Euras J Fam Med 2020;9(4):225-32. doi:10.33880/ejfm.2020090405

Rapid Antigen Detection Test Using Rates of Family Physicians, Test Results and Its Impact on Their Prescription Behaviours

Humeyra Aslaner, Haci Ahmet Aslaner, Bade Erturk Arik, Fahri Alpay Onuk, Ali Ramazan Benli, Selcuk Mistik

https://doi.org/10.33880/ejfm.2020090405

Original Research / Orijinal Araştırma

AUTHORS / YAZARLAR

Hümeyra Aslaner
(*Corresponding Author*)

drhumeyra@hotmail.com

Kayseri City Hospital, Family Medicine, Kayseri, Turkey
ORCID iD:
0000-0002-3710-3893

Haci Ahmet Aslaner
İncesu County State Hospital, İnternal Medicine, Kayseri, Turkey
ORCID iD:
0000-0003-3331-8667

Bade Ertürk Arik
Tomarza Yaşar Karayel County State Hospital, Kayseri, Turkey
ORCID iD:
0000-0002-0898-1099

Fahri Alpay Onuk
Felahiye County State Hospital, Kayseri, Turkey
ORCID iD:
0000-0002-4838-7801

Ali Ramazan Benli
Health Directorate of Kayseri, Kayseri, Turkey
ORCID iD:
0000-0003-0039-1497

Selçuk Mıstık
Department of Family Practice, Faculty of Medicine, Erciyes University, Kayseri, Turkey
ORCID iD:
0000-0003-0657-3881

Date of submission
29.04.2020

Date of acceptance
08.12.2020

ABSTRACT

Aim: The aim of this study is to determine the rates of rapid antigen detection test use, test results and its relationship with Modified Centor Score and investigate the effect of rapid antigen detection test use on prescribing behaviour.

Methods: This research was conducted by scanning the family physicians' information system retrospectively. From the Family Medicine Information System, where polyclinics and prescription records of the family health centers where 12 family physicians work in Kayseri are located, the number and results of rapid antigen detection tests performed between February 2017 and April 2019, the Modified Centor Score automatically calculated by the system, the number of prescribed antibiotics and symptomatic treatment information was recorded.

Results: The positivity of rapid antigen detection test was considered, cut-off value of Modified Centor Score was >2 (ROC EAA:63.9, Cl:0.95,0.61-0.66). Sensitivity rate of the test for diagnostic score was 86% and selectivity rate was 48.8%.

Conclusion: Family physicians should be encouraged to use rapid antigen detection test. The fact that antibiotics are prescribed in rapid antigen detection test negative patients may indicate that confidence level of the test is less than physical examination and clinical findings.

Keywords: sore throat, primary care, score

Aile Hekimlerinin Hızlı Antijen Testi Kullanım Oranları, Test Sonuçları ve Reçetelendirmeye Etkisi

ÖZ

Amaç: Bu çalışmanın amacı, hızlı antijen testi kullanım oranlarını, test sonuçlarını, Modifiye Centor Skoru ile ilişkisini belirlemek ve hızlı antijen testi kullanımının reçete yazma davranışı üzerindeki etkisini araştırmaktır.

Yöntem: Bu araştırma Aile Hekimliği Bilgi Sistemi retrospektif taranarak yapılmıştır. Kayseri'de 12 aile hekiminin çalıştığı aile sağlığı merkezinin poliklinik ve reçete kayıtlarının yer aldığı Aile Hekimliği Bilgi Sistemi'nden, 2017 Şubat ile 2019 Nisan ayları arasında yapılan hızlı antijen testi testi sayısı ve sonuçları, sistem tarafından otomatik hesaplanan Modifiye Centor Skorları, reçetelenen antibiyotik sayıları ve semptomatik tedavi bilgileri kaydedildi.

Bulgular: Hızlı antijen testi pozitifliği dikkate alınarak bakıldığında Modifiye Centor Skoru cut-off değeri >2 idi (ROC EAA:63,9, Cl:0,95,0,61-0,66). Tanı puanı için testin duyarlılığı %86, seçiciliği %48,8'dir.

Sonuç: Aile hekimleri tarafından hızlı antijen testi kullanımı teşvik edilmelidir. Hızlı antijen testi negatif hastalarda da antibiyotik reçete ediliyor olması teste olan güvenin fizik muayeneye ve klinik bulgulara olan güvenden daha az olduğunun bir göstergesi olabilir.

Anahtar kelimeler: boğaz ağrısı, birinci basamak, skor

How to cite / Atıf için: Aslaner H, Aslaner HA, Erturk Arik B, Onuk FA, Benli AR, Mistik S. Rapid antigen detection test using rates of family physicians, test results and its impact on their prescription behaviours. Euras J Fam Med 2020;9(4):225-32. doi:10.33880/ejfm.2020090405.

Conflict of interest: No conflict of interest was declared by the authors.
Financial disclosure: No financial disclosure was declared by the authors.

Introduction

Upper respiratory tract infections are among the most common diseases in primary health care. Group A streptococcus (GAS) is the most common bacterial pathogen that causes acute tonsillopharyngitis. Various methods have been developed to identify the agent more rapidly in patients with tonsillopharyngitis. Rapid antigen test (RAT) is a practical and rapid test to detect GAS antigen. The usage of this test which can yield results within 15-20 minutes is limited due to its high cost (1). RAT is more expensive than throat culture which is the gold standard test. However, it is a very important test as it prevents the spread of GAS and its complications and it allows the patient to return to his or her work life in a shorter time by providing a rapid diagnosis. Nowadays, it is easy to evaluate these tests that are analysed with enzyme or optical immunoassay method and they have a good rate of specificity. This test has a selectivity at a rate above 90% but a sensitivity at a rate of 75-90%. If RAT is positive in a patient who is clinically thought to be GAS, antibiotics can directly be started without asking for any culture test (2). It was revealed that the percentage of appropriate antibiotic use was higher in some patient groups who were diagnosed by RAT (e.g. patients admitted to the emergency department) than in patients who underwent culture test (3). In acute tonsillopharyngitis, the criteria (clinical scores) in which clinical conditions these tests will be used have also been determined (4). Clinical scoring and rapid tests can be helpful in planning of antibiotic treatment. Centor et al. identified four signs and symptoms in order to predict the possibility of acute GAS pharyngitis in adults with sore throat (Table 1) (5).

Table 1. Modified Centor Score

Criterion	Score
Fever > 38º C	1
Lack of cough	1
Cervical lymphadenopathy	1
Tonsillary swelling and exudate	1
Age	
3-14 years	1
15-44 years	0
45 years or older	-1

Physicians can use RAT in patients who have a high probability of streptococcal infection (rapid antigen test recommended Modified Centor Score is 2-3) (6). Early diagnosis and treatment of GAS is important especially in primary care since it may cause suppurative complications such as acute rheumatic fever and acute poststreptococcal nephritis in the course of disease (7).

This study aimed to determine the rates of RAT use, test results and its relationship with Modified Centor Score (MCS) and investigate the effect of RAT use on prescription.

Methods

The study was approved by the local ethics committee according to the principles of the Declaration of Helsinki.

Patients with diagnosed ICD-10 code of acute upper respiratory tract infection, who had applied to a Family Medicine Centre which is located in the centre of Kayseri province between February 2017 and April 2019 were included in the study. Patients were between 3 and 80 years old.

There is an application covering the diagnostic criteria suitable for the Family Medicine Information System (FMIS) used by family physicians. In this application, when a diagnosis ICD-10 code of acute upper respiratory tract infection by the ministry of health is typed in the system after the examination, a template compatible with the MCS comes out automatically. MCS may differ between -1 and 5. According to MCS, 1 and less show that there is no need for antibiotics or further examination, scores of 2 and 3 show that RAT or throat culture is recommended for the patient, and scores of 4 and more show that empirical antibiotic is required.

TOYO in vitro diagnostic tests distributed by the Ministry of Health in January 2017 have been used in family health centers in Turkey.

This study was retrospectively performed in 12 family medicine departments in Kayseri. Patients who had been admitted since the date when RAT started to be used were included in the study. Characteristics and prescriptions of the patients who had received the

diagnosis code for acute upper respiratory tract infections and who underwent RAT were analysed. Firstly, the number of patients who had received the proper ICD-10 code was determined. Out of these patients with the diagnosis code, those who underwent RAT were recorded. Their RAT results were evaluated. Prescriptions of these patients were analysed. Antibiotics, antipyretics, cold medicines and medicines such as gargle or spray in the prescriptions were recorded. The number of medicines in each prescription was noted down. The months when patients presented to the family health centers were recorded.

While descriptive statistics for continuous variables were expressed as mean, standard deviation, and minimum and maximum values, categorical variables were expressed as number and percentiles. Data were given as mean ± standard deviation. Kolmogorov Smirnov test was used to determine whether numerical data belonging to the variables were compatible with the normal distribution. Chi-square test was used to determine the relationship between the groups and categorical variables. Statistical significance level was accepted as 5% in the calculations and SPSS statistical package software was used for calculations. *p* value equal to or lower than this value was commented as "the relationship between the parameters was statistically significant". ROC analysis were applied as well. Cut-off values were determined. The linear relationship between the variables were evaluated by Spearman correlation test. Independent indicators affecting the antibiotic prescription were determined with logistic regression analysis.

Results

The number of patients admitted with stated ICD 10 codes between February 2017 and April 2019 was 24,018. RAT was performed in 1,433 (5%) of the patients. Six hundred and eighty-one (46.5%) of the patients were male and 783 (53.5%) of them were female. There were 822 children (57.4%) and 611 adults (42.6%). Median age of the patients was 13 (3-80). Demographic data, clinical characteristics and treatment modalities are listed in Table 2, diagnostic scores in Table 3, ICD 10 codes in Table 4.

Table 2. Demographic and clinical characteristics of the patients

	n	%
Gender		
Female	785	54.8
Male	648	45.2
RAT		
Positive	428	29.9
Negative	1005	70.1
Number of medicines prescribed		
1	198	13.8
2	692	48.3
3	451	31.5
4	78	5.4
5	14	1.0
Antibiotics		
Prescribed	667	46.5
Not Prescribed	766	53.5
Antibiotic types		
Amoxicillin-clavulanic acid	339	50.8
Penicillin	170	25.5
Cephalosporin	108	16.2
Clarithromycin	17	2.5
Others	33	4.9
Antipyretics		
Prescribed	1187	82.8
Not Prescribed	246	17.2
Antipyretics types		
Paracetamol+antihistaminic+ decongenstant	521	43.9
Ibuprofen+antihistaminic+ decongenstant	456	38.4
Paracetamol+ibuprofen	208	17.5
Metamizole	2	0.2

Two hundred and thirty-five (54.9%) of RAT positive patients were pediatric patients. Mean number of medicines prescribed for the whole patient group who underwent RAT was 2.3 ± 0.8. Among patients who underwent RAT, the number of patients who were not prescribed antibiotics was 766 (53.5%) and that of patients prescribed antibiotics was 667 (46.5%). Oral treatment was initiated in 497 (74.5%) of the patients prescribed antibiotics, while 170 (25.5%) patients started parenteral treatment. Amoxicillin-clavulanic acid was mostly preferred (at a rate of 48.8%) in RAT positive patients.

Ibuprofen+decongestant+antihistaminic medicines were the most preferred medicine group in RAT positive patient group at a rate of 20.3% (n=87).

Table 3. Diagnostic scores

Diagnostic scores	n	%
-1	7	0.5
0	77	5.4
1	174	12.1
2	292	20.4
3	260	18.1
4	269	18.8
5	354	24.7

Diagnostic score of the patient group prescribed antibiotics was 2 and more and this was significantly higher (p<0.001). According to RAT results, diagnostic score was significantly higher in RAT positive group (p<0.000). Diagnostic score of the whole RAT positive patient group was 2 and more.

Table 4. ICD 10 codes

ICD 10 code	n	%
J00 Acute nasopharyngitis	131	9.1
J02 Acute pharyngitis	277	19.3
J03 Acute tonsillitis	490	34.2
J03.0 Streptococcaltonsillitis	175	12.2
J06 Acute upper respiratory infections of multiple and unspecified sites	300	20.9
J02.0 Streptococcal pharyngitis	8	0.6
J02.8 Acute pharyngitis due to other specified organisms	21	1.5
J02.9 Acute pharyngitis, unspecified	12	0.8
J03.8 Acute tonsillitis due to other specified organisms	8	0.6
J03.9 Acute tonsillitis, unspecified	11	0.8

The number of medicines prescribed was significantly higher in the patient group prescribed antibiotics (p<0.001). When we divided the patients who underwent RAT into two groups as pediatric and adult patients, antibiotic prescription rate was significantly higher in pediatric group (n=448, 67.2%) (p<0.000). When we divided the patients into two groups as RAT positive and RAT negative patients, there was a significant difference between the groups as all the patients in RAT positive group were prescribed antibiotics (p<0.001). In RAT negative group, 239 (23.8%) patients were prescribed antibiotics. In RAT negative group, median diagnostic score of the patients prescribed antibiotics was 5 (4-5) and significantly higher (p<0.001) (Figure 1).

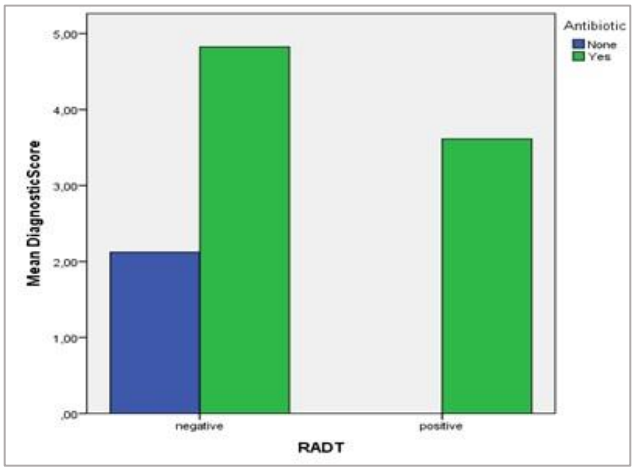

Figure 1: Diagnostic score of patients prescribed antibiotics according to rapid antigen test

In ROC analysis performed by considering RAT positivity, diagnostic cut-off score was >2 and the area under the curve was 70.9% (Cl:0.95,0.68-0.73), (p<0.001). Sensitivity rate of the test for diagnostic score was 86%. Selectivity rate of the test for diagnostic score was 48.8%. Positive predictive value of the diagnostic score test was 41.7% while negative predictive value of the diagnostic scoring test was 89.1%. There was no correlation between diagnostic score and the number of medicines prescribed (p=0.231, r= -0.032). There was a significantly poor negative correlation between diagnostic score and age (p<0.001, r= -0.377). Logistic regression analysis used to evaluate factors affecting antibiotic prescription is given in Table 5.

Table 5. Evaluation of factors affecting antibiotic prescription through logistic regression analysis

Antibiotic Prescription			95%C.I.for EXP(B)	
	p	Exp (B)	Lower	Upper
Age	0.000	0.983	0.977	0.990
Diagnostic Score	0.000	3.497	3.089	3.959
RADT	0.000	13.481	9.355	19.428

Discussion

This study was performed by analysing retrospective records in order to determine the rates of RAT use, tests results and its relationship with MCS and investigate the effect of RAT use on prescription. Acute tonsillopharyngitis is a very common disease and one of the most common causes of admissions to the family health centers. Even experienced physicians

may not be able to diagnose streptococcal tonsillopharyngitis with the medical history, clinical symptoms and signs of the patient (8). The Infectious Diseases Society of America (IDSA) suggested to use throat culture test or RAT in order to detect GAS. They also recommended the use of clinical algorithms in adults with high probability of GAS (9). RAT gives more rapid results compared to throat culture. While positive results allow early diagnosis and treatment, negative results prevent unnecessary antibiotherapy (10).

RAT usage has not been a routine in practice yet among family physicians. Studies revealed that RAT was not sufficiently used in patients with acute tonsillopharyngitis (11). It was found in a study that French family physicians used RAT in only 60.1% of the pediatric patients with tonsillopharyngitis (12). It was revealed that the rates of RAT usage in patients with sore throat were between 7% and 54% (11,13). In our study, the rate of RAT use is 5%.

Lower rate of RAT use compared to literature may be because the time allocated for the test causes disruptions in the routine work of family physicians. It may also be because there is a low level of confidence in the test as stated in some publications in literature (14).

While Topyaka et al. (15) found 23% of RAT positivity in 174 pediatric patients with tonsillopharyngitis; Cabbarpur et al. found RAT positivity in 14% of the patients presenting with complaints of fever, sore throat and swallowing difficulty and having hyperaemia in tonsillo-pharyngeal region and painful cervical lymphadenopathy on physical examination (16). In our study, RAT positivity rate was 29.9%. It was higher than the rate in literature.

The number of studies evaluating the effects of RAT on antibiotic use and the rates of antibiotic use is not much. Worral et al. reported that antibiotic was prescribed at a rate of 38.2% in the group in which clinical score and RAT were used together, 26.7% in the group in which only RAT was used and 58.2% in the control group in which neither of them were used (17). Llor et al. reported that the rate of antibiotic prescription was lower in the group who underwent RAT (43.8%) than in the control group (64.1%) and that 98.3% of RAT positive patients were prescribed antibiotics (18).

In their study with throat culture in 2015, Mıstık et al. reported a high rate (74.8%) of antibiotic prescription despite 18.5% of GAS infection presence in the same population which we performed our study with (19). In our study, clinical score-guided RAT was performed. While the rate of antibiotic prescription was 46.5%, the whole RAT positive group was prescribed antibiotics. The rate of antibiotic prescription in RAT-positive patients was 13,481 times higher than that of RAT-negative patients. Similar to literature, the rates of antibiotic prescription in patients whose test results were positive were higher. We think that RAT gives results faster and more easily than throat culture does, which decreases the rate of antibiotic prescription. Increase in diagnostic score also increases the rate of antibiotic prescription by 3.497 times. In RAT negative group in our study, 23.8% of the patients were prescribed antibiotics. This may be because physicians trusted more in clinical scoring in patients with higher diagnostic scores although RAT was negative. It may also be because patients whose scores were 4 or more could empirically prescribed antibiotics according to MCS.

In which diagnostic scores RAT should be requested has been reported in studies. McIsaac et al. reported that clinical findings and MCS alone were insufficient in bacterial/viral distinction in cases diagnosed with tonsillopharyngitis and that throat culture or RAT was needed in cases with MCS of >2 (20-22). Kose et al. reported in their studies on throat culture that sensitivity was 97.3% and specificity was 16.2% in the detection of MCS as >2. In our study, MCS of >2 was detected as cut off value by considering RAT positivity (23). This suggests that requesting RAT from patients with diagnostic score of >2 in practice of family physicians will be a correct and economical move. While the rate of antibiotic prescription was 46.5% in our study, 100% of RAT positive group was prescribed antibiotics. The rates of

antibiotic prescription were similar with those in studies done with RAT. RAT gives results more rapidly and easily than throat culture, which decreases the rate of antibiotic prescription.

Although the rate of antibiotic prescription decreases with RAT use, inappropriate antibiotic prescribing cannot be completely prevented. Antibiotics may be prescribed for 30.7% of RAT negative patients. In the studies, MCS of the most of RAT negative patients prescribed antibiotics was 4 (18). In our study, 23.8% of the patients in RAT negative group were prescribed antibiotics. This may be because the diagnostic score of the patients who were prescribed antibiotics in RAT negative group was significantly higher, physicians had more confidence in clinical scoring and it was predicted that antibiotics could be empirically prescribed by the system to the patients with a score of 4 or higher according to the MCS.

Since GAS is more common in pediatric age group, the rate of antibiotic prescription is higher especially for children aged between 6 and 11 (23). Physicians prescribe antibiotics to 53% of the children with sore throat, which exceeds the expected maximum prevalence of GAS. RAT sensitivity was reported as 86% and RAT selectivity as 92% among pediatric patients. In the study of Pontin et al. RAT was positive in 18.1% of the pediatric patients (24). Topyaka et al. found that 23% of the pediatric patient group was RAT positive (15). It was reported in the studies performed in pediatric age group that the rates of antibiotic prescription differed between 22% and 28% in patients who underwent RAT (20,21). In our study, 67.2% of the pediatric patients who underwent RAT were prescribed antibiotics, which is higher than the rates in literature. This may be because the rate of RAT positive pediatric patients was 54.9% and may be due to avoiding the development of complications such as acute rheumatic diseases in pediatric age group.

In the study of Llor et al. (18), the most common medicine prescribed was amoxicillin (52.9%) and then penicillin (19.9%), amoxicillin and clavulanic acid (17%) and other antibiotics (3.1%) respectively in patients who underwent RAT (21). In our study, except that the most preferred medicine was amoxicillin clavulanic acid, other antibiotic use preferences were similar. The reason why the combination of clavulanic acid and amoxicillin was preferred more than amoxicillin may be its broader spectrum. It is also known that various medicines are commonly prescribed in addition to antibiotics for symptomatic treatment. While Tiwari et al and Torvi et al. reported that mean 3.4 and 2.2 medicines were prescribed for pediatric patients with upper respiratory tract infection, it was observed that minimum 1 and maximum 6 medicines were prescribed. The rates of patients prescribed 2, 3, 4 and 5 medicines for each prescription were 21%, 37%, 30% and 8% respectively (25,26). In the study in which Mıstık et al. used throat culture, 98.3% (the highest rate) was prescribed one medicine while 5.7% (the lowest rate) was prescribed four medicines (19).

Paracetamol+ antihistaminic+ decongestant medicines were the most used medicine group in sore throat while ibuprofen was mostly preferred for GAS pharyngitis (18,24,27). It was reported in the study of Das et al. that the rate of cough and cold combination medicine use was 47% (28). In another study, the most preferred medicines for upper respiratory tract infections were cough and cold combination medicines (27%) followed by antipyretics (21%) and nasal drops (15%) (25). In our study, the mean number of medicines prescribed was 2.3 ± 0.8. 2 medicines (48.3%) were prescribed at the highest rate. Minimum 1 and maximum 5 medicines were prescribed. The most common medicines prescribed were cold (39.3%) and paracetamol+ antihistaminic+ decongestant medicine group (19.7%). Although the results are similar to those in literature, the reason why there are some tiny differences may be that the population in our group underwent RAT. Similar to the study of Mıstık et al. the most preferred medicine group in RAT positive patient group was ibuprofen+ antihistaminic+ decongestant medicine group (19). The reason of this may be that GAS infection has a severe clinical picture and that the effectiveness of ibuprofen group is higher (29). Analysing

retrospective records and not being able to reach throat culture results of the patients are the limitations of this study.

Conclusion

Clinical score-guided RAT was performed in this study and some patients were prescribed antibiotics although their RAT results were negative. It is more accurate to analyse patients with relevant diagnosis and symptoms according to Modified Centor criteria and then perform RAT in these patients to direct the decision of antibiotic prescription. The use of MCS and RAT together will provide patients who especially need symptomatic treatment to receive immediate treatment. In order to decrease the rate of antibiotic prescription, RAT use should be encouraged by family physicians.

References

1. Tanz RR, Gerber MA, Kabat W, Rippe J, Seshadri R, Shulman ST. Performance of a rapid antigen-detection test and throat culture in community pediatric offices: Implications for management of pharyngitis. Pediatrics 2009;123:437–44. doi: 10.1542/peds.2008-0488.
2. Gerber MA. Comparison of throat cultures and rapid strep tests for diagnosis of streptococcal pharyngitis. Pediatr Infect Dis J 1989;8(11):820-4. doi: 10.1097/00006454-198911000-00032.
3. Lieu TA, Fleisher GR, Schwartz JS. Clinical evaluation of a latex agglutination test for streptococcal pharyngitis: performance and impact on treatment rates. Pediatr Infect Dis J 1988;7(12):847-54.
4. Hashigucci K, Matsunobu T. Etiology of acute pharyngitis in adults: the presence of viruses and bacteria. Nippon Jibiinkoka Gakkai Kaiho 2003;106:532–9. doi: 10.3950/jibiinkoka.106.532.
5. Centor RM, Witherspoon JM, Dalton HP, Brody CE, Link K. The diagnosis of strep throat in adults in the emergency room. Med Decis Mak 1981;1(3):239-46. doi: 10.1177/0272989X8100100304.
6. Pelucchi C, Grigoryan L, Galeone C, Esposito S, Huovinen P, Little P, et al. Guideline for the management of acute sore throat. Clin Microbiol Infect 2012;18:1–27. doi: 10.1111/j.1469-0691.2012.03766.x.
7. Gözüküçük R, Göçmen İ, Nas Y, Yılmazer F, Ünüvar E. Streptokoksik tonsillofarenjit tanısında Strep-A hızlı testinin etkinliği. Çocuk Derg 2011;11(4):157-9. doi.org/10.5222/j.child.2011.157.
8. Choby BA. Diagnosis and treatment of streptococcal pharyngitis. Am Fam Physician 2009;79:383–90. doi: 10.1001/jama.254.7.907.
9. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, et al. Clinical practice guideline for the diagnosis and management of group a streptococcal pharyngitis: 2012 update by the infectious diseases society of America. Clin Infect Dis 2012;55:86–102. doi: 10.1093/cid/cis629.
10. Bisno AL, Peter GS, Kaplan EL. Diagnosis of strep throat in adults: are clinical criteria really good enough? Clin Infect Dis 2002;35:126–9. doi: 10.1086/342056.
11. Gonzales R, Camargo CA, MacKenzie T, Kersey AS, Maselli J, Levin SK, et al. Antibiotic treatment of acute respiratory infections in acute care settings. Acad Emerg Med 2006;13:288–94. doi: 10.1197/j.aem.2005.10.016.
12. Linder JA, Bates DW, Lee GM, Finkelstein JA. Antibiotic treatment of children with sore throat. J Am Med Assoc 2005;294:2315–22. doi: 10.1001/jama.294.18.2315.
13. Portier H, Peyramond D, Boucot I, Grappin M, Boibieux A, Pribil C, et al. Assessing applicability of

guidelines on management of pharyngitis in adults in general practice. Med Mal Infect 2001;31:396–402. doi: 10.1016/S0399-077X(01)00210-4.
14. Pulcini C, Pauvif L, Paraponaris A, Verger P, Ventelou B. Perceptions and attitudes of French general practitioners towards rapid antigen diagnostic tests in acute pharyngitis using a randomized case vignette study. J Antimicrob Chemother 2012;67:1540–6. doi: 10.1093/jac/dks073.
15. Topkaya AE, Uysal S, Johansson CB. Boğaz sürüntü örneklerinde antijen tarama testi ile kültürün karşılaştırılması. Flora 2003;8(4):287–90.
16. Cabbarpur C, Büyüklü F, Çakmak Ö, Haşimoğlu R, Ergin F, Özhan Rz, et al. Akut tonsillofarenjitte rapid strep A testi kullanımı. KBB-Forum 2004;3(1):10–2.
17. 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):666–71.
18. Llor C, Madurell J, Balagué-Corbella M, Gómez M, Cots JM. Impact on antibiotic prescription of rapid antigen detection testing in acute pharyngitis in adults: A randomised clinical trial. Br J Gen Pract 2011;61:244–51. doi: 10.3399/bjgp11X572436.
19. 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;32:263–8. doi: 10.1093/fampra/cmv015.
20. McIsaac WJ, Goel V, Slaughter PM, Parsons GW, Woolnough K V, Weir PT, et al. Reconsidering sore throats - part 2: alternative approach and practical office tool. Can Fam Physician 1997;43:495–500. PMID: 9116521.
21. McIsaac WJ, Goel V, To T, Low DE. The validity of a sore throat score in family practice. Cmaj 2000;163(7):811–5.
22. McIsaac WJ, Kellner JD, Aufricht P, Vanjaka A, Low DE. Empirical validation of guidelines for the management of pharyngitis in children and adults. J Am Med Assoc 2004;291:1587–95. doi: 10.1001/jama.291.13.1587.
23. Kose E, Kose SS, Akca D, Yildiz K, Elmas C, Baris M, et al. The effect of rapid antigen detection test on antibiotic prescription decision of clinicians and reducing antibiotic costs in children with acute pharyngitis. J Trop Pediatr 2016;62:308–15. doi: 10.1093/tropej/fmw014.
24. Pontin IPO, Sanchez DCJ, Di Francesco R. Asymptomatic Group A Streptococcus carriage in children with recurrent tonsillitis and tonsillar hypertrophy. Int J Pediatr Otorhinolaryngol 2016;86:57–9. doi: 10.1016/j.ijporl.2016.03.044.
25. Tiwari P, Ahlawat R, Gupta G. Prescription practice in patients of upper respiratory tract infection at a pediatric outpatient clinic in Punjab. Indian J Pharm Pract 2014;7:26–32. doi: 10.5530/ijopp.7.2.6.
26. Torvi JR, Dambal S. Drug prescription pattern in paediatric out patient clinic in a tertiary hospital. Curr Pediatr Res 2011;15(2):77–80.
27. Le Marechal F, Martinot A, Duhamel A, Pruvost I, Dubos F. Streptococcal pharyngitis in children: A meta-analysis of clinical decision rules and their clinical variables. BMJ Open 2013;3:e001482. doi: 10.1136/bmjopen-2012-001482.
28. Das B, Sarkar C, Majumder AG. Medication use for pediatric upper respiratory tract infections. Fundam Clin Pharmacol 2006;20:385–90. doi: 10.1111/j.1472-8206.2006.00414.x.
29. Sullivan JE, Farrar HC. Fever and antipyretic use in children. Pediatrics 2011;127(3):580–7. doi: 10.1542/peds.2010-3852.