

**Assessing the Diagnostic Accuracy and Validity of the McIsaac Modified Centor Score in Predicting Group A Beta Hemolytic Streptococcal Pharyngitis in A Trial to End Antibiotic Abuse in Children**

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**Abstract**

**Background:** Overuse of antibiotics leads to resistance. Pharyngitis is commonly viral but Group A Streptococcus (GAS) as a significant bacterial cause. GAS infections include suppurative and non-suppurative. Centor criteria assess GAS infection. McIsaac score adjusts for age, reducing antibiotic misuse.

**Objectives:** Assess diagnostic accuracy of McIsaac modified Centor score in predicting GABHS pharyngitis to reduce antibiotic abuse in children.

**Patients and methods:** Study compares modified Centor score to throat swab culture in pediatric pharyngitis. 50 patients sampled from Assiut and Qena university clinics. Inclusion: 3-14 years old, symptomatic. Exclusion: <3 or >14 years, recent antibiotics, immunocompromised, certain conditions. Throat swabs were taken from all patients for culture, analyzed for Streptococcus pyogenes. The modified Centor score was calculated based on tonsillar exudate, anterior cervical lymphadenopathy, absence of cough, fever, and age to assign points, with higher scores indicating a greater likelihood of streptococcal infection. Approved by ethics committee.

**Results:** 50 subjects, with 60% in preschool age and 58% male, were included. 18% positive for GABHS. The modified Centor score threshold of four showed sensitivity of 55.6% and specificity of 70.7% for diagnosing GABHS+ pharyngitis, with an area under the curve of 0.71. Swollen anterior cervical lymph nodes and temperature  $\geq 38^{\circ}\text{C}$  exhibited the highest sensitivity (100%, 88.9%) for GABHS+ pharyngitis, while tonsillar exudate had the highest specificity (61%).

**Conclusion:** Modified Centor score shows fair predictive validity, acceptable specificity. Enhances appropriate antibiotic prescribing but should be cautiously used to avoid missing GABHS+ pharyngitis and complications.

**Keywords:** Diagnostic accuracy; McIsaac modified Centor score; Group A beta hemolytic streptococcal pharyngitis; Antibiotic abuse, Children.

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## Introduction

According to **Ahmed et al. (2020)**, the development of antibiotic resistance is a consequence of the incorrect and excessive use of antibiotics, which renders the treatment procedures that are now useless. Individuals who are experiencing acute pharyngitis are more likely to seek medical assistance from primary care doctors because it is an illness that is rather common. It is a disorder that is characterized by an infection or irritation of the tonsils, hypopharynx, and pharynx. Pharyngitis is a very common ailment. When it comes to youngsters, pharyngitis is typically brought on by a viral illness or Group A Streptococcus (GAS). In spite of this, viral infections remain the most common cause of this disease, according to **Van Brusselen et al. (2019)** research. According to Ahmed et al. research from (2020), the illness can also be caused by other unusual variables, such as the presence of hazardous chemicals, allergic responses, physical traumas, and irregular cell development.

According to **Shulman et al. (2012)**, the most common bacterial pathogen that causes acute pharyngitis is known as Group A beta hemolytic streptococcus (GABHS). This particular infectious agent accounts for around 15-30% of all infections that occur in children. The fact that it is the only prominent symptom of the condition that requires antibiotic therapy is another reason why it is necessary (**Hassan et al., 2015**).

There are a number of suppurative outcomes that are connected with Group A Streptococcus (GAS) pharyngitis. These include tonsillo-pharyngeal cellulitis or abscess, otitis media, sinusitis, necrotizing fasciitis, bacteremia, meningitis, brain abscess, and jugular vein septic thrombophlebitis. There are a number of non-suppurative complications that can arise from Group A Streptococcus (GAS) pharyngitis. These complications include acute rheumatic fever, post-streptococcal

reactive arthritis, scarlet fever, streptococcal toxic shock syndrome, acute glomerulonephritis, and pediatric autoimmune neuropsychiatric disorder that is associated with group A streptococci (**Wolford et al, 2022**). An algorithm known as the Centor criteria is employed to assess the underlying cause of a sore throat and ascertain the probability of Group A  $\beta$  hemolytic Streptococcus (GABHS) being the underlying infection. The examination of patients is based on a set of criteria that includes determining whether or not the patient has tonsillar exudates, swollen and palpable anterior cervical lymph nodes, a lack of cough, and a history of fever measuring more than 38.5 degrees Celsius. According to **Roggen et al. (2013)**, patients receive one point for each sign and symptom that they exhibit, regardless of whether or not they are present.

According to **McIsaac et al. (2004)**, the McIsaac score is a modification of the Centor score that takes into consideration the variance in the occurrence of GAS infection among children aged 3 to 14 in comparison to older individuals. The McIsaac score is calculated by adding one point to the Centor score for patients who are between the ages of three and fourteen, and subtracting one point from the Centor score for patients who are forty-five years old or older respectively. According to information provided by **Van Brusselen et al. (2019)**, the application of the McIsaac Modified Centor score has led to a reduction of roughly 88 percent in the inappropriate consumption of antibiotics.

Within the context of predicting group A beta hemolytic streptococcal pharyngitis, the aim of our research is to provide an evaluation of the diagnostic accuracy and validity of the McIsaac modified Centor score. The purpose of this experiment is to take a look at the problem of youngsters taking an excessive amount of antibiotics.

### Patients and methods

In order to compare the clinical criteria of the modified Centor score to the results of the gold standard of throat swab culture, a research study that was conducted using a cross-sectional design was carried out. Both the pediatrics clinics at Assiut University and the ENT clinic at Qena University were utilized in the course of the inquiry by the respective universities. During the time period of 9-2023 to 2-2023, the research population comprised of fifty individuals who had been diagnosed with pharyngitis.

Using a form of selective sampling that was not random, all of the patients who went to the clinics on Monday and Tuesday during the time period that the data was being collected were either included or excluded, based on the precise criteria under consideration. Those children who meet the inclusion criteria are those who are between the ages of three and fourteen, regardless of gender, and who display signs and symptoms that are characteristic of pharyngitis. Those patients who are less than three years old or older than fourteen years old are not eligible for participation in the study. In patients who are immunocompromised or who are on immunosuppressive drugs and who have a medical history of cancer, liver sickness, renal disease, diabetes mellitus, or major cardiovascular disease, antibiotics should be administered between 24 and 48 hours before the beginning of symptoms. Because the samples were collected in the late summer and fall, when the incidence of pharyngitis is relatively low, the sample size was very small (Kennis et al., 2022). Because of this, the sample size was limited.

The selected patients were subjected to a detailed clinical history including age, sex, complaint, onset and duration of symptoms, grade of fever and presence or absence cough, clinical and physical examination (throat examination and cervical LN), and throat culture with

obtaining definitive results between 24 and 48 hours.

**Specimen collection and microbiological identification:** Clinicians were instructed on taking oropharyngeal swabs using sterile cotton swab. Swabs were transported to the microbiology Laboratory at Assiut University Hospitals.

The specimens were cultured on blood agar (Oxoid, USA) so that after streaking the medium, the blood agar plates were then incubated at 35°C. After 24 hours, the plates were observed to check the grown  $\beta$ -hemolytic colonies. Negative cultures were re-intubated for an additional 24 hours.

The colonies that raised suspicion were subjected to sub-culturing. The identification of *S. pyogenes* was determined by observing the colony shape and  $\beta$ -hemolysis on blood agar plates, as well as its gram stain features. Additionally, the sensitivity to bacitracin and reactivity with group A-specific antiserum were used as further indicators. It was determined that the procedure for the study was acceptable by the Ethics Committee of the Qena Faculty of Medicine at South Valley University. **SVU-MED-ENT030-4-23-9-736** is the code number that should be used. After supplying the patients and their families with all of the pertinent information, the patients and their families were given an explanation of the research, and their consent was obtained.

### Statistical analysis

The statistical program known as the Statistical Package for the Social Sciences (SPSS) was utilized in order to carry out the analyses, especially version 22.0. For the purpose of representing categorical variables, integer values and proportions were utilized. Utilizing the Shapiro-Wilk test, we were able to determine whether or not the continuous data were normal. Data that does not follow a normal distribution can be characterized using the median and the interquartile range (IQR), which are both

statistical measures. In order to compare two categorical variables, either the Pearson chi-squared test or Fisher exact test was utilized. On the other hand, the Mann-Whitney test was utilized in order to compare non-normally distributed continuous data across two groups.

In order to calculate the modified Centor score, the following clinical variables were added together: a body temperature of 38 degrees Celsius or above, the presence of tonsillar exudates, the presence of enlarged anterior cervical lymph nodes, and the lack of a cough. According to **Fine et al. (2012)**, the modified Centor score was increased by one point for people who were less than 14 years old.

According to **Hajian-Tilaki (2013)**, the sensitivity, specificity, and receiver operating characteristic (ROC) of

a diagnostic test are the major markers of the diagnostic accuracy and validity of the test. A receiver operator characteristic (ROC) curve was developed in order to ascertain the most suitable modified Centor score cut-off point. This was accomplished by taking into consideration sensitivity, specificity, and the area under the curve (AUC). Both the area under the curve (AUC) and confidence intervals at 95% were calculated. Each and every statistical test determined that a P value that was lower than 0.05 was statistically significant.

### Results

A total of 50 subjects were recruited into the study, 60% of them was in preschool age, 58% was male, modified Centor Score median (iqr) was 3.0 (2.0). Throat swab culture was positive for 18% of the patients, (**Table 1**).

**Table 1. Background Characters and Modified Centor Score and Criteria, n=50**

Variables		n	%
Age Group	Less Than 5 Years	30	60
	5 -14 Years Old	20	40
Sex	Male	29	58
	Female	21	42
<b>Centor Criteria</b>			
Temperature 38 °C or Above	No Fever	23	46
	Fever	27	54
Absence Of Cough	No	13	26
	Yes	37	74
Tonsillar Exudates	No	29	58
	Yes	21	42
Swollen Anterior Cervical Lymph Nodes	No	24	48
	Yes	26	52
<b>Centor Categories</b>	2.00 And less	15	30
	3.00	18	36
	4.00 And more	17	34
Modified Centor Scores Median (Iqr)**	3.0 (2.0)		
<b>Throat Sample Results</b>	Non- GABHS *	41	82
	GABHS+	9	18

Notes: n = number of respondents; \* GABHS = Group A Streptococcus \*\*Iqr interquartile range as non-parametric data

Using the findings of the throat swab, there is no correlation between the modified Centor criterion and Score. There was a statistically significant correlation

between GABHS+ pharyngitis and age, fever of 38 degrees Celsius or higher, and enlarged lymph nodes, particularly in the anterior cervical region. The other criteria

of the Centor revealed that there was no significant correlation. The Mann Whitney test revealed that those with non-GABHS pharyngitis and those with GABHS+

pharyngitis had a statistically significant difference in their modified Centor Score median, (Table .2).

**Table 2. Association between Modified Centor criteria and score with throat swab results (N = 50)**

Variables		Throat Culture				P-Value*
		Non-GABHS (n=41)		GABHS+ (n=9)		
		n	%	n	%	
Age Group	Less Than 5 Years	30	73.2	0	0	0.00
	5 Years and More	11	26.8	9	100	
Sex	Male	24	58.5	5	55.6	1.00
	Female	17	41.5	4	44.4	
Temperature 38 °C or Above	No	22	53.7	1	11.1	0.02
	Yes	19	46.3	8	88.9	
Absence Of Cough	No	9	22	4	44.4	0.21
	Yes	32	78	5	55.6	
Tonsillar Exudates	No	25	61	4	44.4	0.46
	Yes	16	39	5	55.6	
Swollen Anterior Cervical Lymph Nodes	No	24	58.5	0	0	0.002
	Yes	17	41.5	9	100	
Modified Centor Score median difference(Iqr)			3(2)		4(1)	0.02**

Notes: n = number of respondents; \* Fisher exact test.; GABHS = Group A Streptococcus \*\*Mann Whitney test as non-parametric data Iqr interquartile range

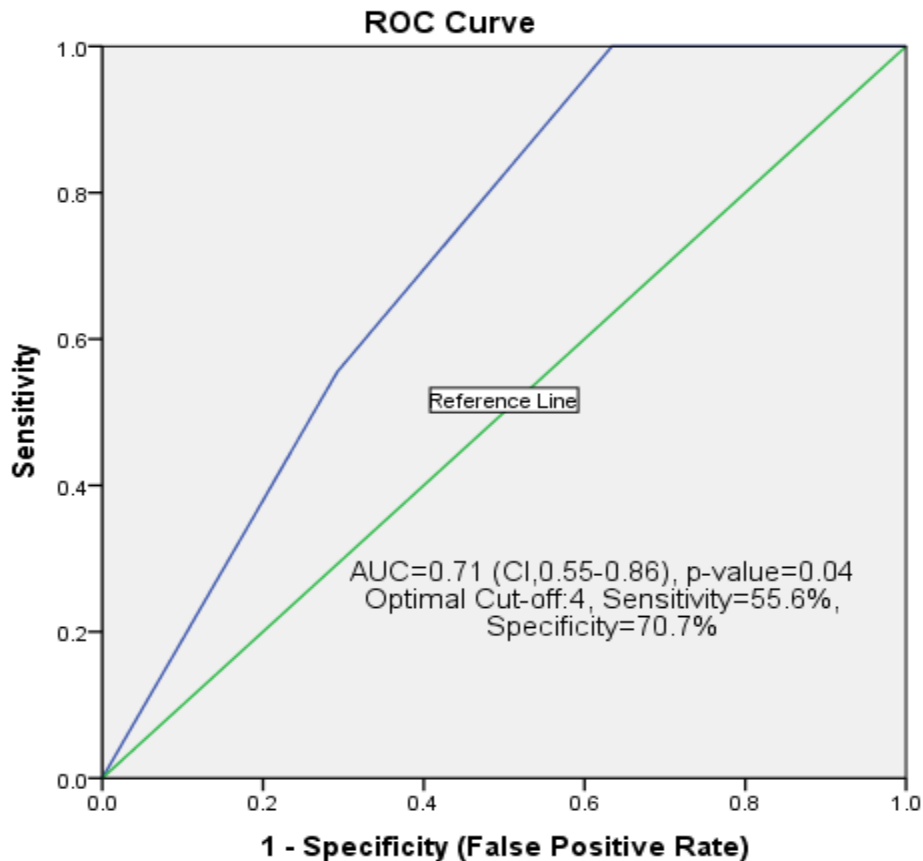
Modified Centor Score of 2 and less significantly associated with non-GABHS pharyngitis, (Table.3). (Fig.1) presents the results of an analysis using receiver operating characteristic (AUC) to evaluate the overall performance of the modified Centor score in the diagnosis of GABHS+ pharyngitis diagnostics. The

value of 0.71 for the area under the curve was determined to be satisfactory (95% confidence interval = 0.55 to 0.86; p = 0.04). The threshold of four, which corresponded to a sensitivity of 55.6% and a specificity of 70.7%, determined the most acceptable level of sensitivity and specificity.

**Table 3. Throat Culture Result and Modified Centor Score Result Association**

Modified Centor Score Result	Non-GABHS (%)	GABHS+ n (%)	P-Value*
Score 2 and less	15 (36.6)	0 (0)	0.04
Score 3	14 (34.1)	4(44.4)	0.7
Score 4 and more	12(29.3)	5 (55.6)	0.24
<b>Total</b>	41	9(18)	50

Notes: n = number of respondents; \* Fisher exact test.; GABHS = Group A Streptococcus



Diagonal segments are produced by ties.

**Fig.1.** ROC Curve for Predictive Validity of Overall Modified Centor Score in Predicting Streptococcal Pharyngitis in Children

Among symptoms table 4 shows that the swollen anterior cervical lymph nodes and temperature 38 °c or above had the highest sensitivity (100%, 88.9%

respectively), with specificity of 58.5% and 53.7% respectively. Tonsillar exudate had the highest specificity by 61%, with 55.6% sensitivity, (Table .4).

**Table 4. Diagnostic Accuracy of Modified Centor Score Criteria in Diagnosis of Streptococcal Pharyngitis**

Centor Criteria	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive Value (%)	AUC under ROC curve (CI)
Temperature 38 °C or Above	88.9	53.7	29.6	95.7	0.71(0.54-0.88) *
Absence Of Cough	55.6	22	13.5	69.2	0.39 (0.17-0.60)
Tonsillar Exudates	55.6	61	23.8	86.2	0.58 (0.37-0.79)
Swollen Anterior Cervical Lymph Nodes	100	58.5	34.6	100	0.79 (0.66-0.91) *

\*Significant with a p value less than 0.05

The diagnostic test results for the modified Centor criteria score are displayed in Table 5. These results are compared to the gold standard, which is the outcome of a throat swab culture. The Centor scores 4 had a sensitivity of 55.6% and a specificity of 70.7%. Additionally,

the negative predictive value (NPV) was 87.9%. The positive predictive value (PPV) was 29.4%. The AUC, which represents the area under the curve, had a value of 0.63. This value indicates that the model performance may be considered fair, (Table .5).

**Table 5. Diagnostic Accuracy of Modified Centor Score at Different Levels in Diagnosis of Streptococcal Pharyngitis**

Centor Criteria	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive Value (%)	AUC under ROC curve (CI)
Score 2 and less	0.0	63.4	0.0	74.3	0.31(0.15-0.47)
Score 3	44.4	56.9	22.2	84.4	0.55 (0.33-0.76)
Score 4 and more	55.6	70.7	29.4	87.9	0.63(0.42-0.84)

## Discussion

It is common practice to identify the diagnosis of pharyngitis by analyzing the clinical symptoms that the patient is experiencing. Neither the usual throat culture nor the rapid test can reliably differentiate between patients who are acutely infected and those who are asymptomatic carriers with intercurrent viral pharyngitis (Hassan et al, (2015). This is the conclusion reached by Hassan et al. In order to improve the diagnosis of Group A beta-hemolytic streptococcal pharyngitis and to offer direction for testing and treatment, a number of clinical decision criteria have been developed. A significant number of people make use of the Centor Score (Wolford et al., 2022).

It is generally agreed that the most reliable approach for diagnosing GABHS+ pharyngitis is doing a culture on a throat swab. In general, it takes between two and three days to determine whether or not bacteria have developed (Anjos et al., 2014). To add insult to injury, throat swab culture is not available at a few of primary care facilities. It is essential to make a prompt and accurate diagnosis of pharyngitis at the initial appointment. This is because untreated pharyngitis often heals within a span of three to five days

once it has been diagnosed. According to Choby (2009), it is vital to take a course of antibiotics for a period of ten days in order to avoid the long-term repercussions of GABHS+ pharyngitis. These implications include rheumatic fever and acute glomerulonephritis.

The ailment known as pharyngitis, which is defined by inflammation of the throat, is one that affects a substantial number of children worldwide each year. This can be related to the growing utilization of antibiotics, which in turn results in the development of resistance to antibiotics (Robinson, 2021). The Centor score is a tool that has been created to aid clinicians in identifying streptococcal pharyngitis and assessing whether or not antibiotics are necessary (Muthanna et al., 2022). This was done in order to address the problem that has been identified.

According to the findings of the current study, the prevalence of GABHS+ pharyngitis was 18%. This finding is in line with the global prevalence range of 15% to 35% in children, as reported by Mustafa and Ghaffari (2020).

According to the findings of our inquiry, the incidence of pharyngitis is significantly higher in males than in girls.

A prior study that was conducted among Pakistani patients also found a greater frequency of acute pharyngitis in males than in females (Rathi and Ahmed, (2014). This conclusion is consistent with that study with regard to the findings.

Comparing GABHS+ pharyngitis with non-GABHS pharyngitis regarding Centor score criteria we detected a significant difference regarding age, fever and swollen anterior lymph nodes. The non-GABHS significantly more prevalent in the preschool aged children. GABHS+ pharyngitis is more common in children older than 5 and it has been considered rare in children younger than 3 years (Pellegrino et al., 2023). This is consistent with Kainth and Krysan, (2011) study that proved that higher prevalence of GABHS disease in older children than preschool children (Kainth and Krysan, (2011). A significant association between GABHS+ pharyngitis with high temperature (38 °C or above). Although the degree of fever cannot differentiate between viral and bacterial diseases, high fever is associated with a greater incidence of bacterial diseases (El-Radhi, (2018). Swollen anterior cervical lymph nodes were more frequent in GABHS+ pharyngitis. It is well-known that swollen and tender lymph nodes favor a bacterial etiology (Harberger and Graber, (2023).

There is a statistically significant difference between the two groups, namely non-GABHS pharyngitis and GABHS+ pharyngitis, in terms of the total modified Centor score median difference. There is a difference between the median score for GABHS+ pharyngitis, which is 4, and the median score for non-GABHS pharyngitis, which is 3. Muthanna et al. (2022) came to the conclusion that a Centor score of three did not offer adequate evidence to confirm the diagnosis of GABHS+ pharyngitis. This was the conclusion reached about their inquiry. According to the findings of the study, all of the patients who were diagnosed with GABHS+ pharyngitis had Centor scores that fell

within the range of 3 to 4, while none of them had Centor values that fell within the range of 0 to 2, as Muthanna et al., (2022) shown in their study.

It is usual practice to use the receiver operator characteristic curve (ROC) to evaluate the overall accuracy of a diagnostic test, and the area under this curve (AUC) is a statistic that is frequently applied for this purpose (Nahm, 2022). An area under the curve (AUC) value of 0.7 is the minimal threshold that should be used for measuring the efficiency of any diagnostic threshold, as stated by Hajian-Tilaki (2013). As evidenced by the Area under the Receiver Operating Characteristic (ROC) curve in this research (AUC=0.71), the modified Centor score exhibited a level of predictive validity that was satisfactory in separating patients who had Group A beta-hemolytic streptococcus (GABHS) from those who did not have the condition. According to the first study conducted by Centor in (1981), the area under the curve (AUC) was 0.78, which is higher than the AUC that was found in our investigation (Centor et al., 1981). According to the findings of the study conducted by Aslaner et al., the ROC curve indicated a significant degree of sensitivity and specificity, with an Area under the ROC curve of 0.91 (Aslaner et al., 2021). The current discovery, on the other hand, appears to contradict these findings. A value of 0.59 for the area under the curve (AUC) indicated that the modified Centor score had a low degree of efficacy, according to the findings of the research that Vasudevan and his colleagues did in India (Vasudevan et al., 2019).

According to the findings of our investigation into the use of the Centor score as a decision-making tool for antibiotic prescribing, the most acceptable levels of sensitivity and specificity were seen when the score was more than 4, with values of 55.6% and 70.7% respectively. Although the Centor score has the potential to facilitate the appropriate prescription of antibiotics, its utilization



need to be approached with caution. It is possible that an excessive amount of antibiotics will be used if all individuals who have a sore throat and a score of more than three are treated.

According to a previous study on GABHS pharyngitis, the diagnostic accuracy of the criteria that were utilized to compute the Centor score in this study is consistent with earlier research. This prior analysis shown that there is not a single sign or symptom that is sufficiently reliable to reliably confirm or reject a diagnosis of GABHS pharyngitis (Aalbers et al., 2011). The results of our research indicate that each individual criterion that contributes to the formulation of the Centor score contains a high capacity for discrimination. To be more specific, the condition known as "swollen anterior cervical lymph nodes" demonstrates the highest concentration, followed by a fever of 38 degrees Celsius or higher. Due to the fact that their sensitivity is higher than their specificity, they are more successful in excluding GABHS pharyngitis when the symptoms are not present. Our research indicates that the interpretation of the Centor score criteria may differ depending on whether the physician objective is to confirm or reject the presence of GABHS pharyngitis (Muthanna et al., 2022). This was found to be the case on different occasions.

It is important to note that the prevalence of rheumatic fever has a role in determining the threshold for beginning antibiotic therapy based on the Centor score. It is possible for doctors to strive for a Centor score that has a high level of specificity in industrialized nations, where rheumatic fever is quite uncommon. If this strategy were used, the number of antibiotic prescriptions would decrease; nonetheless, it is possible that some instances of GABHS pharyngitis might be overlooked. According to Aalbers et al., (2011), a practitioner who is working in a poor nation that has a high incidence of rheumatic fever should make it a top

priority to get a test that has a high level of sensitivity. Rheumatic heart disease (RHD) affects around 300,000 people in Egypt who are between the ages of 5 and 15 who are affected by the condition. According to Sayed et al., (2021) survey, Egypt has the highest number of fatalities that are associated with this ailment among the countries that are located in the East Mediterranean area. It is possible that a lower sensitivity of the Centor score may be regarded acceptable in countries where the incidence of rheumatic fever is relatively low. On the other hand, this is not acceptable in nations with a heavy load, such as Egypt (Sayed et al., 2021). In situations like these, it is essential to confirm the diagnosis by culture since a high level of sensitivity is of significant significance (Sauve et al., 2021).

The small sample size in the study and the purposive sampling technique were major limitations that did not allow controlling of confounding factors associated with culture positive infection. It also that can affect generalizability of these results.

### Conclusion

The new Centor score utilizes a mix of factors to accurately predict the risk of GABHS+ pharyngitis in children. In order to ensure the suitability of this score for application in several nations, it has been effectively modified. Our research findings indicate that it has a strong ability to accurately predict outcomes, is precise enough, and has the potential to improve the right use of antibiotics. Nevertheless, it is crucial to use prudence when using it to prevent overlooking instances of GABHS+ pharyngitis and the associated complications.

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