RESEARCH PAPER

McIsaac Modification of Centor Score in Diagnosis of Streptococcal Pharyngitis and Antibiotic Sensitivity Pattern of Beta-hemolytic Streptococci in Chennai, India

JAISHREE VASUDEVAN, ALEXANDER MANNU AND G GANAVI

From Department of Pediatrics, Chettinad Hospital and Research Institute, Chennai, Tamil Nadu, India.

Correspondence to: Dr Jaishree Vasudevan, Professor, Department of Pediatrics, Chettinad Hospital and Research Institute, Kelambakkam, Chennai 603 103, India. vsdvn_jshr@yahoo.com
Received: January 04, 2017; Initial review: June 14, 2017; Accepted: October 18, 2018.

Objective: To assess the validity of modified Centor Score in predicting streptococcal pharyngitis, and describe the antibiotic sensitivity of streptococcal strains. **Methods:** A cross-sectional study of 120 children (age 1-18 y) with signs and symptoms of pharyngitis was undertaken in the pediatric department of a tertiary care teaching hospital in Chennai from July 2015 to April 2016. Modified Centor score was calculated for all children, and streptococcal sore throat was confirmed by throat swab culture. Predictive validity of Centor score was assessed by Receiver Operating Curve (ROC) analysis. **Results:** Streptococcal culture positivity was 35%. The Area Under the Curve (AUC) value for modified Centor score was 0.589 (95% CI 0.481 to 0.697, *P*=0.11) in predicting streptococcal pharyngitis. Cough had the highest sensitivity (63.4%), but poor specificity (36.7%) for streptococcal pharyngitis confirmed by culture. The specificity was 100% for palatine petechiae, followed by palatine exudates (97.5%) and tender anterior cervical nodes (88.6%) to diagnose streptococcal pharyngitis. The proportion of antibiotic resistance was highest for cotrimoxazole (16.7%). **Conclusion:** Predictive validity of modified Centor score was not satisfactory, and resistance to cotrimoxazole, fluoroquinolones and macrolides was high among *S. pyogenes* strains.

Keywords: *Antimicrobial resistance, Streptococcus pyogenes, Upper respiratory infection*.

Streptococcal pharyngitis can lead to a plethora of suppurative and nonsuppurative complications [1], which can be prevented by prompt diagnosis and institution of appropriate antibiotic therapy. However, due to considerable overlap in clinical presentation, differentiating streptococcal pharyngitis from other causes is difficult. Non-availability of culture and sensitivity in many of the healthcare settings in resource-poor countries precludes its routine use. Delay in diagnosis leads physicians to administer empirical therapy, leading to overuse of antibiotics, which results in a rise in drug-resistant bacterial strains [2]. Various alternative diagnostic methods, including clinical scoring systems [3,4] and rapid antigen detection testing (RADT) [5] have been developed for diagnosis of streptococcal pharyngitis. It is important to validate these scores for effective diagnosis and treatment of GABHS pharyngitis and prevention of subsequent complications. The present study was conducted to assess the utility of various clinical manifestations and McIsaac modification of Centor score in predicting streptococcal pharyngitis in pediatric age group, and describe the sensitivity pattern of isolated streptococcal strains.

METHODS

This cross-sectional study was undertaken in the department of pediatrics of a tertiary-care teaching hospital in Chennai, India, from July 2015 to April 2016. Children aged between 1 to 18 years presenting to the outpatient department with symptoms of pharyngitis and clinically suspected as streptococcal pharyngitis were included in the study. Children who presented with obvious signs of viral respiratory infection (having rhinorrhea, coryza, conjunctivitis, coughing and/or sneezing) were excluded. Children who were already on antibiotics were also excluded.

All screened children were recruited by purposive sampling sequentially, till the sample size was reached. Approval of the Institute Human Ethics Committee was obtained. Informed written consent was obtained from the parents or guardians of all the participants.

All the children were evaluated by a pediatrician. Demographic and clinical data were collected from the children. Clinical examination of the pharynx and tonsils was conducted under flash light illumination. All the variables related to modified Centor score were

documented and score was calculated for each child. The clinician collected the sample from pharyngeal wall (after depressing tongue with tongue depressor) by a sterile cotton swab applied on the tip of 6-7 inches long swab stick. Cotton swab was rubbed gently against pharyngeal mucosa. All precautions to avoid contamination were taken and the samples were immediately transported to the microbiology department in a sterile test tube at room temperature. Smear was examined by Gram staining, and Blood Agar was the culture media used for culture. Any growth observed on culture medium was assessed for morphology (smear examination), colony characteristics and biochemical tests. Isolates were subjected for antibiotic sensitivity as per CLSI guidelines.

Throat swab culture positivity was considered as the primary outcome variable. Various sociodemographic, lifestyle related parameters were considered as exploratory variables. The children with and without culture positive infection were compared with respect to demographic, clinical variables and modified Centor score. The association between the symptoms, signs and modified Centor score with culture positivity was assessed by cross tabulation and chi-square test. IBM SPSS version 21.0 was used for statistical analysis. P <0.05 was considered statistically significant.

RESULTS

A total of 120 participants were included in the analysis. About 35% in the study population had streptococcal sore throat. Only one child had throat swab culture positive for *Staphylococcus aureus*. The streptococcal positivity was 28% among 1 to 5 year, 40% in both 6 to 10 year and more than 11-year-old age groups. The proportion of streptococcal pharyngitis increased with increasing Centor score category. Among the symptoms, cough, throat pain, painful swallowing and difficulty in swallowing showed statistically significant difference among streptococcal and nonstreptococcal pharyngitis (***Table* I**).

The area under the curve value for modified Centor score was 0.589 with a P value 0.11 and 95% CI was 0.481 to 0.697, respectively in the study population. Among symptoms, cough had the highest sensitivity (63.4%), but poor specificity (36.7%). Palatine petechiae had 100% specificity, but very poor sensitivity

TABLE I FACTORS ASSOCIATED WITH STREPTOCOCCAL PHARYNGITIS IN THE STUDY POPULATION (N=120)

Parameter	*Culture positive (n=42), n(%)*	*Culture negative (n=78), n(%)*	*P value*
Male gender	21 (38.9)	33 (61.1)	0.42
Centor score			
-1 to +1	9 (23.7)	29 (76.3)	0.14
2 to 3	13 (34.2)	25 (65.8)	
4 to 5	15 (41.7)	21 (58.3)	
Above 5	5 (62.5)	3 (37.5)	
Symptoms			
Cough	26 (34.2)	50 (65.8)	0.81
Throat pain	28 (43.7)	36 (56.2)	0.03
Fever	26 (40.6)	38 (59.4)	0.16
Rhinorrhea	16 (32)	34 (68)	0.57
Painful swallowing	19 (54.3)	16 (45.7)	0.004
Difficulty in swallowing	13 (56.5)	10 (43.5)	0.02
Signs			
Erythematous pharynx	30 (46.1)	35 (53.8)	0.005
Erythematous tonsils	31 (48.4)	33 (51.6)	<0.001
Enlarged anterior cervical nodes	21 (58.3)	15 (41.7)	<0.001
Tender anterior cervical nodes	13 (59)	9 (40.9)	0.009
Enlarged tonsils	12 (50)	12 (50)	0.08
Tonsilar exudates	3 (75)	1 (25)	0.09
Palatal petechiae	2 (100)	0 (0)	0.05

(4.9%). Tender anterior cervical nodes and palatine exudates also had very high specificity (88.6% and 97.5%, respectively) but poor sensitivity (***Table* II**).

The proportion of antibiotic resistance was highest for Cotrimoxazole (16.7%), followed by tetracycline (9.5%). Ciprofloxacin and Ofloxacin resistance was seen in 7.1% of the study population. Erythromycin resistance was seen in 4.8% of the strains. Intermediate resistance was found for Erythromycin (4.8%), Azithromycin and Ofloxacin (2.4%).

Modified Centor score of 4 had a poor sensitivity (12.2%, 95% CI 4.8% to 26.2%), but very high specificity (96.2%, 95% CI 89.3% to 99.2%) in predicting streptococcal pharyngitis. The overall diagnostic accuracy was 67.5% (95% CI 58.4% to 75.8%). Even though the positive likelihood ratio was 3.21, the 95% confidence interval ranged from 0.81 to 12.77. The negative likelihood ratio was 0.91 (95% CI 0.81 to 1.03).

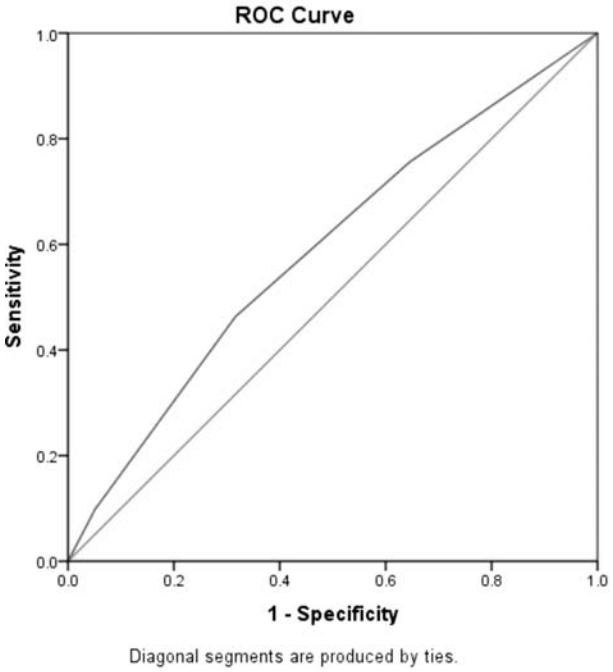

FIG. 1 *ROC analysis of predictive validity of modified Centor score in predicting streptococcal pharyngitis***.**

DISCUSSION

In this study, the overall predictive validity of modified Centor score, as assessed by Area under ROC curve was poor. Palatine petechiae, tonsillar exudates and tender anterior cervical lymph nodes had high specificity and positive predictive value in diagnosis of streptococcal pharyngitis. *Streptococcus pyogenes* strains were sensitive to penicillin. However, resistance to Cotrimoxazole (16.7%), tetracycline (9.5%), fluoroquinolones and macrolides was high.

The AUC reported in the original 1981 study by Centor [3] was 0.78, which is considerably higher compared to our study. McIssac, *et al*. [4] modified the score, and reported high (83.1%) sensitivity. Few other studies from the West have reported AUC value higher than 0.7, indicating good predictive validity [6]. Another study had reported an area under the ROC of 0.633 [7]. A study had reported a strong positive association between tonsillar exudates and culture positive Group A streptococcal (GAS) sore throat [7]. But there are other studies, which have documented sensitivity as low as 3.9% for a modified Centor score of 4, with a high specificity of 96%, as in current study [8]. Similar pattern of low sensitivity and higher specificity has been demonstrated by few other studies [9,10]. Lowering the cut-off level of modified Centor score, has shown to increase the sensitivity, but at the cost of specificity, which may result in increase in unnecessary antibiotic prescription [6].

The reasons for such a wide variation in reported predictive validity needs to be evaluated. The key differences in the demographic characteristics, differences in the clinical presentation, and quality of clinical assessment may be responsible for these differences. The same factors may determine the clinical utility of modified Centor score.

The limited sample size in the study was a major limitation that did not allow for controlling for the effect

TABLE II SENSITIVITY AND SPECIFICITY OF VARIOUS CLINICAL FINDINGS IN DIAGNOSIS OF STREPTOCOCCAL PHARYNGITIS

Factors	*Sensitivity*	*Specificity*	*Positive predictive value*	*Negative predictive value*
Cough	63.4%	36.7%	34.2%	65.9%
Tender anterior cervical nodes	31.7%	88.6%	59.1%	71.4%
Palatine petechiae	4.9%	100%	100%	66.9%
Tonsillar exudates	4.9%	97.5%	50.0%	66.4%
Modified centor score	12.2%	96.2%	62.5%	67.9%

WHAT THIS STUDY ADDS?

- Presence of palatine petechiae, tonsillar exudates and tender anterior cervical lymph nodes may guide in starting antibiotic therapy in children with pharyngitis, but McIssac modification of Centor Score does not seem to perform satisfactorily.

of confounding or detailed analysis of factors associated with culture positive infection. Exclusion of possible viral etiology on clinical grounds alone was another limitation that can affect generalizability of these results.

We conclude that the predictive validity of Centor score for diagnosis of streptococcal pharyngitis is poor, and its utility as screening tool is questionable. Considering very low sensitivity, high proportion of streptococcal sore throat may be missed, if modified centor score is used a screening tool.

Contributors: JV: had conceptualized the idea, prepared the study proposal, engaged in data compilation, analysis and preparation of all the drafts of the manuscripts; AM,GG: have fine-tuned the study proposal, engaged in data collection, reviewed all the drafts and provided their inputs. They have compiled, verified and approved the final draft. All authors have contributed, designed and approved the study.
Funding: None; *Competing interest*: None stated.

REFERENCES

1. Gerber MA. Group A Streptococcus. Nelson Textbook of Pediatrics: Elsevier; 2011. *p*. 914-25.e1.
2. Ayanruoh S, Waseem M, Quee F, Humphrey A, Reynolds T. Impact of rapid streptococcal test on antibiotic use in a pediatric emergency department. Pediatr Emerg Care. 2009;25:748-50.
3. 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;1:239-46.
4. 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.
5. Kundu R. Rapid diagnostic tests in childhood infections. Indian Pediatr. 2018;55:233-7.
6. 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;172:847-52.
7. Atlas SJ, McDermott SM, Mannone C, Barry MJ. The role of point of care testing for patients with acute pharyngitis. J Gen Intern Med. 2005;20:759-61.
8. Orda U, Mitra B, Orda S, Fitzgerald M, Gunnarsson R, Rofe G, *et al*. Point of care testing for group A streptococci in patients presenting with pharyngitis will improve appropriate antibiotic prescription. Emerg Med Australas. 2016;28:199-204.
9. Palla AH, Khan RA, Gilani AH, Marra F. Over prescription of antibiotics for adult pharyngitis is prevalent in developing countries but can be reduced using McIsaac modification of Centor scores: a cross-sectional study. BMC Pulm Med. 2012;12:70.
10. Regoli M, Chiappini E, Bonsignori F, Galli L, de Martino M. Update on the management of acute pharyngitis in children. Ital J Pediatr. 2011;37:10.