Evaluating the Diagnostic Paradigm for Group A and Non–Group A Streptococcal Pharyngitis in the College Student Population

Shannan N. Rich,1,2 Mattia Prosperi,1,3 Emily M. Klann,1 Pavel T. Codreanu,2 Robert L. Cook,1 and Melissa K. Turley1,2

1Department of Epidemiology, College of Public Health and Health Professions and College of Medicine, University of Florida, Gainesville, Florida, USA, 2Student Health Care Center, University of Florida, Gainesville, Florida, USA, and 3School of Physician Assistant Studies, College of Medicine, University of Florida, Gainesville, Florida, USA

Background. Acute pharyngitis is a frequent illness presenting in outpatient settings. Antibiotics are only recommended for bacterial pharyngitis caused by group A β-hemolytic streptococci (GAS); however, infections with non–group A β-hemolytic streptococci (NGAS) have similar clinical presentations and are common in young adult populations. The objective of this study was to analyze the performance of a current (expert) diagnostic algorithm for GAS pharyngitis, the Centor score, and compare it to alternative models developed to predict GAS and NGAS in a college student population.

Methods. Electronic health records were obtained for all patients who received a streptococcal rapid antigen detection test (RADT) and/or a bacterial throat culture (n = 3963) at a southeastern US university in 2014. Bivariate and multivariable regression models (least absolute shrinkage and selection operator [LASSO] and stepwise-selected) were fitted to assess and compare their diagnostic performances for GAS-positive and NGAS-positive infections.

Results. Prevalence of GAS was 18.8%. In the subset of RADT-negative patients who received bacterial throat cultures (n = 313), growth of NGAS occurred in 34.8%, with group C streptococci the most frequent isolate. Mean Centor score was higher for NGAS (3.2) vs GAS (2.9) infections (P = .0111). The area under the curve (AUC) for GAS prediction was 0.64 using the Centor score and 0.70 using the LASSO model. For NGAS, the most important features were cough, pharyngeal erythema, tonsillar exudate, and gastrointestinal symptoms (AUC = 0.63).

Conclusions. GAS and NGAS pharyngitis were indistinguishable among college students in this study utilizing a commonly applied decision score. Alternative models using additional clinical criteria may be useful for supporting diagnosis of this common illness.

Keywords. clinical decision support systems; group A Streptococcus; non–group A Streptococcus; pharyngitis.

Acute pharyngitis ("sore throat") is a frequent illness that accounts for an estimated 4% of all primary care and emergency department visits annually in the United States (US) [1]. Although the majority of pharyngitis cases are attributed to a viral etiology (requiring no antimicrobial treatment), group A β-hemolytic Streptococcus (GAS) is responsible for approximately 5%–10% of these infections in adults and 15%–30% in children in whom antibiotic therapy is indicated [2]. Treatment of GAS pharyngitis with antibiotics is recommended to shorten symptom duration, reduce transmission, and prevent complications that are suppurrative (eg, peritonsillar or retropharyngeal abscess, cervical lymphadenitis, mastoiditis) and nonsuppurrative (eg, acute rheumatic fever) [3].

The clinical presentation of GAS pharyngitis often resembles other respiratory infections [4] and consequently, a clinical decision-making tool known as the Centor score was developed to help clinicians estimate the probability of GAS and judge whether to proceed with laboratory testing. The Centor score is a 4-point algorithm that predicts the likelihood of a GAS infection based on 4 symptoms: fever, absence of cough, cervical lymphadenopathy, and tonsillar exudate [5]. The American College of Physicians (ACP) recommends performing a streptococcal rapid antigen detection test (RADT) for individuals with Centor scores of 2–3 and empiric antibiotic treatment for individuals with Centor scores of 2 and empiric antibiotic treatment for individuals with Centor scores of 4 [4]. Among children, a modified version of the Centor score, the McIsaac score, is employed since it assigns an extra point to children aged 3–14 years, who tend to have the highest prevalence of GAS [6].

Both the ACP and the Infectious Diseases Society of America (IDSA) recommend backup bacterial throat cultures for children and adolescents with symptoms of pharyngitis who
Rich et al

Patient Consent Statement

A waiver of informed consent for record abstraction and secondary data analysis was approved as exempt by the Institutional Review Board at the University of Florida (reference numbers IRB201500184 and IRB201802893). The study was performed in accordance with the Helsinki Declaration.

Study Parameters

Patient demographics (age, gender) were collected and EHR data were extracted for components of the Centor score (fever, cough, cervical lymphadenopathy, and tonsillar exudate), as well as other clinical factors, including history of tonsillectomy, sore throat, sore throat onset (days), pharyngeal erythema, temperature, difficulty swallowing, runny nose/nasal congestion, headache, ear pain, and gastrointestinal symptoms (including abdominal pain, nausea, vomiting, and diarrhea). Fever was defined as reported objective measurement either in clinic or at home of 38°C (100.4°F) or greater. Tactile or subjective fever was excluded. Missing categorical data were coded as unknown in the descriptive analysis and handled with multiple imputation—a method to infer the value of missing data points—prior to fitting the multivariable models. This procedure is described in more detail in the Statistical Analysis section. The proportion of missing data ranged from 0 to 0.1% for demographics and 0 to 38.8% for each symptom.

Laboratory Diagnosis

Diagnosis of GAS pharyngitis was determined using the QuickVue In-Line RADT via throat swab. The sensitivity and specificity of the RADT in the general population have been reported as 64.6% and 96.79%, respectively [15]. A subset of RADT-negative throat swab specimens was sent to external laboratories for routine upper respiratory cultures at the clinical provider’s discretion. In the event the culture results were found positive for GAS, these patients were grouped into the GAS-positive population. Patients with positive throat culture results for group C or G streptococci were included in the NGAS pharyngitis population. The culture-negative control population included patients with no growth or growth of group B or F Streptococcus species (as these species are not known to cause pharyngitis) or non-Streptococcus species (Hemophilus influenzae, routine upper respiratory flora, or Staphylococcus aureus) on the upper respiratory throat culture.

Statistical Analysis

Demographic and clinical characteristics of patients with GAS, NGAS, RADT-negative, and culture-negative infections were compared using $\chi^2$ test for categorical variables. Welch 2-sample $t$ test and Wilcoxon rank-sum test were used for normally and nonnormally distributed continuous variables, respectively. Bonferroni $P$ value correction was applied to adjust for multiple comparison in the descriptive analysis. Univariable
logistic regression was performed to predict GAS infections (vs RADT-negative infections) based on the 4-factor Centor score, which we treated categorically. Multivariable models were fitted to associate uncorrelated variables (ie, with a Pearson correlation coefficient <0.40) with GAS and NGAS infections using 2 feature selection procedures to identify the best model fit: a less restrictive bidirectional (forward and backward) stepwise selection on the basis of Akaike information criterion and least absolute shrinkage and selection operator (LASSO), which is a more restrictive, machine learning–based modeling approach. The RADT-negative population served as the control group in the prediction model for GAS infections, whereas the culture-negative population served as the control group in the prediction model for NGAS infections. Measures of sensitivity, specificity, positive predictive value, and negative predictive value and the receiver operating characteristic (ROC) curves were computed for the multivariable (LASSO and stepwise-selected) models of GAS and NGAS infections and summarized by plotting the area under the curve (AUC). All analyses were conducted using R statistical programming software, version 3.6.0 [16]. The following packages were used: Amelia to perform 5 combinations of multiple imputation for the missing categorical data, MAMI for model selection and averaging over the 5 multiply imputed datasets, and ROCR to compute and visualize ROC curves [17].

RESULTS

Characteristics of Study Population
A total of 3963 patients received a RADT and/or bacterial throat culture at the health care center between 1 January 2014 and 31 December 2014. Of these patients, 18.8% tested positive for GAS. Thirty-four patients who originally tested negative on the RADT were found to be positive for GAS upon bacterial throat culture. Bacterial throat cultures were performed for 407 patients (313 who tested negative on the RADT) in whom growth of NGAS occurred in 34.8% (n = 109). Group C was the most common isolate—attributed to 75.2% of NGAS infections.

Clinical Presentations
In comparing the symptom presentation of patients with GAS-positive vs RADT-negative pharyngitis, we observed symptoms of runny nose/nasal congestion and cough more commonly among RADT-negative patients, whereas pharyngeal erythema, tonsillar exudate, and adenopathy were more common among GAS-positive patients (Table 1). Centor scores tended to be higher in the GAS-positive population, with a mean score of 2.9 in the GAS-positive population compared to 2.3 in the RADT-negative population (P < .0001). In the analysis of GAS vs NGAS pharyngitis, patients with NGAS infections were more likely to present with gastrointestinal symptoms and tonsillar exudate. Similarly, patients with NGAS pharyngitis were also more likely to present with tonsillar exudate when compared to culture-negative patients.

Multivariable Prediction of GAS and NGAS
Centor scores between 1 and 4 were associated with increased odds of GAS compared to RADT-negative infections (P < .05; Table 2). Increasing Centor scores corresponded to increased odds of GAS pharyngitis, with a Centor score of 4 indicating 4.74 times increased odds of GAS infection compared to a score of 0 (95% confidence interval [CI], 3.21–7.02). Likewise, higher Centor scores (eg, scores of 3 and 4) were also predictive of NGAS-positive compared to culture-negative infections at P < .05. A Centor score of 4 was indicative of 3.31 times (95% CI, 1.46–12.71) increased odds of NGAS pharyngitis, compared to a score of 0.

Model Performance
The models for GAS outperformed all the models for NGAS (Figure 1). The area under the ROC curve (AUC) for the bivariable Centor score model prediction accuracy was 0.64 for GAS and 0.59 for NGAS. The mean AUC for the LASSO model prediction accuracy of GAS on all 5 imputed datasets was 0.70 whereas for NGAS it was 0.59. The stepwise model prediction accuracy was comparable for both outcomes (mean AUC = 0.71 for GAS and 0.63 for NGAS), again on all 5 imputed datasets.

DISCUSSION
In this study, we evaluated the diagnostic paradigm for acute bacterial pharyngitis in a population of college students from a university in the southeastern US who presented with symptoms of pharyngitis. The proportion of individuals with acute...
### Table 1. Characteristics of Patients Who Presented With Symptoms of Pharyngitis Stratified by Diagnosis

| Characteristic                      | RADT-Negative Population<sup>a</sup> | GAS-Positive Population<sup>b</sup> | P Value for Difference: RADT-Negative vs GAS-Positive | NGAS-Positive Population<sup>c</sup> | P Value for Difference: GAS-Positive vs NGAS-Positive | Culture-Negative Population<sup>d</sup> | P Value for Difference: NGAS-Positive vs Culture-Negative |
|-------------------------------------|--------------------------------------|-------------------------------------|-------------------------------------------------------|--------------------------------------|-------------------------------------------------------|--------------------------------------|-----------------------------------------------------------|
| Age, y, mean (SD)                   | 20.5 (2.9)                           | 20.4 (2.8)                           | .3481                                                 | 20.9 (3.0)                           | .7642                                                 | 21.1 (3.7)                           | .1666                                                     |
| Gender                              |                                      |                                     |                                                       |                                      |                                                       |                                      |                                                            |
| Female                              | 1958 (60.9)                          | 432 (58.1)                          | .1633                                                 | 70 (64.2)                            | .2646                                                 | 129 (63.5)                          | 1.0000                                                    |
| Male                                | 1256 (39.1)                          | 312 (41.9)                          |                                                       | 39 (35.8)                            |                                                       | 74 (36.5)                           |                                                            |
| Symptoms                            |                                      |                                     |                                                       |                                      |                                                       |                                      |                                                            |
| History of tonsillectomy            | 208 (6.5)                            | 30 (4.1)                            | .0162                                                 | 7 (6.4)                              | .3863                                                 | 12 (6.0)                            | 1.0000                                                    |
| Fever                               | 1490 (47.0)                          | 361 (49.3)                          | .2762                                                 | 60 (55.0)                            | .3109                                                 | 99 (49.0)                           | .3697                                                     |
| Difficulty swallowing               | 355 (11.0)                           | 106 (14.5)                          | .0172                                                 | 18 (23.7)                            | .6665                                                 | 27 (13.9)                           | .6319                                                     |
| Runny nose/nasal congestion         | 1563 (48.6)                          | 272 (36.6)                          | <.0001                                                | 37 (38.5)                            | .4566                                                 | 89 (49.7)                           | .0996                                                     |
| Cough                               | 1356 (42.1)                          | 208 (28.0)                          | <.0001                                                | 21 (21.6)                            | .0646                                                 | 65 (34.9)                           | .0298                                                     |
| Headache                            | 966 (30.0)                           | 213 (28.6)                          | .6989                                                 | 38 (45.8)                            | .1383                                                 | 67 (43.2)                           | .8090                                                     |
| Ear pain                            | 366 (11.4)                           | 73 (9.8)                            | .4745                                                 | 14 (19.4)                            | .2967                                                 | 27 (18.0)                           | .9403                                                     |
| Gastrointestinal symptoms           | 434 (13.5)                           | 74 (9.9)                            | .0286                                                 | 23 (25.6)                            | .0023                                                 | 28 (17.0)                           | .1404                                                     |
| Pharyngeal erythema                 | 2340 (72.8)                          | 683 (91.9)                          | <.0001                                                | 103 (95.4)                           | .2865                                                 | 178 (87.7)                          | .0473                                                     |
| Tonsillar exudate                   | 666 (20.7)                           | 304 (41.0)                          | <.0001                                                | 66 (60.6)                            | .0002                                                 | 86 (42.6)                           | .0037                                                     |
| Adenopathy (any)                    | 1549 (48.2)                          | 562 (75.6)                          | <.0001                                                | 87 (79.8)                            | .4034                                                 | 161 (79.3)                          | 1.0000                                                    |
| Sore throat onset, d, mean (SD)     | 3.9 (4.6)                            | 3.4 (3.6)                           | .0030                                                 | 3.6 (3.7)                            | .7365                                                 | 4.6 (7.6)                           | .1206                                                     |
| Temperature, °C, mean (SD)          | 370 (1.5)                            | 370 (3.6)                           | .9600                                                 | 37.3 (0.7)                           | .0594                                                 | 372 (0.8)                           | .5468                                                     |
| Centor score                        |                                      |                                     | <.0001                                                |                                      | .1066                                                 |                                      | .0707                                                     |
| 0                                   | 687 (21.3)                           | 79 (10.6)                           | 8 (7.3)                                               | 32 (15.8)                            |                                                       |                                      |                                                            |
| 1                                   | 1280 (39.8)                          | 202 (27.2)                          | 23 (21.1)                                             | 52 (25.6)                            |                                                       |                                      |                                                            |
| 2                                   | 816 (25.3)                           | 248 (33.3)                          | 33 (30.3)                                             | 58 (28.6)                            |                                                       |                                      |                                                            |
| 3                                   | 326 (10.1)                           | 155 (20.8)                          | 31 (28.4)                                             | 48 (23.6)                            |                                                       |                                      |                                                            |
| 4                                   | 110 (3.4)                            | 60 (8.1)                            | 14 (12.8)                                             | 13 (6.4)                             |                                                       |                                      |                                                            |
| Centor score (continuous), mean (SD)| 2.3 (1.0)                            | 2.9 (1.1)                           | <.0001                                                | 3.2 (1.1)                            | .0111                                                 | 2.8 (1.2)                           | .0044                                                     |

Data are presented as No. (%) unless otherwise indicated. Missing values were retained as unknown for this table and therefore, not all proportions and inverse proportions add up to 1. P values are for χ² test (categorical variables), Wilcoxon rank-sum test (age, sore throat onset), or Welch 2-sample t test (temperature, Centor score). Only P values significant after Bonferroni correction (at P < .00098) are shown in bold.

Abbreviations: GAS, group A Streptococcus; NGAS, non-group A Streptococcus (includes groups C and G streptococci); RADT, rapid antigen detection test; SD, standard deviation.

<sup>a</sup>RADT-negative population includes all RADT-negative patients, less those positive for GAS on the throat culture.

<sup>b</sup>GAS-positive population includes patients positive for GAS on the RADT or throat culture.

<sup>c</sup>NGAS-positive population includes patients who tested RADT negative and culture positive for NGAS species.

<sup>d</sup>Throat culture-negative population includes patients who tested RADT negative and had no growth or growth of non-Streptococcus species (Hemophilus influenzae, routine upper respiratory flora, or Staphylococcus aureus) on the throat culture.
Table 3. Prediction of Group A Streptococcus and Non–Group A Streptococcus Infections Based on Symptom Presentation Using Multivariable Logistic Regression

| Characteristic                  | GAS-Positive vs RADT-Negative Infection | GAS-Positive vs NGAS-Positive Infection | NGAS-Positive vs Culture-Negative Infection |
|---------------------------------|----------------------------------------|----------------------------------------|--------------------------------------------|
|                                 | LASSO Model                            | Stepwise Model                          | LASSO Model                                | Stepwise Model                          | LASSO Model                            | Stepwise Model                          |
| Age (years)                     | ...                                    | ...                                     | ...                                        | ...                                      | ...                                    | ...                                     |
| Gender (male vs female)         | ...                                    | ...                                     | ...                                        | ...                                      | ...                                    | ...                                     |
| Symptoms (ref. = no)            | ...                                    | ...                                     | ...                                        | ...                                      | ...                                    | ...                                     |
| History of tonsillectomy        | ...                                    | ...                                     | ...                                        | ...                                      | ...                                    | ...                                     |
| Fever                           | ...                                    | ...                                     | ...                                        | ...                                      | ...                                    | ...                                     |
| Cough                           | 0.70 (0.59–0.85)                       | 0.75 (0.59–0.95)                        | ...                                        | 1.38 (0.89–2.77)                        | ...                                    | 0.91 (0.47–1.77)                        |
| Adenopathy                      | 2.35 (1.94–2.85)                       | 2.37 (1.96–2.88)                        | ...                                        | ...                                      | ...                                    | ...                                     |
| Pharyngeal erythema             | 2.63 (1.97–3.50)                       | 2.58 (1.94–3.44)                        | ...                                        | ...                                      | 2.43 (0.89–6.65)                       | ...                                     |
| Tonsillar exudate               | 1.68 (1.40–2.02)                       | 1.69 (1.41–2.03)                        | 0.45 (0.30–0.68)                           | 0.46 (0.30–0.71)                        | 2.08 (1.29–3.34)                       | 1.91 (1.17–3.12)                        |
| Difficulty swallowing           | ...                                    | ...                                     | ...                                        | ...                                      | ...                                    | ...                                     |
| Runny nose/nasal congestion     | ...                                    | ...                                     | ...                                        | ...                                      | ...                                    | ...                                     |
| Headache                        | ...                                    | ...                                     | ...                                        | 0.79 (0.38–1.65)                        | ...                                    | ...                                     |
| Ear pain                        | ...                                    | ...                                     | ...                                        | ...                                      | ...                                    | ...                                     |
| Gastrointestinal symptoms (any) | ...                                    | ...                                     | ...                                        | 0.57 (0.34–0.97)                        | ...                                    | 1.10 (0.55–2.17)                        |
| Sore throat onset (days)        | ...                                    | ...                                     | ...                                        | ...                                      | ...                                    | ...                                     |

Results are presented as odds ratio (95% confidence interval).

Abbreviations: GAS, group A Streptococcus; NGAS, non-group A Streptococcus (includes groups C and G streptococci); RADT, rapid antigen detection test.
NGAS, *Fusobacterium necrophorum*, an anaerobic bacterial pathogen, has recently been recognized as an emerging pharyngitis pathogen of importance, particularly among young adults and adolescents [10, 19]; however, this bacterium was not tested for in the present study as it is not currently included in the standard upper respiratory culture. Future research should investigate the longitudinal trends and outcomes of pharyngitis infections arising from non–group A *Streptococcus* (NGAS) and *β*-hemolytic groups C and G (*S. dysgalactiae* subspecies *equisimilis*), and *F. necrophorum* to determine whether prevalence of these pathogens is increasing over time and whether treatment should be indicated.

This study also had limitations. Since bacterial throat cultures were ordered on a case-by-case basis, and not for all RADT-negative patients, this study likely suffered from misclassification bias as the number of NGAS infections is likely an underestimation. Furthermore, the number of true GAS infections may have also been underestimated given the relatively low sensitivity of the RADT (64.6%). Although the nonrandom selection of individuals who received cultures reflects current clinical practice, it likely resulted in a study population with more severe illness than would otherwise be expected in the general population as clinicians may have been more likely to order throat cultures for patients with acute or persistent symptoms. This may explain why tonsillar exudate, a Centor score criterion, was associated with higher odds of NGAS than GAS in the study; however, this finding has also been observed in a prior meta-analysis [18]. Future studies should retrieve throat cultures from all RADT-negative patients to eliminate sources of misclassification bias. Additionally, medical record abstraction by multiple assessors can lead to information bias, and therefore, assessor agreement (such as through calculation of κ statistic) should be considered when validating data. Last, this analysis was also limited due to its retrospective nature and the use of incomplete EHR data, which required imputation on multiple variables. Multivariable estimates were averaged across 5 multiply imputed datasets to account for the uncertainty associated with both the imputation process and the variable selection procedures, however, and thus, this source of bias is likely minute.

**CONCLUSIONS**

In this study, GAS and NGAS pharyngitis were indistinguishable among college students using a commonly applied (expert) decision score, the Centor score. The prevalence of GAS
among college students with symptoms of pharyngitis is more reflective of the expected prevalence in pediatric, rather than in adult, populations. Taken together, closer attention to the diagnostic paradigm and development of new clinical decision support systems, such as those presented in this study, to predict GAS and NGAS pharyngitis in the college student population is warranted. Given the high occurrence of NGAS among college students evidenced in both the current and previous studies, and the potential for shared gene content between Streptococcus species, further study of the long-term consequences of untreated NGAS infections is also warranted.

Notes

Acknowledgments. We would like to acknowledge the early contributions of Salma Rawof, MD, Rose Michele Emery, MD, Cheri Sellers, PA-C, and Alyson Listhaus, MPH, to the initial design of the study. Additionally, we would like to thank the health support technicians at the Student Health Care Center for their role in extracting the data for the analysis.

Financial support. This work has been supported in part by the National Institute of Allergy and Infectious Diseases (grant number 1-R01-AI141810-01 to M. P.); and the University of Florida’s (UF) “Creating the Healthiest Generation” Moonshot initiative, supported by the UF Office of the Provost, UF Office of Research, UF Health, UF College of Medicine, and UF Clinical and Translational Science Institute (to M. P.).

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Barnett ML, Linder JA. Antibiotic prescribing to adults with sore throat in the United States, 1997-2010. JAMA Intern Med 2014; 174:138.
2. Bisno AL, Gerber MA, Gwaltney Jr JM, et al. Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis. Clin Infect Dis 2002; 35:113–25.
3. Centers for Disease Control and Prevention. Pharyngitis (strep throat). In: Group A streptococcal (GAS) disease. 2018. https://www.cdc.gov/groupastrep/diseases-hcp/strep-throat.html. Accessed 11 June 2019.
4. Dingle TC, Abbott AN, Fang FC. Reflexive culture in adolescents and adults with group A streptococcal pharyngitis. Clin Infect Dis 2014; 59:643–50.
5. Centor RM, Withenspoon JM, Dalton HP, et al. The diagnosis of strep throat in adults in the emergency room. Med Decis Making 1991; 1:239–46.
6. McIsaac WJ, White D, Tannenbaum D, Low DE. A clinical score to reduce unnecessary antibiotic use in patients with sore throat. CM AJ 1998; 158:75–83.
7. Shulman ST, Bisno AL, Clegg HW, et al; Infectious Diseases Society of America. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis 2012; 55:e66–102.
8. Ramirez C, Turner J, Chance JE. Non-group A streptococci as common isolates from throat culture among college students with pharyngitis. J Am Coll Health 2011; 59:237.
9. Mitchell MS, Sorrentino A, Centor RM. Adolescent pharyngitis: a review of bacterial causes. Clin Pediatr (Phila) 2011; 50:1091–5.
10. Centor RM. Expand the pharyngitis paradigm for adolescents and young adults. Ann Intern Med 2009; 151:812.
11. Turner JC, Hayden GJ, Kielca D, et al. Association of group C beta-hemolytic streptococci with endemic pharyngitis among college students. JAMA 1990; 264:2644–7.
12. Turner JC, Hayden FG, Lobo MC, et al. Epidemiologic evidence for Lancefield group C beta-hemolytic streptococci as a cause of exudative pharyngitis in college students. J Clin Microbiol 1997; 35:1–4.
13. Chandrani HK, Jain R, Pammasundari P, Group C. Streptococcus causing rheumatic heart disease in a child. J Emerg Med 2015; 49:12–4.
14. Babbar A, Itzek A, Pieper DH, Nitsche-Schmitz DP. Detection of Streptococcus pyogenes virulence genes in Streptococcus dysgalactiae subsp. equisimilis from Vellore, India. Folia Microbiol (Praga) 2018; 63:581–6.
15. Gurol Y, Akan H, Izbirak G, et al. The sensitivity and the specificity of rapid antigen test in streptococcal upper respiratory tract infections. Int J Pediatr Otorhinolaryngol 2010; 74:591–3.
16. R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, 2019.
17. Sing T, Sander O, Beerenwinkel N, Lengauer T. ROC: visualizing classifier performance in R. Bioinformatics 2005; 21:3940–1.
18. Thai TN, Dale AP, Ebell MH. Signs and symptoms of group A versus non-group A strep throat: a meta-analysis. Fam Pract 2018; 35:231–8.
19. Centor RM, Akinson TP, Ralliff AE, et al. The clinical presentation of Fusobacterium-positive and streptococcal-positive pharyngitis in a university health clinic: a cross-sectional study. Ann Intern Med 2015; 162:241.