

**Case report****Accuracy of Centor scoring system in diagnosing group a-beta haemolytic streptococcal (GABHS) infection**

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**ABSTRACT**

**Background:** At present, the standard examination for diagnosing streptococcal upper respiratory tract infection is throat culture. As throat culture is time-consuming and relatively expensive, efforts are made to develop certain criteria that will still lead to proper diagnosis and rational use of antibiotics, that is Centor score. Even so, the accuracy of Centor score is still debatable. **Purpose:** To provide evidence on the accuracy of Centor scoring system compared to throat culture in diagnosing Group A Beta-Haemolytic Streptococcal (GABHS) upper respiratory tract infection. **Case Report:** A 25-years old male come to primary health care with primary complain of sore throat. Centor score was used to diagnose GABHS infection and as a guide to give antibiotics. **Clinical question:** In patients with score throat, how accurate is the centor score compared to throat culture in GABHS Infection? **Methods:** Literature searching was conducted through 4 databases. Critical appraisal based on the Centre of Evidence-based Medicine (CEBM) - University of Oxford, Diagnostic Critical Appraisal Sheet and Systematic Review Sheet. **Results:** All the selected studies were considered valid. They revealed a high specificity, low sensitivity, high negative predictive value (NPV), and low positive predictive value (PPV) in the importance aspect assessment. The Centor scoring system was applicable to our patient. It was available, affordable, and accurate in adult patients, yet less accurate in children. **Conclusion:** Patient with score throat and suspicion of GABHS infection could be diagnosed with Centor scoring system as the first line diagnosis in primary care and as a guide to whether giving antibiotics or not.

**Keywords:** Streptococcal, Centor Score, Throat Culture, Diagnosis

**ABSTRAK**

**Latar belakang:** Saat ini, kultur tenggorok merupakan pemeriksaan baku emas yang digunakan untuk mendiagnosis infeksi saluran napas atas yang disebabkan oleh bakteri *Streptococcus*. Namun, kultur tenggorok merupakan pemeriksaan yang mahal dan hasilnya memakan waktu yang lama, sehingga berbagai kriteria dikeluarkan untuk dapat dipakai sebagai alat diagnostik dan sebagai panduan penggunaan antibiotik yang rasional pada kasus infeksi saluran napas atas. Salah satunya yaitu Centor score, tetapi akurasi masih kontroversial. **Tujuan:** Menyediakan laporan kasus berbasis bukti terhadap akurasi dari Centor score sebagai alat diagnostik infeksi saluran napas atas yang disebabkan oleh bakteri *Streptococcus* dibandingkan dengan pemeriksaan kultur tenggorok. **Laporan kasus:** Seorang laki-laki berusia 25 tahun datang ke fasilitas kesehatan tingkat pertama dengan keluhan utama nyeri tenggorokan. Centor score digunakan untuk mendiagnosis pasien ini dan sebagai panduan pemberian antibiotik. **Pertanyaan klinis:** Pada pasien dengan skor tenggorokan, seberapa akurat Centor score dibandingkan dengan kultur tenggorokan pada Infeksi GABHS?. **Metode:** Pencarian literatur dilakukan melalui 4 database dan telaah kritis literatur menggunakan tilikan dari CEBM, University of Oxford. **Hasil:** Seluruh studi yang ditelaah valid. Seluruh studi menunjukkan spesifisitas dan negative predictive value (NPV) yang tinggi, serta sensitivitas dan positive predictive

value (PPV) yang rendah. Centor score dapat diaplikasikan untuk pasien pada skenario klinis karena bersifat mudah digunakan, biaya yang dikeluarkan terjangkau, dan akurat khususnya pada pasien dewasa. **Kesimpulan:** Pasien dengan nyeri tenggorok yang dicurigai memiliki infeksi saluran napas atas yang disebabkan oleh bakteri *Streptococcus* dapat ditegakkan diagnosisnya melalui penilaian Centor score di fasilitas layanan tingkat pertama, serta dapat menjadi panduan dalam pemberian antibiotik.

**Kata kunci:** *Streptococcus*, Centor Score, kultur tenggorok, diagnosis

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## INTRODUCTION

Upper respiratory tract infections (URI), is the most common diagnosis found in health centers (40-60%) and hospitals (15-30%). One hundred and fifty six million cases occur annually worldwide, of which 151 million (96.7%) occur in developing countries, one of which is Indonesia. Based on data from the National Basic Health Research of the Indonesian Ministry of Health, the prevalence of URI was 25.5% in 2007, and 25% in 2013. This figure shows that there is no significant change and indicates that control and management of URI is not optimal. Acute pharyngitis which is included in URI, contributes about 2-5% of patient visits to health facilities. In 2004, acute pharyngitis was one of the top 10 diseases in outpatient visits in Indonesia (1.5% or around 214,781 patients). The prevalence of acute pharyngitis is most common in children in the 5-15 year age range compared to adults.<sup>1</sup>

Acute pharyngitis / tonsillitis is an infectious disease characterized by inflammation of the posterior pharynx and tonsils. The main symptoms most often complained of by patients are sore throat and fever.<sup>2</sup> In acute pharyngitis cases, 40-60% of them are caused by viruses and 5-40% are caused by bacteria. Thus, antibiotic therapy is not always recommended in this case because acute pharyngitis could be cured even without intervention. However, it should be noted that acute pharyngitis might be caused by *Streptococcus pyogenes*, a bacterium

that belongs to group A beta-haemolytic streptococcus, most commonly found in patients suffering from acute pharyngitis due to bacteria.<sup>1</sup> This is because *S. pyogenes* has important clinical significance because it can cause systemic complications after infection including acute rheumatic fever and post-streptococcal glomerulonephritis, which usually occurs 1-3 weeks after infection in the pharynx.<sup>2</sup> Referring to guidelines from the US and UK, if acute pharyngitis caused by *S. pyogenes*, antibiotic management is needed to reduce the possibility of risk of complications, duration of symptoms, and spread of the disease.<sup>3</sup> Although guidelines for antibiotic use in cases of infection have been clearly stated, the phenomenon of excessive and irrational antibiotic prescribing is still common in Indonesia. A study conducted by Yuniar, et al.<sup>1</sup> at two public health centers in Bandung and Cimahi, showed an association between irrational drug use and the incidence and prevalence of acute pharyngitis. It is known that excessive antibiotic prescription occurred at around 80.01%, of which 8.98% included antibiotics as a non-treatment option, and 62.43% of irrational use of corticosteroids. Excessive use of antibiotics can cause resistance which has a negative impact on health.

Identifying the causes of acute pharyngitis is the key to determining optimal management for patients, especially in terms of use.<sup>1</sup> This can be achieved by doing the right diagnosis. At present, the standard examination for

diagnosing streptococcal pharyngitis (GABHS pharyngitis) is throat culture. In addition to throat culture, the use of rapid streptococcal antigen test has also been widely used in the diagnosis of GABHS pharyngitis, especially in children. However, because throat culture procedure is time-consuming and relatively

more expensive, efforts are made to develop certain criteria that will lead to proper use of antibiotics without the need for throat culture. The scoring system that has been developed is the Centor score. **Figure 1** shows the criteria in Centor Score.<sup>3,4</sup>

Symptoms	Points	Score	Post-test probability
Tonsillar exudates	1	0	2.5%
Tender anterior cervical adenopathy	1	1	6.5%
Absence of cough	1	2	15.4%
History of fever (> 38.0°C)	1	3	31.6%
		4	55.7%

**Figure 1. The Centor score<sup>5</sup>**

The Centor Score was developed in 1980 and consists of 4 criteria to predict the likelihood of GABHS pharyngitis, especially in adults. When the 4 criteria in the Centor Score are met, the probability of GABHS pharyngitis is >50%. However, if only 2 criteria or less are met, the probability is <15%.<sup>3,4</sup> Even so, the accuracy of the Centor score in diagnosing GABHS infection is still debatable. Based on the problems described above, we would like to report a case of a patients with sore throat in purpose of finding and assessing the evidences, to find out the accuracy of the Centor Score in diagnosing GABHS infection compared to throat culture in patients with sore throats.

## CASE REPORT

A 25-years old male came to the primary health care with complaints of sore throat, coughing, fever, chills, and body aches for the past 3 days. From physical examination, his body temperature was 38,5°C, his tonsils were swollen T3-T3, hyperemic, no exudates, and there were no neck lymph nodes enlargement on palpation. Throat culture as the gold standard for this diagnosis is time-consuming and relatively expensive. Centor score was

used to determine whether this is a viral or bacterial pharyngitis to decide the prescription of antibiotics to this patient. This patient's Centor score is in the value of 1, so he was not given any antibiotics. He was given symptomatic treatments, such as antipyretic. Three days after, the patient came back for control and his symptoms have improved.

## CLINICAL QUESTION

“In patients with sore throat, how accurate is the Centor score compared to throat culture in diagnosing Group A Beta-Haemolytic Streptococcal (GABHS) Infection?”

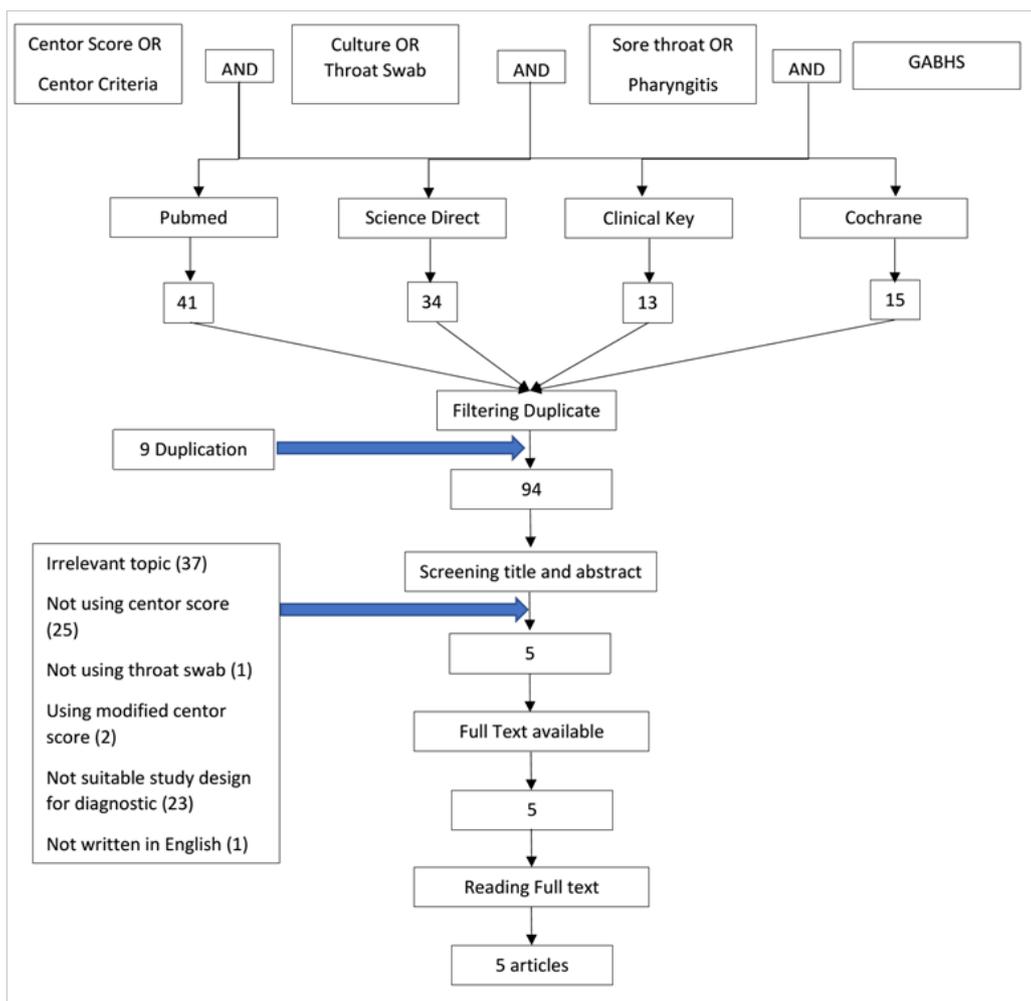
## REVIEW METHOD

To draw a valid conclusion regarding this case report, it was essential to gather evidences systematically and evaluate them. We carried out literature searching, selected articles relevant to answer the clinical question, and assessed the validity, importance, and applicability of each article.

Literature searching was conducted on 4 databases, including Pubmed, Cochrane, Clinical Key, and Science Direct. Key words used are listed in Table 1.

**Table 1. Searching strategy**

Database	Key Words	Hits	Selected
Pubmed	((((((((centor score) OR centor score[MeSH Terms]) OR centor) OR centor[MeSH Terms]) OR centor scoring) OR centor scoring[MeSH Terms])) AND (((((((((pharyngitis) OR pharyngitis[MeSH Terms]) OR bacterial pharyngitis) OR bacterial pharyngitis[MeSH Terms]) OR streptococcal) OR streptococcal[MeSH Terms]) OR streptococcus) OR streptococcus[MeSH Terms]) OR sore throat) OR sore throat[MeSH Terms])) AND ((throat culture) OR throat culture[MeSH Terms])) AND (((((diagnosis) OR diagnosis[MeSH Terms]) OR detect) OR detect[MeSH Terms]) OR assess) OR assess[MeSH Terms])	41	5
ScienceDirect	“Centor score” AND Pharyngitis” AND (“Culture” OR “Throat swab”) AND Diagnostic	34	0
Cochrane	Adult in All Text AND Centor criteria in All Text OR Centor score in All Text AND “Pharyngitis” in All Text (Word variation have been searched)	15	0
ClinicalKey	(Centor score OR Centor criteria) AND (Culture OR Throat swab) AND Diagnostic AND Pharyngitis	13	0



**Figure 2. Article selection flow**

One hundred and three articles in total was retrieved. Nine duplications were found and sorted out. Titles and abstracts were screened to exclude articles that were not suitable for this study. From there, we retrieved 5 articles from Pubmed, including 4 diagnostic studies and 1 systematic review.

Validity, importance, and applicability of the selected studies were assessed using the

Centre of Evidence-based Medicine (CEBM) - University of Oxford, Diagnostic Critical Appraisal Sheet and Systematic Review Sheet.

## RESULT

The summary of the studies selected was displayed in **Table 2**.

**Table 2. Table of summary**

First author	Aalbers et al. <sup>5</sup>	Orda U et al. <sup>6</sup>	Alper Z et al. <sup>7</sup>	Roggen I et al. <sup>4</sup>	Fine et al. <sup>8</sup>
<b>Study design</b>	Systematic review	Diagnostic study	Cross-sectional	Cross-sectional	Cross-sectional
<b>Level of Evidence</b>	1a	1b	1b	1b	1b
<b>Number and characteristics of subjects</b>	21 studies (Pubmed and Embase Database) incorporating 4,839 patients with sore throat complaint	Children aged 3-15 years with sore throat, no antibiotics	Patients > 7 years old (May 2007-April 2008), with sore throat and no antibiotics in the past 3 days (n=287)	All medical records of children aged 2-16 years diagnosed with pharyngitis, tonsillitis, or sore throat, and have a throat swab culture for GABHS, no prior antibiotics treatment (n=441)	All patients above 15 years old with symptoms of GAS pharyngitis and no multiple visit
<b>Index test</b>	Centor score	Centor score	Centor score	Centor score	Centor score
<b>Reference test</b>	Throat culture	Throat culture	Throat culture	Throat culture	Throat culture
<b>Outcome</b>	Diagnosis of Groups A-beta Hemolytic Streptococcus (GABHS) pharyngitis	Diagnosis of Groups A-beta Hemolytic Streptococcus (GABHS) pharyngitis	Diagnosis of Groups A-beta Hemolytic Streptococcus (GABHS) acute tonsillo-pharyngitis	Diagnosis of Groups A-beta Hemolytic Streptococcus (GABHS) pharyngitis	Diagnosis of Groups A-beta Hemolytic Streptococcus (GABHS) pharyngitis
<b>Strength of the study</b>	Pooling results of Centor score thus able to make quantitative validation	Blinding was done for the physician thus minimizing information bias	Blinding was done for the physician thus minimizing information bias	Large number of children included	Large amount and uniformity of data
<b>Limitation of the study</b>	Moderate heterogeneity, possibility of missed articles	Small number of subjects	Excluding Centor score 1 and 2 on the calculation thus might affect the diagnostic values	Selection bias as not all children in the medical records with sore throat had throat cultures result	Asymptomatic streptococcal carriers are not addressed

**Validity****Table 3. Validity of diagnostic studies**

<b>Validity of diagnostic studies</b>				
<b>Parameters</b>	<b>Orda U et al.<sup>6</sup></b>	<b>Alper Z et al<sup>7</sup></b>	<b>Roggen I et al<sup>4</sup></b>	<b>Fine et al<sup>8</sup></b>
Clearly defined question	Yes	Yes	Yes	Yes
Independent and blind comparison with the reference standard	Yes	Yes	Unclear	Yes
Performing the diagnostic test in an appropriate spectrum of patients	Yes	Yes	Yes	Yes
Reference standard was applied regardless of the diagnostic test result	Yes	Yes	No	Yes
<b>Validity of systematic review</b>				
<b>Parameters</b>	<b>Aalbers et al<sup>5</sup></b>			
Clearly defined PICO	Yes			
Finding all relevant evidences	No			
Critical appraisal of the studies	Yes			
Inclusion of high quality studies for the type of question asked	Yes			
Summary table or plot to total up the result	Yes			
Heterogeneity analysis	Yes			

The study by Roggen et al.<sup>4</sup> did not state whether the clinician collecting the information for Centor score was blinded for the throat culture result. In their study, it was also stated that not all children that are eligible for the inclusion criteria had a throat culture result in their medical records as only those with a higher Centor score tend to have the throat culture result. However, they excluded those without the throat culture result and all the children who were finally analyzed in the study were the ones who had both information for Centor score and result of throat culture. Thus, the five studies assessed in Table 3 are considered valid. It was stated

in the limitation of the systematic review by Aalbers et al.<sup>5</sup> that there was a possibility of missing out relevant articles because of imprecise keywords. However, in the method section, it was also stated that the authors have supplemented the search by hand-checking, looking through the references list, searching in Google Scholar and Cochrane Library, and they put no restrictions on language. Thus, actually they had minimized the possibility of missing out relevant articles. Based on this information, the study by Aalbers et al.<sup>5</sup> is considered valid.

**Importance****Table 4. Importance of diagnostic studies and systematic review**

<b>Importance of diagnostic studies</b>				
<b>Parameters</b>	<b>Orda U et al<sup>6</sup></b>	<b>Alper Z et al<sup>7</sup></b>	<b>Roggen I et al<sup>4</sup></b>	<b>Fine et al<sup>8</sup></b>
Sensitivity	23%	40.60%	51.10%	48.60%
Specificity	91%	84.80%	42.10%	81.20%
Likelihood Ratio for positive test result (LR+)	2.56	2.67	0.88	2.59
Likelihood Ratio for negative test result (LR-)	0.85	0.7	1.16	0.63
Positive Predictive Value (PPV)	46%	25.50%	29%	43%
Negative Predictive Value (NPV)	77%	92%	65.10%	84.40%
Pre-test Probability (Prevalence)	25%	11.30%	31.50%	22.60%
Pre-test-odds	33%	12.80%	81.50%	87%
Post-test-odds	85%	34.10%	35%	15.60%
Post-test Probability	46%	25.50%	98.90%	99.90%
<b>Importance of systematic review</b>				
<b>Parameters</b>	<b>Aalbers et al<sup>5</sup></b>			
Sensitivity	49% (38% - 60%)			
Specificity	82% (72% - 88%)			
Likelihood Ratio for positive test result (LR+)	2.68 (1.92 – 3.75)			
Likelihood Ratio for negative test result (LR-)	0.62 (0.52 – 0.74)			
Pre-test Probability (Prevalence)	15%			
Pre-test-odds	18%			
Post-test-odds	50%			
Post-test Probability	33%			
Heterogeneity Test	I <sup>2</sup> = 11%			

Studies by Orda et al,<sup>6</sup> Alper et al,<sup>7</sup> and Fine et al<sup>8</sup> showed similar trend in that they all presented low sensitivity and low positive predictive value (PPV), yet high specificity and high negative predictive value (NPV). Although a diagnostic tool is considered good if they have high values in all four aspects, these results can still be considered important according to the objective of using Centor score to minimize the irrational use of antibiotics as high NPV created confidence in making sure that the patients with negative result (Centor score lower than 3) did not have the disease and did not need antibiotics. Study by Roggen et al<sup>4</sup> showed a different trend compared to the three studies. The higher

sensitivity compared to specificity shown here could be due to the selection bias in this study, as only children who has higher Centor score tends to have the throat culture result. Therefore, there was a lesser possibility of a negative Centor score had a negative throat culture result, thus further will affect the proportion of the true negatives.

The study by Aalbers et al.<sup>5</sup> showed similar trend in with the reviewed cross-sectional studies that it presented low sensitivity and low positive predictive value, yet high specificity and high negative predictive value. Based on the forest plot there was also the evaluation of risk ratio between

predicted and observed of Centor score which was insignificant (CI passed through 1). The result of this reasoning cannot be determined because there was a lack of patient data level in the reviewed studies.

### *Applicability*

All five studies had sufficient information thus allowing the replicability of the index test.

**Table 5. Applicability of selected studies**

Parameters	Orda U et al <sup>6</sup>	Alper Z et al <sup>7</sup>	Roggen I et al <sup>4</sup>	Fine et al <sup>8</sup>	Aalbers et al <sup>5</sup>
Replicability of the index test	Yes	Yes	Yes	Yes	Yes

## DISCUSSION

From all five papers, both in adult and children population, it was found that the Centor score had low sensitivity, high specificity, low PPV, and high NPV. In clinical practice, we focused on predictive values rather than sensitivity and specificity.

In adults, the low PPV and high NPV suggest that the Centor score can be used to ensure that a patient with negative result is truly not having the disease, yet it cannot be used to ensure that a patient with positive result is truly having the disease. To ensure that a patient with positive result is truly having the disease requires further testing with other additional methods, such as rapid diagnostic assay for GABHS or throat culture. The certainty of a negative diagnosis means that we can rule out unnecessary antibiotics use in patients with negative Centor score (score lower than 3) results.

In children, however, while the PPV is similar, the NPV is lower. This means that the scoring system is not accurate enough

to be used in diagnosing GABHS infection in children. The use of other diagnostic modalities is paramount in these cases, especially since children are more susceptible to non-suppurative complications of GABHS infection, such as glomerulonephritis and rheumatic heart disease; a missed diagnosis would be extremely fatal.<sup>11</sup>

Although this diagnostic tool is not really good in detecting GABHS infections, its high NPV raises the confidence in ruling out negative results, therefore decreasing antibiotics misuse and the risk of antibiotics resistance in the population.

To assess applicability in our patient, we adjust the PPV and NPV to data of the Indonesian prevalence of upper respiratory tract infection which are 11% in adults and 26% in the pediatric population, as seen in Table 6.<sup>9</sup> In general, there's no significant difference between the disease prevalence in the studies and in Indonesia, therefore the adjusted PPV and NPV remains similar.

**Table 6. Predictive values after adjustment with Indonesian's prevalence**

Parameters	Orda U et al <sup>6</sup>	Alper Z et al <sup>7</sup>	Roggen I et al <sup>4</sup>	Fine et al <sup>8</sup>
Positive Predictive Value (PPV)	46.2%	27.8%	29%	22.7%
Negative Predictive Value (NPV)	77%	92.7%	65%	92.3%

In our case, this patient had a Centor score value of 1 and considered as negative Centor score. As the NPV of Centor score is high, therefore we could be certain to rule out bacterial infection and antibiotic was not given to this patient. After three days of follow up, the patient came with improved symptoms although he was only received symptomatic treatments. Hence, viral infection was likely the cause of this patient's symptoms, which did not require antibiotics.

In conclusion, from the evidence above, patients with sore throat and suspicion of GABHS infection could be diagnosed with Centor score as first line diagnosis. If the result of Centor score is positive (score 3 or above), the patients need to undergo additional test before they can be prescribed with antibiotics. Whereas patients with negative score (score below 3), antibiotics should not be given to them. This method could be applied in primary health care

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