had associations and statistically significant for streptococcal pharyngitis ($P < 0,05$). Therefore those five clinical features above specifically considered as clinical predictors for childhood streptococcal pharyngitis. **Table 2** summarizes all variables analyzed.

In this study, the risk for suffering streptococcal pharyngitis in children was identical with OR value of every clinical predictors for streptococcal pharyngitis. The higher the value, the more the risk for a child to suffer. From five clinical predictors, tonsillar exudates and tender anterior cervical adenopathy shared the biggest risk (OR 55.05, 31.82). Although high grade fever contributed the risk as much as 2.96 times, it couldn't be selected absolutely for the clinical predictor due to the value of its 95% CI(0.96;8.51). Risks for suffering streptococcal pharyngitis at children are listed on **Table 3**.

Combinations of every clinical predictors or baseline characteristics with clinical predictors can result in more accurate probability and those finally create a model in diagnosing childhood streptococ-

cal pharyngitis. Due to their bigger reliability among the others, clinical predictors such as absence of cough, tonsillar exudates and tender anterior cervical adenopathy were selected for. Combination of those three shared 99.3% probability and that was higher

Table 2. Distribution of subjects based on baseline characteristics and clinical features

	Streptococcal pharyngitis n (%)	Nonstreptococcal pharyngitis n (%)	P
Age 6-13 years			
Yes	6 (15)	34 (85)	0.750
No	7 (12)	48 (87)	
Undernourished			
Yes	8 (15)	45 (85)	0.653
No	5 (11)	37 (88)	
Male			
Yes	5 (10)	44 (89)	0.308
No	8 (17)	38 (82)	
High grade fever			
Yes	7 (24)	22 (75)	0.049*
No	6 (9)	60 (91)	
Chills			
Yes	4 (2)	12 (75)	0.149
No	9 (11)	70 (88)	
Runny nose			
Yes	7 (10)	61 (89)	0.127
No	6 (22)	21 (77)	
Nasal congestion			
Yes	5 (15)	28 (85)	0.761
No	8 (13)	54 (87)	
Sore throat			
Yes	11 (65)	6 (35)	<0.001
No	2 (3)	76 (97)	
Absence of cough			
Yes	10 (53)	9 (47)	<0.001
No	3 (4)	73 (96)	
Hoarseness			
Yes	0 (0)	3 (100)	0.483
No	13 (15)	79 (84)	
Tonsillar exudates			
Yes	12 (70)	5 (29)	<0.001
No	1 (1)	77 (99)	
Pharyngeal exudates			
Yes	2 (40)	3 (60)	0.079
No	11 (12)	79 (88)	
Tender anterior cervical adenopathy			
Yes	11 (79)	3 (21)	<0.001
No	2 (3)	79 (98)	

Table 3. Risk for suffering streptococcal pharyngitis based on clinical predictors

Clinical predictor	Odds ratio	95%CI
Absence of cough	14.21	6.25; 56,92
Sore throat	25.23	12.46; 113,32
Tonsillar exudates	55.05	19.84; 272,26
Tender anterior cervical adenopathy	31.82	21.72; 165,55

than combination of one or two clinical predictors only.

Bigger probability also could be achieved by combining one clinical predictor and one baseline characteristic of patient. In this study, if a child aged 6-13 years was found to have tonsillar exudates or sore throat, the probability of streptococcal pharyngitis case would reach 100%. If there was tonsillar exudates or sore throat in a boy as well as tonsillar exudates or tender anterior cervical adenopathy in a wellnourished child, the cases probability would also reach 100%. Probability percentage of streptococcal pharyngitis cases can be seen in **Tables 4 and 5**.

Discussion

Group A *β-haemolyticus streptococcus* is the main pathogenic microorganism of childhood's acute pharyngitis, accounts for 15-30% of all causes.^{2,3,8} Many factors play role in GABHS infection in children, such as age, nutritional stage, socioeconomic level and climates.⁹⁻¹¹ Due to the great influence of those external factors, there will be a difference in the prevalence of streptococcal pharyngitis in different places.

Our study in Dr. M. Djamil Hospital Padang showed that the prevalence of childhood streptococcal pharyngitis was 14%, lower than that found

by McIsaac, Martin and Sahin. With similar subject characteristics and laboratory methods, they found the prevalence of 36.2%, 15.5% and 26.5%, respectively.^{12,19,20} Compared to the results of the study of *Nandis*²¹ (13.4%) or *Chi*¹⁴ (1.7%), the prevalence is higher and it is possibly caused by the smaller number of samples enrolled in our study, covering only 40-50% of other studies total samples.

There are many bacterial causes of childhood's acute pharyngitis. On pharyngeal swab, the culture result doesn't always show single bacterial growth. Frequently, there are two or more growths of bacterial pathogens or normal floras of throat found as combination. Bacterial pathogens as the cause of acute pharyngitis cover only a small number compared to total bacteria found on pharyngeal swab.^{14,22,23} Our data in Dr. M. Djamil Hospital showed that normal flora accounted for 84% of total growth. This was nearly similar with Hables, that found 89% normal flora growth in specimen cultured from his entirely cases of childhood pharyngitis.²³

The incidence of acute pharyngitis in Padang is higher in girls than boys and it doesn't seem far different from Halls (52% vs 47%).²⁴ Both data above were contradictive to results of Chi, Hamza, Sahin, Van Limbergen or dos Santos. They all found that acute pharyngitis were more prevalent in boys than girls (55-60% vs 40-45%).^{14,17,20,25,26}

Many studies reported that childhood streptococcal pharyngitis are more prevalent in boys, 5-15 years old, undernourished, lower socioeconomic level children or in winter/ early spring.^{3,7,10,11} In Padang during November '06-March '07, the incidence of streptococcal pharyngitis in girls, less than six years old and undernourished children was 62%, 54% and 62%, respectively.

Datas from Padang were much different from that of WHO (in 3 countries), Hamza and Sauver.

Table 4. Probability percentage of streptococcal pharyngitis based on clinical predictors

Clinical predictors	Probability (%)
Absence of cough + tender anterior cervical adenopathy	43
Absence of cough + tonsillar exudates	67
Tonsillar exudates + tender anterior cervical adenopathy	99
Absence of cough + tonsillar exudates + tender anterior cervical adenopathy	99

Table 5. Probability percentage of streptococcal pharyngitis based on combination of clinical predictors and baseline characteristics

Clinical predictor	Age		Sex		Nutritional stage	
	<6 years (%)	6-13 years (%)	Male (%)	Female (%)	Wellnourished (%)	Undernourished (%)
Sore throat	71	100	100	75	80	87
Absence of cough	72	83	80	75	80	75
Tonsillar exudates	86	100	100	88	100	86
Tender anterior cervical adenopathy	85	83	87	79	100	75

They found that boys or children aged more than five years were more prevalent to suffer from streptococcal pharyngitis, but unfortunately it was not statistically significant ($P > 0.05$).^{15,17,27} Lin¹⁶ also found that streptococcal pharyngitis was more prevalent in boys or children aged 6-11 years ($P < 0.05$). Mean age of streptococcal pharyngitis in Padang was 6.1 (SD 1.83) years, nearly similar with other data studies from Lin, Hamza, Attia or Sauver i.e. 7.8 (SD 2.3) years, 5.2 (SD 1.6) years, 6.2 (SD 3.4) years and 5.8 (SD 3.7) years respectively.^{16,17,28,29} All results above are compatible with literatures.

There are many clinical predictors of streptococcal pharyngitis proposed in studies and new important innovations in simplifying the diagnosis, especially in places with limited facility of laboratories.^{17,28-30} Only a little part of clinical features of acute pharyngitis were representative for clinical predictors of streptococcal pharyngitis. In Padang it was found only four clinical predictors are representative and those are sore throat, absence of cough, tonsillar exudates and tender anterior cervical adenopathy. Some studies abroad also indicated sore throat, tonsillar exudates, tender anterior cervical adenopathy and even high grade fever as the clinical predictors associated significantly with streptococcal pharyngitis.²⁸⁻³⁰ Our study in Padang showed that tonsillar exudates and tender anterior cervical adenopathy were the strong clinical predictors and these were similar with other data from study abroad.^{28,29}

In our study, combination of more than two clinical predictors would increase probability of streptococcal pharyngitis (up to 99%). McIsaac with his clinical score (0-4), got 38-63% probability of childhood streptococcal pharyngitis case with score 4, whereas Attia only counted 65-95% probability if found four clinical predictors in his patients.^{12,28}

Age, sex and nutritional status in acute pharyngitis patients in Padang are not significantly associated with streptococcal pharyngitis. Those characteristics would be meaningful and result in bigger probability of streptococcal pharyngitis (up to 100%) if combined with one clinical predictor. Due to the lack of data from studies abroad, we couldn't compare our results as 100% probability to others.

It is unclear why the probability of childhood streptococcal pharyngitis is bigger in wellnourished and tonsillar exudative children than that in undernourished one (100% vs 87.5%). It was

presumably associated with the higher content of protein found in cells or tissues of wellnourished children. Theoretically, every cell damages will always be followed by proteolysis process and these events more easily occur in wellnourished than undernourished children.^{13,31}

Because the majority of childhood acute pharyngitis are not caused by GABHS, empiric antibiotics therapy would result in substantial overtreatment. Combination of one or some clinical predictors, and one baseline characteristic of children will enlarge the probability of streptococcal pharyngitis.^{1,4,5} The widespread availability of accurate, inexpensive clinical predictors offers both cost-effective and efficient diagnostic strategy for streptococcal pharyngitis, and avoids the overuse of antibiotics.^{12,29}

In conclusion, childhood streptococcal pharyngitis in Padang contributes a small part of all acute pharyngitis. High grade fever, sore throat, absence of cough, tonsillar exudates and tender anterior cervical adenopathy were considered as clinical predictors for children streptococcal pharyngitis. Combination of some clinical predictors will strengthen the probability of streptococcal pharyngitis.

References

1. Smeesters PR, Campos D, Van Melder L, de Agular E, Vanderpas J, Vergison A. Pharyngitis in low resource setting: A pragmatic clinical approach to reduce unnecessary antibiotic use. *Pediatrics* 2006;118:1607-11.
2. Schwartz B, Marcy M, Phillips WR, Gerber MA, Dowell SF. Pharyngitis. Principles of judicious use of antimicrobial agents. *Pediatrics* 1998;101:171-4.
3. Vincent MT, Celestin N, Hussain AN. Pharyngitis. *Am Fam Physician* 2004;69:1465-70.
4. Dowell SF, Schwartz B, Phillips WR. Appropriate use of antibiotics for URIs in children: Part II. Cough, pharyngitis and the common cold. *Am Fam Physician* 1998;58:1335-47.
5. McCaig LF, Besser RE, Hughes JM. Trends in antimicrobial prescribing rates for children and adolescents. *JAMA* 2002; 267:3096-102.
6. Rossenstein N, Phillips WR, Gerber MA, Marcy SM, Schwartz B, Dowell SF. The common cold. Principles of judicious use of antimicrobial agents. *Pediatrics* 1998;101:181-4.
7. Bisno AL, Kaplan EL. Appropriate use of antibiotics. *Pharyngitis*. *Ann Intern Med* 2002;136:489-90.

8. Bisno AL, Gerber MA, Gwaltney JM, Kaplan EL, Schwartz RH. Practice guidelines for diagnosis and management of group A streptococcal pharyngitis. *Clin Infect Dis* 2002;35:113-25.
9. American Academy of Pediatrics. Group A streptococcal infection. In: Pickering L, editor. *Red Book 2003*. Report of the Committee on Infectious Disease, 26th ed. Elk Grove Village, IL: American Academy of Pediatrics;2003: p. 576-8.
10. Pichichero ME. Group A beta-hemolytic streptococcal infections. *Pediatr Rev* 1998;19:291-303.
11. Hayes CS, Williamson H Jr. Management of group A beta-hemolytic streptococcal pharyngitis. *Am Fam Physician* 2001;63:1557-65.
12. McIsaac WJ, White D, Tannenbaum D, Low DE. A clinical score to reduce unnecessary antibiotic use in patients with sore throat. *Can Med Assoc J* 1998;158:75-83.
13. Bisno AL. Acute pharyngitis. *N Engl J Med* 2001;344:205-11.
14. Chi H, Chiu NC, Li WC, Huang FY. Etiology of acute pharyngitis in children: Is antibiotic needed? *J Microbiol Immunol Infect* 2003;36:26-30.
15. Rimoin AW, Hamza HS, Vince A, Kumar R, daCunha ALA, Walker CF, et al. Evaluation of the WHO clinical decision rule for streptococcal pharyngitis. *Arch Dis Child* 2005;90:1066-70.
16. Lin MH, Fong WK, Chang PF, Yen CW, Huang KL, Lin SJ. Predictive value of clinical features in differentiating group A β -hemolytic streptococcal pharyngitis in children. *J Microbiol Immunol Infect* 2003;36:21-5.
17. Hamza H. Group A streptococcal pharyngitis (GRASP) study. Available from: URL:<http://www.ph.ucla.edu/epi/faculty/rimoin/CV-Rimoin.pdf>.
18. Park SY, Gerber MA, Tanz RR, Hickner JM, Galliher JM, Chuang I, et al. Clinicians' management of children and adolescents with acute pharyngitis. *Pediatrics* 2006;117:1871-8.
19. Martin JM, Green M, Barbadora KA, Wald ER. Group A streptococci among school-aged children. Clinical characteristic and the carrier state. *Pediatrics* 2004;114:1212-9.
20. Sahin F, Ulukol B, Aysef D, Suskan E. The validity of diagnostic criteria for streptococcal pharyngitis in integrated management of childhood illness (IMCI) guidelines. *J Trop Pediatr* 2003;49:377-9.
21. Nandi S, Kumar R, Ray P, Vohra H, Ganguly NK. Group A streptococcal sore throat in a periurban population of northern India: A one year prospective study. *Bull World Health Organ* 2001;79:528-33.
22. Ruppert SD. Differential diagnosis of common causes of pediatric pharyngitis. *Nurse Pract* 1996;21:38-48.
23. Bourbeau PP. Role of the microbiology laboratory in diagnosis and management of pharyngitis. *Minireview. J Clin Microbiol* 2003;41:3467-72.
24. Hall MC, Kieke B, Gonzales R, Belongia EA. Spectrum bias of rapid antigen detection test for group A β -hemolytic streptococcal pharyngitis in a pediatric population. *Pediatrics* 2004;114:182-6.
25. Van Limbergen J, Kalima P, Taheri S, Beattie TF. Streptococcus A in pediatric accident and emergency: Are rapid streptococcal tests and clinical examination of any help? *Emerg Med J* 2006;23:32-4.
26. dos Santos AG, Berezin EN. Comparative analysis of clinical and laboratory methods for diagnosing streptococcal sore throat. *J Pediatr (Rio J)* 2005;81:23-8.
27. Sauver JLS, Weaver AL, Orvidas LJ, Jacobson RM, Jacobsen SJ. Population-based prevalence of repeated group A β -hemolytic streptococcal pharyngitis episodes. *Mayo Clin Proc* 2006;81:1172-6.
28. Attia M, Zaoutis T, Eppes S, Klein J, Meier F. Multivariate predictive models for group A β -hemolytic streptococcal pharyngitis in children. *Acad Emerg Med* 1999;6:8-13.
29. Nawaz H, Smith DS, Mazhari R, Katz DL. Concordance of clinical findings and clinical judgement in the diagnosis of streptococcal pharyngitis. *Acad Emerg Med* 2000;7:1104-9.
30. DiMatteo LA, Lowenstein SR, Brimhall B, Reiquam W, Gonzales R. The relationship between the clinical features of pharyngitis and the sensitivity of a rapid antigen test: Evidence of spectrum bias. *Ann Emerg Med* 2001;38:658-52.
31. Thompson LDR, Wenig BM, Kornblut AD. Pharyngitis. In: Bailey BJ, Healy GB, Johnson JT, Jackler RK, Calhoun KH, Pillbury HC, Tardy ME, editors. *Head & neck surgery-otolaryngology*, 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 543-54.