

Acute exudative tonsillitis in adults: the use of the Centor score and some laboratory tests

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Background/aim: The aim of our study was to determine the usefulness of the Centor score and some basic laboratory tests (complete blood count and C-reactive protein) for the differential diagnosis of exudative tonsillitis due to Group A β -hemolytic streptococcus (GABHS) or due to non-GABHS agents.

Materials and methods: The data of clinical and laboratory characteristics of the patients diagnosed with exudative tonsillitis were collected and statistically compared between those having positive GABHS throat culture result and those who were negative for any bacterial agent.

Results: Totally 899 adult patients were included in our study; 56 (6.2%) of them were positive for GABHS, while 34 (3.8%) of the cases had a bacterial cause other than GABHS. The remaining 809 (90%) were accepted as non-GABHS cases. The percentages of patients having Centor score of 3 or greater, neutrophilia, lymphocytopenia, and CRP values of greater than 5-fold normal upper reference range were significantly higher in GABHS patients.

Conclusion: Centor score of 3 or more together with high CRP, neutrophilia, and lymphocytopenia is predictive for GABHS tonsillopharyngitis.

Key words: Pharyngitis, streptococci, throat culture, Centor score

1. Introduction

Upper respiratory tract infections are common and important diseases with low mortality but high morbidity rates (1). Acute tonsillopharyngitis is one of the most common respiratory tract infections (2). Although the cause of acute pharyngitis in the majority of patients is viral, approximately 5%–17% of cases have a bacterial causative agent, β -hemolytic streptococci being the most common ones (3). Group A β -hemolytic streptococcus (GABHS), namely *Streptococcus pyogenes*, is responsible for almost all bacterial tonsillopharyngitis cases. Other rare bacterial causes of pharyngitis, such as Group B, C, and G β -hemolytic streptococci, *Acrobacterium haemolyticum*, *Neisseria gonorrhoeae*, *Corynebacterium diphtheriae*, and *Fusobacterium necrophorum*, can also be observed. According to US and UK guidelines, antibiotic treatment is recommended only for GABHS pharyngitis (4,5). Throat cultures are currently considered to be the 'reference standard' for the diagnosis of streptococcal pharyngitis (6,7). Rapid streptococcal antigen testing is also widely used

for the diagnosis of GABHS pharyngitis, especially in the pediatric age group. Acute tonsillopharyngitis can initiate an immunologic process that can result in sequelae such as acute rheumatic fever and acute glomerulonephritis. Antibiotic treatment reduces the risk of complications, the duration of symptoms, and the spread of the disease (8–10). Incidence of GABHS varies due to several factors like socioeconomic status, geographic region, and the season (11–15).

Because throat culture is time-consuming and relatively expensive, an attempt was made to develop certain criteria that will lead to appropriate antibiotic use without the need for throat culture (16). The Centor score was developed as a result and it is recommended by guidelines as a decision aid for empirical antibiotic use. In 1980, Centor et al. developed four criteria to predict the probability of GABHS pharyngitis in adults (17). When all four criteria (swollen, tender anterior cervical lymph nodes; fever >38.5 °C; the presence of tonsillar exudate; and the absence of cough) are present, the probability of

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GABHS is just above 50%. When two or fewer criteria are present, the probability is below 15%. Hence, Centor criteria are often used as a tool to assess the absence of GABHS, rather than its presence (3–5). McIsaac et al. developed modified criteria where the score ranged from 0 to 4 and the age of the patient was also included (+1 if age is 3–14 years, 0 if age is 15–44, and –1 if age is ≥ 45), taking into account the fact that GABHS is more prevalent in the age group of 5–15 years (6–10).

Still, several studies have shown that signs and symptoms, neither separately nor combined as prediction rules, were not reliable enough to distinguish between GABHS pharyngitis and non-GABHS pharyngitis (18). In the UK, the National Institute for Health and Clinical Excellence (NICE) recommends that clinicians consider immediate treatment with antibiotics for patients who have three or more Centor criteria (19).

Mistik et al. defined the Mistik score for rapid diagnosis of viral sore throat. The predictive model for positive viral analysis included the following variables: absence of headache, stuffy nose, sneezing, temperature of ≥ 37.5 °C, and tonsillar exudate and/or swelling. The probability of a positive viral analysis for a score of 5 was 82.1%. They suggested its use either alone or in combination with the modified Centor score (20).

The aim of our study was to analyze whether the Centor score and routine laboratory test results would be useful in the diagnosis of GABHS pharyngitis.

2. Materials and methods

We planned our study as a retrospective cohort study. The patient cohort was defined as the patients diagnosed with exudative tonsillitis at the Internal Medicine and Ear-Nose-Throat outpatient clinics between 15 February 2010 and 25 August 2015 in a 300-bed teaching hospital in İstanbul, Turkey. Inclusion criteria were to be within the age range of 16 to 70 years and diagnosed with exudative tonsillitis. Exclusion criteria were to be outside of that age range and using antibiotics at the time of the outpatient visit.

After receiving the approval of the local ethics committee, files were screened and all patients diagnosed with exudative tonsillitis, being 493 females and 406 males, in total 899 patients with mean age of 23 ± 7 years, were included. All patients were tested for GABHS by throat culture, the swabs of which were taken by a doctor with the standard procedure and sent to the microbiology laboratory where they were inoculated on 5% sheep blood agar and incubated at 37 °C overnight. Before incubation, a sinking technique was applied to several inoculated areas to observe increased beta-hemolysis, and bacitracin (0.04 U, Sigma) and SXT (trimethoprim, 1.25 µg, plus sulfamethoxazole, 23.75 µg; Sigma) disks were placed on

the plate to observe the presence of the inhibition zones. After incubation for 24 h and, for the plates found negative at 24 h after total incubation of 48 h, the growth of small colonies with a large β -hemolytic zone and enhanced hemolysis at sunken areas together with the presence of an inhibition zone around the bacitracin disk and the absence of inhibition around the SXT disk confirmed the growth of GABHS. Although some other bacterial causes were also determined, they were not included in statistical comparisons of clinical and laboratory characteristics of the patients; only the patients having positive GABHS culture results and non-GABHS cases were compared.

The clinical characteristics recorded were the presence of painful cervical lymphadenopathy, fever of >38.5 °C, cough, and tonsillar exudate. Laboratory results recorded were C-reactive protein (CRP, as normal or abnormal if greater than 5-fold of the upper reference value), white blood cell count (WBC, as normal or abnormal if $>10,000/\text{mm}^3$), neutrophil count (NEU, as normal or abnormal if $>5380/\text{mm}^3$), lymphocyte count (LYM, as normal or abnormal if $<1320/\text{mm}^3$), mean platelet volume (MPV, as normal or abnormal if >10.8 fL), and platelet distribution width (PDW, as normal or abnormal if >19 fL).

The clinical and laboratory data were compared between two groups statistically using the chi-square test. The arhythmical means with standard deviation were also calculated. The significance value was determined by choosing alpha as 0.01.

3. Results

Among the patients fitting the inclusion criteria, being 899 in number (493 females and 406 males), 56 (6.2%) were positive for GABHS, while 34 (3.8%) had bacterial causes of tonsillitis other than GABHS (Group C and G β -hemolytic streptococci, *Acranobacterium haemolyticum* and *Fusobacterium necrophorum*). There was no statistically significant difference in sex in the GABHS group (26 females and 30 males, $P < 0.01$). Furthermore, 809 (90%) patients were found negative for any bacterial cause and these were accepted as non-GABHS cases.

The clinical and laboratory characteristics of the two groups are presented in the Table.

Among clinical characteristics compared, a Centor score of 3 or greater, the presence of exudative tonsillitis, and the absence of cough were found significantly different. The presence of fever and cervical lymphadenopathy, although more frequent in the GABHS group, was not statistically significant.

In laboratory results, having a CRP value of greater than 5-fold normal upper reference value and the presence of neutrophilia and lymphocytopenia were found significantly different between the two groups compared. The presence of leukocytosis and high MPV and PDW

Table. The clinical and laboratory characteristics of GABHS-positive and GABHS-negative groups.

Variables	Patients with GABHS (n = 56)	Non-GABHS patients (n = 809)	P
Centor score ≥ 3 , n (%)	35 (83.2)	386 (47.7)	<0.001
Fever $>38.5^{\circ}\text{C}$, n (%)	46 (82.1)	623 (77)	NS
Presence of exudative tonsillitis, n (%)	56 (100)	453 (55.9)	<0.001
Presence of cervical lymphadenopathy, n (%)	44 (78.5)	568 (70.2)	NS
Absence of cough, n (%)	48 (85.7)	404 (50)	<0.001
CRP $>5\times$ upper normal range, n (%)	53 (94.6)	631 (77.9)	<0.001
Leukocytosis $>10,000/\text{mm}^3$, n (%)	35 (62.5)	469 (57.9)	NS
Neutrophilia $>5380/\text{mm}^3$, n (%)	60 (93.3)	615 (76)	<0.001
Lymphocytopenia $<1320/\text{mm}^3$, n (%)	38 (67.8)	389 (48)	<0.001
MPV $>10.8\text{ fL}$, n (%)	37.5 (21)	291 (35.9)	NS
PDW $>19\text{ fL}$, n (%)	25 (44.6)	323 (39.9)	NS

values were not significantly different between GABHS patients and non-GABHS tonsillitis patients.

4. Discussion

GABHS is accepted to be the most important pathogenic bacterium that causes acute exudative tonsillitis because of its sequela and complications. Tonsillopharyngitis due to streptococci is a potentially serious disease as it can cause suppurative complications like rheumatoid valvular heart disease and acute glomerulonephritis. As a result, rapid diagnosis and adequate treatment are necessary (1,2). For 50 years, the fundamental test has been throat swab culture. It detects 90%–99% of positive cases and is accepted as the gold standard in GABHS diagnosis (2,21). Rapid streptococcal antigen testing is a reliable method for diagnosis and immediate treatment. It was shown that the sensitivity and the positive predictive value of rapid streptococcal tests are quite lower in adult patient groups than the pediatric age group (22). Although throat culture is a routine procedure for the diagnosis of bacterial pharyngitis in adults, rapid antigen testing is not always ordered in our hospital and those data were not included.

GABHS incidence in upper respiratory tract infections differs between populations. Those differences are due to socioeconomic changes, regions, seasons, and many other factors. Prevalence of acute tonsillopharyngitis due to GABHS was reported to be approximately between 5% and 40% all around the world (2,12,23–25). Estimates of carrier state in GABHS infection range between 2% and 40%. Those carriers are important reservoirs for the spread of infection all around the world (1,12,14,15).

Brunton and Pichichero reported that pharyngitis in adults consists of 30%–65% idiopathic, 30%–60% viral, and 5%–10% bacterial cases, and they declared GABHS infection rates to be 15%–36% in children and 5%–10% in adult cases in the United States (26).

Besides culture, the Centor criteria were described for clinical diagnosis of GABHS tonsillopharyngitis; these criteria were found to be more useful in adult patient populations than children (17,27). McIsaac et al. strengthened the Centor criteria with some modifications and Mistik et al. proposed some parameters for the diagnosis of viral pharyngitis (8,9).

In our study, besides evaluation of the usefulness of Centor scoring in our patient population, we also aimed to determine the laboratory tests that can be used for differentiation between tonsillopharyngitis due to GABHS and non-GABHS causes. In our group of patients with tonsillopharyngitis due to GABHS, we found a greater percentage of high Centor scores in comparison with non-GABHS pharyngitis group (83.2% in the GABHS group and 47.7% in the non-GABHS group, $P < 0.01$). Among the Centor criteria, the presence of tonsillar exudate and the absence of cough were found to be most significant for the use of differentiation from viral infections.

Leukocytosis was not found to be a significant parameter among laboratory tests evaluated, while neutrophilia as found to be significantly more frequent in GABHS cases than non-GABHS cases (93.3% vs. 76%, $P < 0.01$) and lymphocytopenia was more frequent in GABHS patients (67.8% vs. 48%, $P < 0.01$).

CRP increases when there is inflammation throughout the body. In our study, the patients with 5-fold increase of CRP were compared with the rest but the other causes of CRP increase were not investigated. CRP was found to be high in significantly more patients in the GABHS group than the non-GABHS cases group (94.6% vs. 77.9%, $P < 0.01$). Taking into consideration that when low-level increases in CRP are included, it would be difficult to obtain meaningful results, we defined high CRP as a CRP value that 5-fold the normal upper reference value and a significant difference was found between GABHS and non-GABHS cases.

Recent studies revealed the association between platelet indices (PLT, MPV, and PDW) and inflammation

(28). We analyzed MPV and PDW values of our patients for a possible relationship but no significant result that would be useful for the differentiation between GABHS tonsillopharyngitis and non-GABHS pharyngitis was found.

In conclusion, for the differential diagnosis of streptococcal and viral throat infections in adults, a Centor score of 3 or greater was found to be a significant parameter, and in laboratory tests having CRP levels greater than 5-fold the normal value, neutrophilia and lymphocytopenia are good predictors of bacterial infection.

References

- West JV. Acute upper airway infections. *Br Med Bull* 2002; 61: 215-230.
- Santos O, Weckx LL, Pignatari AC, Pignatari SS. Detection of Group A beta-hemolytic *Streptococcus* employing three different detection methods: culture, rapid antigen detecting test, and molecular assay. *Braz J Infect Dis* 2003; 7: 297-300.
- De Meyere M, Matthys J. Acute keelpijn: WVVH-aanbeveling voor goede medische praktijkvoering. *Huisarts Nu* 1999; 28: 193-201 (in Dutch).
- Zwart S, Rovers M, De Melker R, Hoes AW. Penicillin for acute sore throat in children: randomised, double blind trial. *BMJ* 2003; 327: 1324-1328.
- Bisno A, Peter G, Kaplan E. Diagnosis of strep throat in adults: are clinical criteria really good enough? *Clin Infect Dis* 2002; 35: 126-129.
- Schroeder B. Diagnosis and management of group A streptococcal pharyngitis. *Am Fam Physician* 2003; 67: 880-883.
- Ruppert S. Differential diagnosis of common causes of pediatric pharyngitis. *Nurse Pract* 1996; 21: 38-42.
- McIsaac W, Kellner J, Aufricht P, Vanjaka A, Low DE. Empirical validation of guidelines for the management of pharyngitis in children and adults. *JAMA* 2004; 291: 1587-1595.
- McIsaac W, Goel V, To T, Low DE. The validity of a sore throat score in family practice. *CMAJ* 2000; 163: 811-815.
- Vincent M, Celestin N, Hussain A. Pharyngitis. *Am Fam Physician* 2004; 69: 1465-1470.
- Lindbaek M, Høiby EA, Lermark G, Steinsholt IM, Hjortdahl P. Clinical symptoms and signs in sore throat patients with large colony variant beta-haemolytic streptococci groups C or G versus group A. *Br J Gen Pract* 2005; 55: 615-619.
- Dawson KP, Ameen AS, Nsanze H, Bin-Othman S, Mustafa N. The prevalence of group A streptococcal throat carriage in Al Ain, United Arab Emirates. *Ann Trop Paediatr* 1996; 16: 123-127.
- St Sauver JL, Weaver AL, Orvidas LJ, Jacobson RM, Jacobsen SJ. Population-based prevalence of repeated group A beta-hemolytic streptococcal pharyngitis episodes. *Mayo Clin Proc* 2006; 81: 1172-1176.
- Gunnarsson RK, Holm SE, Söderström M. The prevalence of beta-haemolytic streptococci in throat specimens from healthy children and adults. Implications for the clinical value of throat cultures. *Scand J Prim Health Care* 1997; 15: 149-155.
- Sevinc I, Enoz M. The prevalence of group A beta hemolytic *Streptococcus* in healthy Turkish children in day-care centers in Ankara. *Chang Gung Med J* 2008; 31: 554-558.
- Snow V, Mottur-Pilson C, Cooper RJ, Hoffman JR. Principles of appropriate antibiotic use for acute pharyngitis in adults. *Ann Intern Med* 2001; 134: 506-508.
- Centor R, Witherspoon J, Dalton H, Brody CE, Link K. The diagnosis of strep throat in adults in the emergency room. *Med Decis Making* 1981; 1: 239-246.
- Shaikh N, Swaminathan N, Hooper E. Accuracy and precision of the signs and symptoms of streptococcal pharyngitis in children: a systematic review. *J Pediatr* 2012; 160: 487-493.
- NICE Short Clinical Guidelines Technical Team. Respiratory Tract Infections - Antibiotic Prescribing. Prescribing of Antibiotics for Self-Limiting Respiratory Tract Infections in Adults and Children in Primary Care NICE Clinical Guideline 69. London, UK: National Institute for Health and Clinical Excellence; 2008.
- Mistik S, Gokahmetoglu S, Balci E, Onuk FA. Sore throat in primary care project: a clinical score to diagnose viral sore throat. *Fam Pract* 2015; 32: 263-268.
- McDonald M, Towers R, Fagan P, McKinnon M, Bengner N, Andrews R, Curie BJ, Carapetis J. Recovering streptococci from the throat, a practical alternative to direct plating in remote tropical communities. *J Clin Microbiol* 2006; 44: 547-552.

22. Gurol Y, Akan H, Izbirak G, Tekkanat ZT, Gunduz TS, Hayran O, Yilmaz G. The sensitivity and specificity of rapid antigen test in streptococcal upper respiratory tract infections. *Int J Pediatr Otorhinolaryngol* 2010; 74: 591-593.
23. Treebupachatsakul P, Tiengrim S, Thamlikitkul V. Upper respiratory tract infection in Thai adults: prevalence and prediction of bacterial causes, and effectiveness of using clinical practice guidelines. *J Med Assoc Thai* 2006; 89: 1178-1186.
24. Enöz M, Sevinç I, İnançlı HM. The incidence of group A beta haemolytic streptococci in upper respiratory tract infections in Erzurum. *Kulak Burun Bogaz İhtis Derg* 2009; 19: 285-288 (in Turkish with English abstract).
25. Sevinc I, Enoz M. The incidence of group a beta hemolytic streptococci in throat specimens from upper respiratory infections. *Acta Medica* 2007; 50: 243-244.
26. Brunton S, Pichichero M. Considerations in the use of antibiotics for streptococcal pharyngitis. *J Fam Pract* 2006; 55: 9-16.
27. Roggen I, van Berlaer G, Gordts F, Pierard D, Hubloue I. Centor criteria in children in a paediatric emergency department: for what it is worth. *BMJ Open* 2013; 3: e002712.
28. Santimone I, Di Castelnuovo A, De Curtis A, Spinelli M, Cugino D, Gianfagna F, Zito F, Donati MB, Cerletti C, De Gaetano G, Lacoviello L, MOLI-SANI Project Investigators. White blood cell count, sex and age are major determinants of heterogeneity of platelet indices in an adult general population: results from the MOLI-SANI project. *Haematologica* 2011; 96: 1180-1188.