McIsaac criteria for diagnosis of acute group-A β-hemolytic streptococcal pharyngitis

Imanuel Y. Malino¹, Dwi Lingga Utama¹, Yati Soenarto²

Abstract

Background The early use of antibiotics for acute upper respiratory infections is controversial because most of these infections are caused by viruses. A strategy is needed to correctly identify the causative agents of acute pharyngitis, so that antibiotics can be prescribed appropriately.

Objective To assess McIsaac criteria for diagnosing acute group-A β-hemolytic streptococcal (GABHS) pharyngitis in children.

Methods This diagnostic study was conducted from August 2011 to February 2012, to compare clinical criteria of McIsaac to throat swab culture results as the gold standard for diagnosis. Subjects were children aged 3-14 years who visited the pediatric outpatient clinic or emergency ward at Sanglah Hospital and the pediatric outpatient clinic at Wangaya Hospital.

Results There were 550 cases of acute pharyngitis during the study period, with 313 patients aged 3-14 years and 199 patients excluded due to a history of taking antibiotics in the two weeks prior to the hospital visit. Hence, 114 subjects were eligible for the study. GABHS prevalence in this study was 7.9%. McIsaac’s area under the curve (AUC) from receiver operating characteristic (ROC) curve was 78.1%(95%CI 60.3 to 96%, P= 0.005). A McIsaac score ≥4 had a 66.7% (95%CI 49 to 97%) sensitivity, 87.6% (95% CI 81 to 94%) specificity, 31.6% (95% CI 11 to 52%) positive predictive value (PPV), 96.8% (95% CI 93 to 100%) negative predictive value (NPV), 86.0% accuracy, 5.4 (95% CI 2.7 to 10.7) positive likelihood ratio (LR+) and 0.4 (95% CI 0.2 to 0.9) negative likelihood ratio (LR-).

Conclusion A McIsaac criteria total score of <4 is favorable for excluding a diagnosis of GABHS pharyngitis. A McIsaac total criteria score of ≥4 requires further examination to confirm a diagnosis of GABHS pharyngitis. [Paediatr Indones. 2013;53:258-63].

Keywords: diagnostic testing, pharyngitis, group-A β-hemolytic streptococcus (GABHS), McIsaac
GABHS pharyngitis. Practical diagnostic tools may comprise of clinical criteria and rapid lab tests. We hope that a feasible, less more affordable, yet accurate diagnostic tool will reduce unnecessary antibiotic usage.

The Centor Criteria have been widely accepted and validated as clinical criteria for diagnosis of GABHS bacterial pharyngitis in adults since 1981. This criteria was modified by McIsaac et al. in 1998, with the addition of age criteria. McIsaac criteria have a sensitivity and specificity of 70.6% and 91.7%, respectively.

A study on McIsaac criteria, particularly on acute GABHS pharyngitis in primary care in the tropics, is still limited while the incidence of acute pharyngitis is high. We aimed to compare the McIsaac diagnostic criteria to throat swab culture results for diagnosing acute GABHS pharyngitis in children.

**Methods**

This cross-sectional diagnostic study was performed to assess the McIsaac criteria for diagnosing acute GABHS pharyngitis with throat swab culture results as the gold standard. Subjects were children aged 3-14 years with symptoms of acute pharyngitis who visited the outpatient clinic or emergency ward of Sanglah Hospital and the outpatient clinic of Wangaya Hospital, Denpasar, from August 1, 2011 until February 6, 2012.

The inclusion criteria were clinical symptoms of acute pharyngitis in patients aged 3-14 years and parental agreement to participate in the study. We excluded patients with a history of antibiotic administration within the two weeks prior to enrollment. Subjects were collected by consecutive sampling.

Trained examiners who met the reliability test were hired for the study and blinded to the results from the trained laboratory officers at Prodia Labs who took throat swab specimens. Interobserver reliability tests were carried out on the trained examiners for ten subjects before the study began. Laboratory officers from Prodia Labs took throat swabs immediately after examiners evaluated subjects based on the McIsaac criteria. Researchers collected the questionnaires, McIsaac scores, and throat swab culture results at the end of the study. Subjects who scored ≥ 4 in the McIsaac criteria were treated with antibiotics. The McIsaac criteria are shown in Table 1.

The sample size was calculated with single sample proportion each for sensitivity and specificity of McIsaac score ≥ 4, previously reported to be 70.6% and 91.7%, respectively, with Z score for $\alpha = 0.05$ of 1.96 and 10% acceptable deviation of P value. The minimum required sample size was calculated to be 110 subjects.

This study was approved by the Research Ethics Committee of Udayana Medical School, Sanglah and Wangaya Hospitals, Denpasar, and Warren J. McIsaac.

**Table 1. McIsaac criteria (modified)**

| Criteria | Point |
|----------|-------|
| Temperature > 38°C | 1 |
| No cough | 1 |
| Tender anterior cervical adenopathy | 1 |
| Tonsillar swelling or exudate | 1 |
| Age 3–14 years | 1 |
| Age 15–44 years | 0 |
| Age ≥45 years | -1 |

**Results**

During the study period, there were 4,067 hospital visits, with 550 cases of acute pharyngitis (13.5%). Three hundred thirteen patients were children aged 3-14 years. We excluded 199 children due to their past history of antibiotic usage within the two weeks prior to the study. Hence, 114 patients were eligible for the study (Figure 1).

Characteristics of the study subjects are presented in Table 2. Most subjects were male (56.1%) and 6 years of age (18.4%). Fever (73.7%) was the most common clinical problem observed, followed by tonsillar swelling or exudates, anterior cervical lymph node swelling, and the absence of cough. The majority of subjects had total McIsaac scores of 3 (50%), followed by a score of 2 (33.3%). Acute pharyngitis is more frequent during the first 3-6 years of life.

Figure 2 shows the ROC curve of McIsaac scores. McIsaac criteria had an AUC value of 78.1%
Table 2. Baseline characteristics of subjects

| Variables                | n=114 | %   |
|--------------------------|-------|-----|
| Male gender, n           | 64    | 56.1|
| Age in years, n          |       |     |
| 3                        | 15    | 13.2|
| 4                        | 18    | 15.8|
| 5                        | 17    | 14.9|
| 6                        | 21    | 18.4|
| 7                        | 6     | 5.3 |
| 8                        | 7     | 6.1 |
| 9                        | 7     | 6.1 |
| 10                       | 7     | 6.1 |
| 11                       | 12    | 10.5|
| 12                       | 1     | 0.9 |
| 13                       | 2     | 1.8 |
| 14                       | 1     | 0.9 |

McIsaac's clinical criteria
- Temperature > 38°C: 84 (73.7)
- No cough: 23 (20.2)
- Tender anterior cervical adenopathy: 26 (22.8)
- Tonsillar swelling or exudate: 81 (71.1)

Total McIsaac criteria scores
- 2: 38 (33.3)
- 3: 57 (50.0)
- ≥4: 19 (16.7)

Table 3. Diagnostic test of McIsaac criteria confirmed with throat swab culture results

| McIsaac's criteria total score | n  | Positive culture results | Sn (%) | Sp (%) | PPV (%) | NPV (%) | Ac (%) | LR (+) | LR (-) |
|--------------------------------|----|--------------------------|--------|--------|---------|---------|--------|--------|--------|
| 2                              | 38 | 1                        | 11.1   | 64.4   | 2.6     | 89.3    | 59.6   | 0.3    | 1.4    |
| 3                              | 57 | 2                        | 22.2   | 47.6   | 3.5     | 87.7    | 45.6   | 0.4    | 1.6    |
| ≥4                             | 19 | 6                        | 66.7   | 87.6   | 31.6    | 96.8    | 86.0   | 5.4    | 0.4    |

Sn=sensitivity; Sp=specificity; PPV=positive predictive value; NPV=negative predictive value; Ac=accuracy; LR=likelihood ratio

Figure 1. Study flow chart

Figure 2. ROC curve of McIsaac criteria

Diagonal segments are produced by ties
(95%CI 60.3 to 96%). We found that the prevalence of acute GABHS pharyngitis was 7.9%. Table 3 shows the diagnostic test results of McIsaac criteria scoring, compared to the gold standard of throat swab culture results.

A total McIsaac score ≥4 had a sensitivity of 66.7% (95%CI 49 to 97%), specificity 87.6% (95%CI 81 to 94%), positive predictive value 31.6% (95%CI 11 to 52%), negative predictive value 96.8% (95% CI 93% to 100%), accuracy 86.0%, positive likelihood ratio 5.4 (95%CI 2.7 to 10.7), negative likelihood ratio 0.4 (95 CI 0.2 to 0.9), pre-test odds 0.09, post-test odds 0.05, and post-test probability 0.32.

Discussion

We found that more boys suffered from acute pharyngitis than girls, similar to results of a previous Indonesian study. However, two studies from other countries found that more females than males suffered from acute pharyngitis. Some studies on acute GABHS pharyngitis did not display data on gender, possibly due to the lack of a significant difference in numbers of males and females.

Acute pharyngitis was more common in subjects aged 3-6 years in our study. Similarly, an Indian study found that the highest incidence of GABHS pharyngitis was at 4-6 years (14.1%). Tanz et al. reported that GABHS pharyngitis occurs in all age groups, but especially during school age, 5-11 years, possibly due to high transmissibility from one child to another.

Fever or a history of fever of >38°C in our study was the most common symptom accompanying pharyngitis, followed by tonsil swelling or exudates, enlarged lymph nodes, and absence of cough. Similarly, Tanz et al. found that 90% of GABHS pharyngitis was accompanied by fever. In contrast, McIsaac et al. found the most common symptom occurring in acute GABHS pharyngitis to be enlarged lymph nodes with or without pain, followed by absence of cough, history of fever >38°C and tonsil enlargement or exudates. Clinical manifestations of acute pharyngitis vary among studies. Steinhoff suggested that the classic pattern of acute GABHS pharyngitis, such as enlarged tonsils and/or exudates and tender lymphadenopathy are rare in some areas, such as Egypt. As such, diagnostic tests to determine the validity of the clinical criteria in our setting must be undertaken.

We found that most of our subjects had total McIsaac criteria scores of 3. McIsaac had similar findings, in contrast to another UK study that reported a total score of 2 as the most common, followed by 3 and 4.

The area under curve (AUC) values were between 50% (no discriminative value) and 100% (best discriminative value). The ROC curves showed that the McIsaac score has good diagnostic value because the curve away from the line of 50% and nearly 100%. McIsaac criteria has AUC value of 78.1% means that if the McIsaac score is used to diagnose GABHS in 100 children with acute pharyngitis, the correct conclusions that will be obtained in 78 patients. AUC value of 70-80% have moderate interpretation that tends to good. The AUC value has statistically significant difference (P=0.005) to AUC value of 50%.

The prevalence of acute GABHS infections differs among regions and time periods. A longitudinal study in North America reported that the proportion of GABHS pharyngitis tended to not vary over the past 50 years, although the incidence of rheumatic fever and rheumatic heart disease in the US decreased. In Edinburgh (Scotlandia), Ross et al. found an incidence of 30.0%, but McIsaac et al. reported that an incidence of 17.0% in Canada increased by 29.0% in 2004. In addition, Jain et al. found an incidence of 12.6% in India in 2008. The incidence of GABHS pharyngitis in Indonesia appears to be lower than that of other countries. A Central Jakarta study reported a prevalence of 6.1%, while a Yogyakarta study found it was as high as 10.2%. We found an incidence of 7.9% in our study.

McIsaac scores in our study and previous studies tended to have low sensitivity, but high specificity. The sensitivity of a McIsaac score of ≥4 in our study was 66.7% (95%CI 49 to 97%), higher than that of Jurianti who reported a sensitivity of 56%. However, the specificity was 87.6% (95%CI 81 to 94%), similar to that of Jurianti (87%). This high specificity is more meaningful due to the low prevalence of acute GABHS pharyngitis in our population, indicating that in cases with McIsaac score of ≥4, there is higher likelihood that the acute pharyngitis is caused by GABHS, for which a selective antibiotic should be given.
For clinicians, PPV and NPV are more relevant than sensitivity and specificity. The PPV of McIsaac criteria in our study was 31.6% (95% CI 11 to 52%), lower than that of a Yogyakarta study (33%). However, the NPVs of our study and the Yogyakarta study were 96.8% (95% CI 93 to 100%) and 95%, respectively. High NPV in our study indicates that for total McIsaac score of <4, then there is a 96.8% likelihood that the results are actually negative. It means McIsaac score has a good role in excluding acute GABHS pharyngitis diagnosis.

Positive predictive value and NPV are influenced by disease prevalence that may vary among population settings. Therefore, LR(+) and LR(-) are useful as parameters unaffected by disease prevalence. Higher and further LR(+) from one indicates a strong positive results of diagnostic tests and more likely confirm the presence of disease. The LR(+) in our study was 5.4 (95% CI 2.7 to 10.7), indicating that for McIsaac score of ≥4, the ratio of positive results in the positive group compared with the positive results in the negative group was 5.4. There is a high likelihood of GABHS infection for LR(+) values between 5-10 for McIsaac score ≥4, hence McIsaac score can be used to contribute moderately to the acute GABHS pharyngitis diagnosis. Our results were lower than that of McIsaac (6.43), but higher than that of Jurianti (4.39).

Pretest probability (prevalence) of acute GABHS pharyngitis in children prior to diagnostic testing was 0.079. The possibility of a child with acute GABHS pharyngitis after McIsaac score (post-test probability) was 0.32. Post-test probability values within the range of 0.25-0.65 of test-treatment thresholds mean further tests are needed to determine therapy based on the post-test. The low post-test probability may be the reason that McIsaac recommends throat swab cultures for all total scores, even though empirically antibiotics may be given for total scores ≥4.

The combination of McIsaac clinical criteria and rapid detection tests improve sensitivity in diagnosing acute GABHS pharyngitis up to 100%. This combination is greater than the sensitivity of rapid tests alone (85.8%) and expected to improve post-test probability, hence, the use of antibiotics can be decided empirically. However, these rapid detection tests are not widely available in Indonesia.

A limitation of our study was that the subjects were within the age range of 3-14 years, while according to the McIsaac criteria, the scope of children's health extends to the age of 18 years. Studies with a wider age range, involving the ages of 0-3 years and 14-18 years are needed to improve the application of this study to the population. Another limitation was that the throat swab culture was performed only once. A second culture could be used to rule out the possibility of contaminants.

In conclusion, a total McIsaac criteria score of <4 may be useful for excluding a diagnosis of acute GABHS pharyngitis. Suspected cases of acute GABHS pharyngitis with total scores ≥4 require further investigation, such as a rapid strep detection test or throat swab culture as the gold standard, in order to confirm acute GABHS pharyngitis.

Acknowledgements

Our highest gratitude to I Gde Raka Widiana, MD, for his help in constructing methodology and statistical analysis for this study, as well as to Warren J. McIsaac, MD, for his kind permission to use the McIsaac criteria.

References

1. Wantania JM. Infeksi respiratori akut. In: Rahajoe NN, Supriyatno B, Setyanto DB, editors. Buku ajar respirologi anak. 1st ed. Jakarta: BP IDAI; 2008. p. 268-77.
2. Humair JP, Revaz SA, Bovier P, Stalder H. Management of acute pharyngitis in adults, reliability of rapid streptococcal tests and clinical findings. Arch Intern Med. 2006;166:640-4.
3. Hadi U, Duerink DO, Lestari ES, Nagelkerke NJ, Keuter M, Huis In’t veld D, et al. Audit of antibiotic prescribing in two governmental teaching hospitals in Indonesia. Clin Microbiol Infect. 2008;14:698-707.
4. Chazan B, Shaabi M, Bishara E, Colodner R, Raz R. Clinical predictors of streptococcal pharyngitis in adults. Isr Med Assoc J. 2003;5:413-5.
5. McIsaac WJ, White D, Tannenbaum D, Low DE. A clinical score to reduce unnecessary antibiotic use in patients with sore throat. CMAJ. 1998;158:75-83.
6. Puponegoro HD. Uji diagnostik. In: Sastroasmoro S, Ismael S, editors. Dasar-dasar metodologi penelitian klinis. 3rd ed. Jakarta: CV Sagung Seto; 2010. p. 193-216.
7. Jurianti A. Faringitis grup-A β-hemolitik streptokokus
8. McIsaac WJ, Kellner JD, Aufricht P, Vanjaka A, Low DE. Empirical validation of guidelines for the management of pharyngitis in children and adults. JAMA. 2004;291:1587-95.

9. Lindbaek M, Hoiby EA, Lermark G, Steinsholt IM, Hjortdahl P. Clinical symptoms and signs in sore throat patients with large colony variant β-haemolytic streptococci groups C or G versus group A. Br J Gen Pract. 2005;55:615-9.

10. Steinhoff MC, Rimoin AW. Epidemiology, clinical presentations, and diagnosis of streptococcal pharyngitis in developing countries of the world. In: Pachere JC, Kaplan EL, editors. Streptococcal pharyngitis optimal management. 3rd ed. Basel: Karger; 2004. p.49-65.

11. Jain A, Shukla VK, Tiwari V, Kumar R. Antibiotic resistance pattern of group-A beta hemolytic streptococci isolated from north Indian children. Indian J Med Sci. 2008;62:392-6.

12. Tanz RR, Shulman ST. Sore throat. In: Kliegman RM, Greenbaum LA, Lye PS, editors. Practical strategies in pediatric diagnosis and therapy. 2nd ed. Philadelphia: Elsevier Saunders; 2004. p.3-15.

13. Dahlan MS. Analisis penelitian diagnostik. In: Seri evidence-based medicine 5: penelitian diagnostik. 1st ed. Jakarta: Salemba Medika; 2009. p.19-30.

14. Dahlan MS. Memperoleh nilai area under the curve dengan prosedur receiver operating characteristic. In: Seri evidence-based medicine 5: penelitian diagnostik. 1st ed. Jakarta: Salemba Medika; 2009. p.55-60.

15. Dahlan MS. Menentukan titik potong dengan prosedur receiver operating characteristic. In: Seri evidence-based medicine 5: penelitian diagnostik. 1st ed. Jakarta: Salemba Medika; 2009. p.61-74.

16. Gitawati R, Isnawati A. Pola sensitivitas kuman dari isolat hasil usap tenggorok penderita tonsilofaringitis akut terhadap beberapa antimikroba betalaktam di Puskesmas Jakarta Pusat. Cermin Dunia Kedokteran. 2009;144:20-3.

17. Ross PW, Chisty SM, Knox JD. Sore throat in children: its causation and incidence. Br Med J. 1971;2:624-6.