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Group A Streptococcal Tonsillopharyngitis: The Diagnostic Power of the Centor and McIsaac Clinical Prediction Models at Different Pre-probability

ABSTRACT

Background: The power of diagnostic tests is affected by pre-test probability, and clinical prediction models must be validated in different populations. The aim of this study was to determine the diagnostic value of symptoms and signs for group A Streptococcus tonsillopharyngitis and diagnostic power of Centor and McIsaac criteria in a patient population with different pre-probability.

Methods: The study was conducted between September 2019 and February 2020 in Adnan Menderes University Hospital's outpatient clinics. A total of 405 patients older than 36 months who presented with one of the complaints of acute tonsillopharyngitis participated in the study. Throat swab samples were taken from each patient. The diagnostic value of symptoms and signs was determined by performing univariate analysis and multiple logistic regression analysis.

Results: The mean age of 405 patients was 24.7 (3-81 years). While group A Streptococcus positivity was 7.9% over the age of 3, the frequency of group A Streptococcus was 16.8% in children under the age of 15 and 4.7% in adolescents and adults. Group A Streptococcus positivity was 45.8% in those with a Centor score of 4 and 35.7% in those with a McIsaac score of 4-5. In regression analysis, only 4 criteria included in the Centor score entered the model ($P < .05$).

Conclusions: Centor and McIsaac clinical prediction models were found to be valid in our patient group with low group A Streptococcus positivity. However, although the diagnostic power of both clinical prediction models does not change in the patient population with low group A Streptococcus positivity, they cannot increase the post-test probability above 40-50%.

Keywords: Centor clinical prediction model, diagnostic power, group A Streptococcus, sore throat

INTRODUCTION

Acute tonsillopharyngitis is a common cause of patient–physician encounters worldwide, and sore throat is one of the most common presenting complaints of these cases seen in primary care.[1,2] Acute pharyngitis is the second most common acute infection seen by family physicians, with 3-6% of all office visits.[1,3,4]

Self-limiting viral infections are responsible for the vast majority of sore throats in adults. On the other hand, the most common bacterial cause is group A Streptococcus (GAS); it occurs with a frequency of 15-30% in children and 5-15% in adults globally.[2,4]

The patients, especially children with acute GAS pharyngitis, present with acute onset of fever and sore throat. In untreated cases of GAS pharyngitis, suppurative complications such as necrotizing fasciitis and peritonsillar abscess can be seen, and very few of them can trigger acute rheumatic fever (ARF). On the other hand, ARF and its most important sequelae, rheumatic heart disease, continue to be an important public health problem especially in low- and middle-developed countries and among minority groups in developed countries.[2,5]

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In acute pharyngitis cases, clinicians face with the dilemma of prescribing antibiotics to reduce the risk of ARF or withholding antibiotics to minimize antibiotic-related harms.[2] The guidelines of North America, Finland, and France recommend that a microbiological investigation in suspected cases should be performed and that antibiotics should be given for the cases with confirmed GAS to prevent suppurative complications and ARF. However, other European guidelines do not routinely recommend microbiological tests and limit antibiotic treatment to selected cases.[6-8]

Oropharynx examination is not sufficient for the differential diagnosis of acute pharyngitis. So, many international organizations recommend the use of clinical prediction models in diagnosis.[5,9]

Although the 4-point Centor criteria have been shown to be effective in predicting GAS pharyngitis in pre-adolescent children, the model is controversial in adolescent and young adult patients.[10] On the other hand, it has been suggested that clinical prediction models may not be effective in new settings and their validity should be demonstrated at different times and in different populations.[5,11] It is also known that the power of diagnostic tests is affected by pre-test probability.[12]

Therefore, in this study, we aim to determine the strength of the Centor and McIsaac criteria and diagnostic value of symptoms and signs for GAS pharyngitis in a patient population with different pre-probability.

METHODS

This prospective study of the methodological design was conducted between September 2019 and February 2020 in Aydın Adnan Menderes University (ADU) Hospital's Family Medicine, Ear-Nose-Throat (ENT), Pediatrics, and Emergency outpatient clinics. Patients aged 3 years or more, and presented with sore throat or other acute tonsillopharyngitis complaints of at least 1-day duration, comprised the target population of the study. Patients and parents giving written consent were enrolled in the study. Patients were excluded if they had had their complaints for more than 21 days or high risk of serious infection or had participated in another study within the last 3 weeks.

Considering the potential number of patients in hospital outpatient clinics during the study period, the manpower and the budget for the study, as well as the 10-case rule per variable suggested in the literature,[13] the sample size of our study has been determined as 300. However, since the study includes both children and adults, the sample size has been increased by 1/3 to 400 in order to increase the power of statistical analysis.

Following the informed written consent, the symptoms and demographic characteristics of the patients who participated in the study were recorded on a standardized data collection form by one of the researchers (MDB). Upper respiratory tract physical examination was performed in all patients by the same investigator. Data were non-systematically collected by the same investigator over a period of 6 months and in 4 different practice settings. As a result of questioning and physical examination, the scores of all patients were calculated according to the Centor and McIsaac scores. One point was given in the case of measuring fever above 38°C, presence of exudate in the tonsillar and oropharynx area, presence of sensitive anterior cervical lymph nodules, or no cough complaint. For McIsaac score calculation, one score was added if the patient was between 3 and 14 years old, and no score was given if the patient was between 15and 45 years old. One point was subtracted from the total score obtained in patients over the age of 45.

Throat swabs for throat culture were obtained from all patients. Throat cultures were studied in Aydın ADU Practice and Research Hospital's Medical Microbiology Laboratories.

Necessary administrative permissions for the study were obtained from ADU Practice and Research Hospital Chief Physician, and ethics committee permissions were obtained from ADU Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (protocol no: 2019/64). The study has been funded by ADU Scientific Research Projects Department (TPF-19001).

The data of the study were evaluated with the Statistical Package for the Social Sciences 18.0 statistical program, and $P < .05$ was considered statistically significant. Categorical variables were presented as numbers and percentages, and numerical variables as mean and standard deviation. The frequency of GAS was calculated according to the risk levels determined by Centor and McIsaac criteria for the pediatric age group and adults who presented for sore throat or at least one of the complaints of acute pharyngitis. The relationship between the total scores obtained for each patient and GAS positivity was evaluated using Kendall's tau-b correlation test. Univariate analysis (chi-square test, Fisher's exact test, *t* test) and multiple logistic regression analysis were performed to determine the diagnostic value of symptoms and signs based on the diagnosis of GAS pharyngitis (laboratory-confirmed GAS culture positivity). For the relationship of each predictor to the main outcome, odds ratios were given with 95% CIs. The diagnostic power of the Centor and McIsaac clinical prediction model components was determined by taking into account the sensitivity and selectivity for diagnostic accuracy and the possibility of GAS pre-test and post-test by taking a single throat culture as the gold standard for diagnosing GAS infection (diagnostic power = post-test probability − pre-test probability/prevalence). In addition, the area under the receiver operating characteristic (ROC) curve (AUC) was calculated by performing ROC analysis to determine the general performance of clinical predictive models.

MAIN POINTS

- The only four predictors in Centor scores among symptoms and signs for GAS pharyngitis in a patient population with lower pre-probability have been found to have a diagnostic value of GAS positivity.
- The Centor score is valid in the patient group with lower frequency of GAS positvity.
- However the diagnostic power of Centor and McIsaac predictive systems appears to be weakening in low prevalence groups.
- Our results does not support Centor's aggressive antibiotic treatment recommendations at higher scores.

RESULTS

Descriptive Data (Characteristics of the Study Population)

A total of 418 volunteers were reached within the scope of the purpose and inclusion criteria during the study period, of whom 13 patients were excluded from the study because they had started taking antibiotics previously. Approximately half of the patients (52.35%; 212 patients) were admitted to the adult emergency department. Most of the patients were admitted during the winter months (76.30%; 309 patients). Nearly all of the patients included in the study had sore throat (386 patients; 95.31%). The mean duration of the complaints was 2.63 ± 2.00 days.

The most common findings on physical examination in patients with pharyngitis were hyperemic pharynx (402 patients; 99.26%) and hypertrophic tonsils (203 patients; 50.12%). Among the predictors included in the Centor criteria, fever was the one that was observed with the highest rate (47.16%; 191 patients). The majority of cases were in the low-probability group compared to the Centor (60.00%) and McIsaac (55.56%) predictive systems (Table 1).

Effectiveness of Centor and McIsaac Clinical Prediction Models in Recognizing Group A Streptococcus Tonsillopharyngitis

In throat culture, 7.90% of the patients had GAS and 3.46% had non-GAS streptococci. Group A Streptococcus positivity in culture was 16.82% in children and 4.70% in adolescents and adults. Group A Streptococcus positivity in culture according to age groups and Centor scores is shown in Table 2. For those who live in rural areas (5.69% vs. 14.15%; $P = .010$), those who have 12 years or less education (3.70% vs. 10.70%), and those who do not work actively (2.75% vs. 9.80%), GAS was produced significantly more ($P < .05$). Gender and marital status were not associated with GAS positivity ($P > .05$).

Table 1. Centor and McIsaac Criteria Scores and Categories, n = 405

Predictors	Number	Percent
Fever (>38.0°C)	191	47.16
Exudate	82	20.25
Absence of cough	152	37.53
Sensitive cervical LAP	117	28.89
CENTOR Scores Mean ± SD; Median (25-75%)	1.3 ± 1.1; 1.0 (0-2.0)	
Centor Categories	Number	Percent
Score 0-1	243	60.00
Score 2-3	137	33.83
Score 4	25	6.17
McIsaac Age Groups	Number	Percent
Age < 15	107	26.42
15 ≤ Age ≤ 45	248	61.23
Age > 45	50	12.35
McIsaac Scores Mean ± SD; Median (25-75%)	1.5 ± 1.5; 1.0 (0-2.0)	
Mc Isaac Categories	Number	Percent
Score ≤1	225	55.56
Score 2-3	138	34.07
Score ≥4	42	10.37

LAP, lymphadenopathy.

Group A Streptococcus positivity was higher in the patients who came in the spring months compared to those who came in the winter months (5.83% vs. 14.58%; $P = .010$), and it was higher in the patients who came to outpatient clinics (family medicine, pediatrics, and ENT) compared to those who came to emergency services (5.28% vs. 11.95%; $P = .025$).

In the presence of fever (13.09%; $P = .001$), exudate (26.25%; $P < .001$), and sensitive lymphadenopathy (LAP) (17.95%; $P < .001$) and in the absence of cough (16.20%; $P < .001$), more GAS were grown in the culture. There was a moderate positive correlation between Centor and McIsaac total scores and GAS positivity in culture. As the Centor ($r = 0.305$; $P < .001$) and McIsaac ($r = 0.306$; $P < .001$) scores (predictor) increased, the probability of GAS reproduction in culture increased.

The presence of tonsillar exudate increased the probability of having GAS pharyngitis from 7.90% to 25.61%, sensitive anterior cervical LAP to 17.95%, absence of cough to 15.79%, absence of throat-clearing to 13.64%, fever to 13.09%, hypertrophic tonsils to 12.81%, the absence of nasal discharge to 12.57%, and the history of temperature increase to 10.29%. The power of other clinical and demographic characteristics was not found to be significant in diagnosing GAS positivity. Although it was significant in binary analysis, the probabilities were very low in diagnosing GAS pharyngitis. When we performed multiple analysis, only 4 predictors that constitute the Centor criteria provided a significant increase: fever above 38°C (sensitivity 78.13% and selectivity 55.50%), presence of tonsillar exudate (sensitivity 65.63% and selectivity 83.65%), absence of cough (sensitivity 75.00% and selectivity 65.68%), and presence of sensitive anterior cervical LAP (sensitivity 65.63% and selectivity 74.26%).

The percentage of patients showing GAS positivity according to the clinical scores obtained in our study are shown in Table 3, in comparison with the results of the studies published in the literature.

Logistic Regression Analysis

Increased temperature, absence of throat clearing, absence of cough, absence of nasal discharge, exudate, fever, sensitive LAP, anterior cervical LAP, and hypertrophic tonsils were independent variables associated with our dependent variable, which is the GAS positivity in culture in patients with pharyngitis.

Multiple logistic regression analysis was performed to determine the effects and degree of effect of independent variables that were related in binary analysis to GAS positivity in culture, independent of other confounders. The second variable was excluded from the regression analysis because the sensitive anterior cervical LAP variable was highly correlated with the anterior cervical LAP variable with no sensitivity.

In the regression analysis where 8 variables were taken into account, only 4 variables included in the Centor criteria entered the model. Possibility of GAS positivity in culture in patients with pharyngitis was 4.33 times more in patients with exudate than in patients without exudate ($P = .001$), 3.21 times

Table 2. Risk of GAS and Non-GAS Pharyngitis by Age Group with 0, 1, 2, 3, or 4 Centor Points, n = 405

	Number GAS Positive/Total (%) and Non-GAS Positive/Total (%) by Age Group					
Centor Points	Child Positive/Total, n (%)		Adolescent and Adult Positive/Total, n (%)		Overall Positive/Total, n (%)	
	GAS+	Non-GAS+	GAS+	Non-GAS+	GAS+	Non-GAS+
0 Points	0/6 (0)	0/6 (0)	0/102 (0)	7/102 (6.9)	0/108 (0)	7/108 (6.5)
1 Points	4/30 (13.3)	2/30 (6.7)	1/112 (0.9)	1/112 (0.9)	5/142 (3.5)	3/142 (2.1)
2 Points	3/39 (7.7)	1/39 (2.6)	3/51 (5.9)	1/51 (2.0)	6/90 (6.7)	2/90 (2.2)
3 Points	4/18 (22.2)	1/18 (5.6)	6/23 (26.1)	1/23 (4.3)	10/41 (24.4)	2/41 (4.9)
4 Points	7/14 (50.0)	0/14 (0)	4/10 (40.0)	0/10 (0)	11/24 (45.8)	0/24 (0)
Overall	18/107 (16.82)	4/107 (3.7)	14/298 (4.70)	10/298 (3.46)	32/405 (7.90)	14/405 (3.46)

GAS, group A Streptococcus.

Table 3. Group A Beta Hemolytic Streptococcus Positivity According to the Clinical Scores Obtained in Our Study Compared to the Results of Studies Published in the Literature

Score	Our Study Age ≥ 15, n = 298 (95% CI)	Centor (1981) (Original Study), n = 286 (95% CI)	Wigton (1996) (Validation Study), n = 516 (95% CI)	Andrew (2012) Validation Study, n = 142 081 (95% CI)
Centor 0, s = 102	0 (0-0)	3 (0-16)	3 (0-14)	7 (7-8)
Centor 1, s = 112	0.9 (0-2.9)	7 (2-14)	14 (9-21)	12 (11-12)
Centor 2, s = 51	5.9 (0-12.8)	16 (8-27)	23 (17-30)	21 (21-22)
Centor 3, s = 23	26.1 (8.3-45.0)	34 (20-46)	45 (36-54)	38 (38-39)
Centor 4, s = 10	40.0 (11.1-72.7)	56 (35-77)	54 (42-67)	57 (56-58)
General	4.7 (2.3-7.2)	17 (14-23)	26 (24-32)	23 (22-23)
	Our Study Age ≥ 3, n = 405 (95% CI)	McIsaac (1998) (Original Study), n = 521 (95% CI)	McIsaac (2000) (Validation Study), n = 619 (95% CI)	Andrew (2012) Validation Study n = 206 870 (95% CI)
McIsaac 0, s = 126	0 (0-0)	3 (1-6)	1 (0-4)	8 (8-9)
McIsaac 1, s = 99	1 (0.0-3.6)	5 (2-10)	10 (6-16)	14 (13-14)
McIsaac 2, s = 80	10 (4.1-17.6)	11 (6-19)	17 (11-25)	23 (23-23)
McIsaac 3, s = 58	13.8 (5.2-23.6)	28 (18-41)	35 (25-45)	37 (37-37)
McIsaac 4, s = 42	36.6 (22.5-52.4)	53 (40-66)	51 (40-62)	55 (55-56)
General	7.9 (5.2-10.6)	14 (11-17)	17 (14-20)	27 (27-27)

more in patients with no cough than in patients with cough ($P = .012$), 2.58 times more in patients with fever above 38.0°C than in patients without fever ($P = .045$), and 2.42 times more in patients with sensitive cervical LAP than those without it ($P = .037$) (Table 4).

The overall performance of the model was assessed by AUC. Area under the curve was obtained as 0.845 (95% CI = 0.778-0.912; SE = 0.034; $P < .001$) when the Centor score was applied in patients over 14 years old, and AUC was obtained as 0.859 (95% CI = 0.807-0.912; SE = 0.027; $P < .001$) when the McIsaac score was applied in all patients over 3 years old (Figure 1).

DISCUSSION

In this study, our aim was to determine the diagnostic value of symptoms and signs for GAS pharyngitis and the effectiveness (diagnostic power) of the Centor and McIsaac criteria (scores). We considered patients who applied to the Family Medicine, Pediatrics, and ENT outpatient clinics and emergency of our university hospital with sore throat or at least one of other complaints of tonsillopharyngitis.

Our study has shown that Centor score is also valid in the patient group with pharyngitis in the hospital outpatient and emergency departments whose GAS positivity is much lower than that of the original Centor study performed only in the adult emergency department. In the logistic regression analysis, the same 4 predictors in Centor scores, among the variables that were found to have a significant relationship with GAS positivity in binary analysis, entered the model (Table 4). While the GAS positivity obtained in our study was outside the 95% CI of that of the original Centor study in low Centor scores, it was within this range in scores 3 and 4. This can be interpreted as the weakening of the Centor prediction model's ability to distinguish GAS pharyngitis in scores 1 and 2 at low pre-probabilities.

The original Centor model was developed by considering the GAS-positive culture result as the gold standard in the study group with 17% GAS positivity. The authors concluded that the

Table 4. Factors Affecting GAS Positivity in Culture in Binary and Multiple Analyses

Dependent Variable: GAS Positivity in culture

	Binary Analysis			Multiple Analysis (Forward LR)		
Independent Variables	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Absence of cough (Ref: presence of cough)	5.742	2.508-13.145	<.001	3.208	1.288-7.993	.012
Presence of exudate (Ref: absence of exudate)	9.765	4.479-21.288	<.001	4.332	1.802-10.413	.001
Presence of fever (Ref: absence of fever)	4.454	1.880-10.552	.001	2.578	1.022-6.504	.045
Presence of sensitive cervical LAP (Ref: absence of sensitive cervical LAP)	5.509	2.562-11.844	<.001	2.419	1.057-5.540	.037
Presence of hypertrophic tonsils (Ref: absence of hypertrophic tonsils)	4.798	1.930-11.929	.001	-	-	.337
Absence of nasal discharge (Ref: presence of nasal discharge)	3.163	1.457-6.870	.004	-	-	.448
Presence of fever in history (Ref: absence of fever in history)	2.539	1.071-6.019	.034	-	-	.619
Absence of throat-clearing (Ref: presence of throat-clearing)	2.345	1.098-5.007	.028	-	-	.305

GAS, group A Streptococcus; LR: likelihood ratio; OR, odds ratio; LAP, lymphadenopathy; NS, not significant.

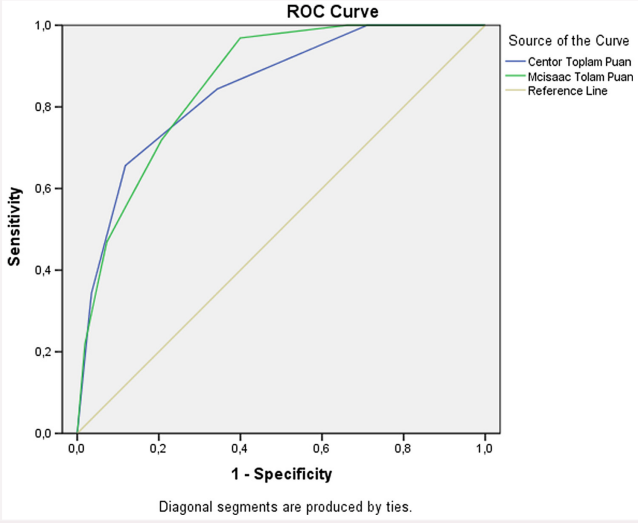

Figure 1. Receiver operating characteristic curves showing the performance of the Centor and McIsaac clinical prediction models for recognizing group A Streptococcus pharyngitis.

model helps the clinician to group patients for management decisions.[14] McIsaac et al[9,15] then developed a clinical prediction model in which the age of the patient was taken into account in addition to the symptoms and signs in the Centor prediction model and showed that the model was valid.

Apart from these studies where 2 prediction models were developed and validated in limited populations and small patient groups, the largest-scale validation study was conducted by Andrew et al in the United States. The validity of Centor and McIsaac clinical prediction systems was also shown in this study conducted with 206 870 patients with pharyngitis aged 3 years and older. As shown in Table 3, our results are well below the values obtained in these studies. The results of GAS positivity obtained in our country vary considerably and the values we obtain in children and adults are at the lower limits of the distribution range. Whatever the cause of low prevalence, there is an important problem raised by our study. The diagnostic power of Centor and McIsaac predictive systems appears to be weakening in low prevalence groups.

The contribution of clinical prediction models to clinical decisions in the diagnosis of GAS pharyngitis is controversial in the international literature. Cohen suggests that the McIsaac score alone can neither exclude nor confirm the diagnosis of GAS in children. He thinks that the 25% frequency in score 1 is too high to exclude the diagnosis, the 44% frequency in score 5 is too low to confirm the diagnosis, and the 52% selectivity also does not meet our current need to reduce antibiotics use.[16,17] According to Centor, the 4-point system is a good clinical prediction model in pre-adolescent tonsillopharyngitis, but the reliability of the model in adolescents and young adults becomes controversial. In GAS pharyngitis, penicillin treatment provides a significant reduction in symptom duration in adolescents and adults, unlike in children, and non-GAS bacterial agents (other Streptococcus groups and *Fusobacterium necrophorum* (FN)) are more common in adolescents and adults as possible reasons for this.[18]

On the other hand, there is a controversy in the management of adult patients with pharyngitis. The guidelines agree that no testing or treatment is appropriate for patients with low scores (0 and 1) but differ for patients with higher scores. They do not agree on empirical antibiotic therapy or testing in the presence of severe signs of pharyngitis (Centor 3 and 4).[19] At this point, it is useful to look at the diagnostic power of Centor scores according to the values obtained in different studies. For example, the power of the score 4 to recognize GAS pharyngitis has been obtained between 28% and 39% for both models according to the results in the studies given in Table 3. Although the frequency of GAS pharyngitis is low, the diagnostic power of score 4 for GAS pharyngitis in our study is within this range (35.3% in Centor and 28.7% in McIsaac). In conclusion, although the diagnostic power

does not change much, the contribution of predictive systems to clinical decisions is affected by the prevalence (pre-probability) of GAS pharyngitis in the study group. Especially in the patient groups with low pre-probability, both models of clinical prediction seem unable to move us beyond the 40-60% threshold at which we remain indecisive. Therefore, it is beneficial to consider the prevalence of GAS in the population of pharyngitis patient with high scores at the point of making decision to give empirical antibiotic treatment. On the other hand, some authors have stated that Lemierre syndrome is a serious problem, but that they do not agree with Centor's aggressive antibiotic treatment recommendation, and that they do not know the clinical course of FN pharyngitis and the effect of treatment on the course of symptoms or on the prevention of transmission.[20] Our data does also not support Centor. In our study, streptococcal groups other than Group A beta hemolytic streptococci have been studied in culture, but not FN. Non-GAS streptococci are more common in patients with low clinical scores. Therefore, considering all bacteria, it seems that Centor prediction model does not make an additional contribution to clinical decisions at high scores.

Strengths and Limitations of Our Study

The positive side of our study is that the study data have been collected prospectively and by a single researcher. In addition, the detection of streptococcal groups other than GAS in culture has enabled us to partially contribute to the discussions on the effect of non-GAS bacteria on clinical decisions, even if FN culture is not performed. On the other hand, our study has some limitations. Our study data have been collected only during autumn and winter months, so it is limited to cover all seasonal variations. Also, it does not consider an important situation such as GAS carriage.

CONCLUSION

While GAS positivity has been found to be 7.9% in the whole group over 3 years old, the frequency of GAS is 16.8% in children under 15 years old and 4.7% in adolescents and adults over 15 years old. The frequency increases as the Centor score increases. While GAS positivity in throat culture is 35.7% in participants of all ages with a McIsaac score of 4 and above, it has been found to be 40% in adolescents and adults with a Centor score of 4. In multivariate analysis, only symptoms and signs included in Centor criteria have been found to be associated with GAS positivity.

Although the diagnostic power of Centor and McIsaac predictive models does not change in clinical practice settings where the frequency is low, the probability after the test does not seem to reach the desired levels. Considering that pharyngitis cases have started to be evaluated using the Centor prediction model, new studies should be carried out on GAS positivity and the diagnostic power of clinical prediction systems in primary care family medicine practice in our country.

Ethics Committee Approval: Ethics committee permissions were obtained from the ADU Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (protocol no: 2019/64).

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REFERENCES

1. Aalbers J, O'Brien KK, Chan WS, et al. Predicting *Streptococcal pharyngitis* in adults in primary care: a systematic review of the diagnostic accuracy of symptoms and signs and validation of the Centor score. *BMC Med*. 2011;9:67. [CrossRef]
2. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. *Lancet Infect Dis*. 2005;5(11):685-694. [CrossRef]
3. Worrall G, Hutchinson J, Sherman G, Griffiths J. Diagnosing streptococcal sore throat in adults randomized controlled trial of in-office aids. *Can Fam Physician*. 2007;53(4):666-671.
4. Worrall GJ. Acute sore throat. *Can Fam Physician*. 2007;53(11):1961-1962.
5. Fine AM, Nizet V, Mandl KD. Large-scale validation of the Centor and McIsaac scores to predict group A streptococcal pharyngitis. *Arch Intern Med*. 2012;172(11):847-852. [CrossRef]
6. Chiappini E, Regoli M, Bonsignori F, et al. Analysis of different recommendations from international guidelines for the management of acute pharyngitis in adults and children. *Clin Ther*. 2011;33(1):48-58. [CrossRef]
7. Matthys J, De Meyere M, van Driel ML, De Sutter A. Differences among international pharyngitis guidelines: not just academic. *Ann Fam Med*. 2007;5(5):436-443. [CrossRef]
8. Gulliford MC, Dregan A, Moore MV, et al. Continued high rates of antibiotic prescribing to adults with respiratory tract infection: survey of 568 UK general practices. *BMJ Open*. 2014;4(10):e006245. [CrossRef]
9. McIsaac WJ, White D, Tannenbaum D, Low DE. A clinical score to reduce unnecessary antibiotic use in patients with sore throat. *CMAJ*. 1998;158(1):75-83.
10. Centor RM. Adolescent and adult pharyngitis: more than strep throat. *Arch Intern Med*. 2012;172(11):852-853. [CrossRef]
11. Laupacis A, Sekar N, Stiell IG. Clinical prediction rules: a review and suggested modifications of methodological standards. *JAMA*. 1997;277(6):488-494. [CrossRef]
12. *McWhinney's Textbook of Family Medicine. Thomas Freeman*. 4th ed. Sf:203-265.
13. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. *Am J Epidemiol*. 2007;165(6):710-718. [CrossRef]
14. Centor RM, Witherspoon JM, Dalton HP, Brody CE, Link K. The diagnosis of strep throat in adults in the emergency room. *Med Decis Making*. 1981;1(3):239-246. [CrossRef]
15. McIsaac WJ, Goel V, To T, Low DE. The validity of a sore throat score in family practice. *CMAJ*. 2000;163(7):811-815.

16. Cohen JF, Chalumeau M, Levy C, et al. Spectrum and inoculum size effect of a rapid antigen detection test for group A streptococcus in children with pharyngitis. *PLoS ONE*. 2012;7(6):e39085. [CrossRef]
17. Cohen JF, Cohen R, Levy C, et al. Selective testing strategies for diagnosing group a streptococcal infection in children with pharyngitis: a systematic review and prospective multicentre external validation study. *CMAJ*. 2015;187(1):23-32. [CrossRef]
18. Centor RM. Adolescent and adult pharyngitis: more than "strep throat". *ArchIntern Med/Vol*. 2012;172(11):852-853.
19. Centor RM, Cohen SJ. Pharyngitis management focusing on where we agree. *Arch Intern Med*. 2006;166(13):1345-1346. [CrossRef]
20. De Meyere EM, Matthys J. Should we expand the pharyngitis paradigm for adolescents and young adults? *Ann Intern Med*. 2010;152(7):477-8; author reply 478. [CrossRef]