

Original Article

Trends in the use of antibiotics for pharyngitis in Saudi Arabia

Rawaa Ibrahim Olwi^{1,2}, Duaa Ibrahim Olwi^{3,4,5}

¹ Department of Family and Community Medicine, University of Toronto, Toronto, Canada

² King Faisal Specialist Hospital and Research Center, Jeddah, Saudi Arabia

³ MRC Epidemiology Unit, Institute of Metabolic Science, University of Cambridge, Cambridge, United Kingdom

⁴ King Abdullah International Medical Research Center, Jeddah, Saudi Arabia

⁵ King Saud bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia

Abstract

Introduction: Pharyngitis is one of the most common diagnoses for antibiotic prescriptions worldwide. Antibiotics should be prescribed for bacterial pharyngitis to reduce its complications. The aims of this study were to assess antibiotic prescriptions for pharyngitis cases, and their relationship with physicians' knowledge regarding its diagnosis and management.

Methodology: A cross-sectional study was conducted. First, prescriptions for pharyngitis cases using the modified Centor criteria was evaluated at primary care centers in Saudi Arabia. Second, physicians' knowledge of the modified Centor score and the diagnosis and management of pharyngitis was assessed using a self-administered questionnaire.

Results: Out of 104 pharyngitis cases, 79% (n = 82) were prescribed antibiotics, of which 28% were evidence-based prescriptions. First-line antibiotics were prescribed in 34% of patients, and second-line (broad-spectrum) antibiotics such as amoxicillin/clavulanate were prescribed in half of the patients. The main significant predictors of antibiotic prescriptions were age < 3 years (odds ratio, 0.13; 95% CI, 0.02 to 0.97), tonsillar exudate (odds ratio, 21.14; 95% CI, 2.88 to 155.09), and throat erythema (odds ratio, 9.30; 95% CI, 1.18 to 73.41). Overall, physicians (n = 29) had adequate knowledge about the modified Centor score and the management of pharyngitis.

Conclusions: Most prescribed antibiotics for pharyngitis were unnecessarily prescribed; the majority being broad-spectrum antibiotics. Despite physicians' adequate knowledge of the modified Centor score and the management of pharyngitis, their practice failed to demonstrate that. Induction of the Saudi Antimicrobial Stewardship Program in the primary care centers, accessibility to diagnostic tools, and educational programs may help in reducing unnecessary antibiotic prescriptions.

Key words: antibiotics; Centor score; group A streptococci; pharyngitis; primary care centers.

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Introduction

Pharyngitis, caused by various types of viruses and bacteria, is a common upper respiratory tract infection involving the oropharynx [1]. The predominant bacterial pathogen is *Streptococcus pyogenes* or Group A *Streptococcus* (GAS) [2]. Complications of GAS infections, though not common, are very serious [3]. They involve rheumatic fever, scarlet fever, streptococcal toxic shock syndrome, acute glomerulonephritis, and pediatric autoimmune neuropsychiatric disorders. The main purpose for treating GAS pharyngitis, which is achieved by taking the right type of antibiotics [3], is to prevent its complications [1]. Identifying cases of GAS pharyngitis is based on patient history, clinical examination, and diagnostic tools [3].

Only cases with GAS pharyngitis should be treated with antibiotics [3]. For suspected GAS cases, a

modified Centor score is calculated. A score higher than three indicates potential need for antibiotics, and a score between two and three requires further confirmation by diagnostic tools, such as throat cultures and rapid antigen detection tests (RADTs) [1]. Proper diagnosis and appropriate choice of antibiotics is vital for proper treatment of GAS [3,4]. Although the Centers for Disease Control and Prevention (CDC) recommend amoxicillin and penicillin V as first-line antibiotics [3], antibiotics have been unnecessarily prescribed [1,5]. This malpractice has been associated with bacterial resistance [6], where geographical areas with more antibiotic use have higher antibiotic resistance rates [7].

In Saudi Arabia, antibiotic prescription rates have been high [8]. Most of these antibiotics are being used for the treatment of upper respiratory tract infections [9]. Studies show that antibiotic prescriptions ranged between 40% and almost all cases of pharyngitis

diagnoses [10,11]. Therefore, several measures have been employed to reduce inappropriate antibiotic prescriptions and use. These include prohibiting self-prescriptions of antibiotics in private pharmacies, publishing the Saudi Acute Respiratory Infections guidelines, and establishing the Saudi Antimicrobial Stewardship Program [12–14]. The latter was published in 2014 by the Ministry of Health (MoH) and aims to improve clinical outcomes of infectious diseases, decrease resistance rates, and reduce economic burden [13].

Despite all such efforts of the Saudi MoH to reduce the inappropriate use of antibiotics, the rates of antibiotic prescriptions are still high. To our knowledge, there have been no studies assessing the knowledge and practice of physicians regarding antibiotic prescriptions for pharyngitis based on the modified Centor score. The aims of this study were to evaluate the evidence regarding antibiotic prescriptions for pharyngitis in primary care centers, and to assess the knowledge of physicians and associated factors regarding antibiotic prescriptions.

Methodology

Setting and participants

This was a cross-sectional study conducted at primary care centers (PCCs) of the MoH, Jeddah, Saudi Arabia, between February 1st and March 2nd, 2018. There are 46 PCCs in Jeddah, four of which are accredited by the Central Board for Accreditation of Healthcare Institutions. For the purpose of this study, proper and organized documentation was deemed vital to ensure a reliable source of data. Therefore, only accredited PCCs were included in the study.

Patients with a diagnosis of pharyngitis were identified retrospectively using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) [15]. Sociodemographic (age and sex) and clinical data (history, examination, diagnosis, and management) of patients were documented from the medical records.

A structured self-administered questionnaire was distributed to physicians. As the relation between the physicians' knowledge and practice of managing pharyngitis was an important aspect of the study, only physicians responsible for included medical records were enrolled. The questions were developed from different studies [16–18], and the questionnaire was reviewed by five family medicine consultants. The questionnaire consisted of three parts: sociodemographic questions, knowledge of the modified Centor score, and management of pharyngitis.

The questionnaire was piloted among physicians at one PCC that was not included in the study.

Centor score

The modified Centor/McIsaac score was calculated out of five to cases of pharyngitis to diagnose patients at high risk for GAS infection [19,20]. As the score was not documented in any of our files, the modified Centor score was calculated from the patients' records based on their history and examination. The input value is -1 if the patient's age is greater than or equal to 45 years and 0 if the patient's age is between 15 and 44 years [20]. A value of 1 is given if the patient's age is between 3 and 14 years, there is an absence of cough, a fever > 38°C, exudate or swelling are noted on tonsils, or the anterior lymph nodes are tender and swollen [20]. In cases of no documented history or examination related to the modified Centor score, a value of 0 was given.

Statistical analysis

Descriptive statistics were presented as frequencies and percentages for categorical variables and as median and interquartile range for continuous variables. Crude and adjusted analyses for antibiotic prescriptions were performed using logistic regression models. The association between physicians' knowledge and practice was assessed using the Pearson correlation coefficient. The significance level was set at 0.05, and the data were analyzed using STATA version 13.0 (Stata Corp., College Station, Texas, USA).

Results

Patients

All patients with pharyngitis diagnoses during the study period were included, for a total of 104 patients. The baseline characteristics of the patients show that 12% of the patients were under three years old, 48% were 3 to 14 years old, 34% were 15 to 44 years old, and 7% were \geq 45 years old (the age was categorized similar to the modified Centor score criteria). For sex, 44% of the sample was male. None of our patients were reported to be allergic to penicillin.

The patients' clinical characteristics and prescribed antibiotics are summarized in Table 1. The median duration of illness was 1.5 days (interquartile range, 0 to 5). The most common symptoms were sore throat (79%), fever (69%), runny nose (50%), and cough (46%). On examination, 63%, 62%, and 11% of patients presented with exudate on their tonsils, throat erythema, and fever (temperature \geq 38°C), respectively. Antibiotics were prescribed for pharyngitis in 79% of patients; of which 51% were composed of

amoxicillin/clavulanate (a second-line and broad-spectrum antibiotic), 34% amoxicillin (first-line), 11% azithromycin, and 4% others.

The unadjusted model for antibiotic prescriptions shows that the presence of exudate on the tonsils increased the likelihood for antibiotic prescriptions (odds ratio, 5.18; 95% confidence interval, CI, 1.88 to 14.29; $p = 0.002$) (Table 1). The adjusted odds ratio for antibiotic prescriptions was 0.046 (95% CI, 0.003 to 0.71; $p = 0.027$) for age < 3 years, 41.82 (95% CI, 3.14 to 557.51; $p = 0.005$) for exudate on the tonsils, and 17.85 (95% CI, 1.27 to 251.02; $p = 0.033$) for throat erythema.

The estimates of antibiotic prescriptions for pharyngitis based on the modified Centor score are presented in Table 2. Out of the 79% of patients receiving antibiotic prescriptions, only 28% of the cases were justifiable by evidence (using the Saudi Acute Respiratory Infections guidelines). In general, most of the patients (72%) received antibiotics despite no supporting evidence.

Physicians

Demographics of the physicians (n = 29) in the survey sample show that the majority of them were between 30 and 40 years old (55%), with the sex ratio being relatively close, and approximately 55% were general physicians. Sixty-seven percent of the physicians were familiar with the Saudi Acute

Table 2. Trends for prescribing antibiotics for pharyngitis based on the modified Centor score guidelines.

Patients received antibiotics (n = 82, 79%)		n (%)
Based on evidence		23 (28)
Despite nonsupporting evidence		59 (72)
Patients did not receive antibiotics (n = 22, 21%)		
Based on evidence		18 (82)
Despite supporting evidence		4 (18)

Respiratory Infections guidelines. However, only one-third of the physicians indicated that the guidelines were available at their PCCs, and the rest were not sure if the guidelines were available at their PCCs or indicated that the guidelines were not accessible. Only 34% of the physicians indicated that a lack of clinical support tools, such as RADT, provoked prescribing antibiotics for pharyngitis.

Physicians’ knowledge of the modified Centor score is presented in Table 3. Most of the modified Centor criteria were correctly answered. However, responses varied considerably for the age and cough criteria. Physicians were asked when antibiotics should be prescribed based on the modified Centor score (Figure 1). The majority (38% and 41%) indicated a score of 3 and 4, respectively. This is contradictory to their practice, where most antibiotics (40% and 31%) were prescribed at modified Centor scores of 1 and 2, respectively. Physicians’ responses (i.e., knowledge) on when to prescribe antibiotics and their practice was weakly negatively correlated ($r = -0.14$; $p = 0.178$).

Table 1. Unadjusted and adjusted odds ratios for antibiotic prescriptions in pharyngitis cases.

Variable	Unadjusted odds ratio (95% CI)	P-value	Adjusted odds ratio (95% CI)	P-value
Age (years)				
<3	0.49 (0.11-2.26)	0.359	0.13 (0.02-0.97)	0.047
3 - 14	Reference		Reference	
15 - 44	0.47 (0.16-1.41)	0.179	0.41 (0.11-1.56)	0.193
≥ 45	0.22 (0.04-1.18)	0.078	0.38 (0.04-3.80)	0.409
Gender				
Female	Reference		Reference	
Male	0.51 (0.19-1.33)	0.168	0.55 (0.17-1.80)	0.324
Duration of illness in days-median (interquartile range)	1.13 (0.80-1.61)	0.477	0.92 (0.62-1.37)	0.69
Symptoms				
Sore throat*	2.78 (0.98-7.87)	0.055	NA	NA
Fever	1.78 (0.69-4.72)	0.249	1.47 (0.43-5.06)	0.538
Runny nose	0.63 (0.24-1.63)	0.339	0.61 (0.15-2.37)	0.471
Cough	0.82 (0.32-2.11)	0.684	0.71 (0.18-2.78)	0.626
Sneezing	0.38 (0.06-2.43)	0.306	0.12 (0.01-1.47)	0.098
Examination				
Exudate on tonsils	5.18 (1.88-14.29)	0.002	21.14 (2.88-155.09)	0.003
Throat erythema	0.89 (0.34-2.37)	0.82	9.30 (1.18-73.41)	0.034
Fever (temperature ≥ 38°C)*	1.23 (0.25-6.17)	0.799	NA	NA
Lymph nodes	2.27 (0.27-19.19)	0.452	1.39 (0.13-14.95)	0.787

* Symptoms of sore throat and temperature at examination ≥ 38°C were not included in the logistic regression model for collinearity.

Discussion

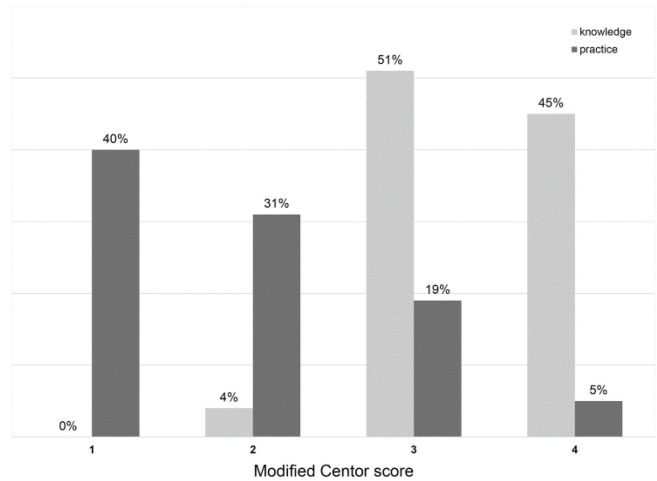
Although most cases of pharyngitis are viral and bacterial cases account for only a small percentage of cases, antibiotics are unnecessarily prescribed for its treatment [1]. In this study, we evaluated the trend of antibiotic use in pharyngitis cases and its' relation with physicians' knowledge and management using the modified Centor criteria.

In suspected cases of bacterial pharyngitis caused by GAS, it is recommended to use RADT or throat culture to confirm the diagnosis before introducing antibiotics [3]. However, such diagnostic testing is not available in the MoH's PCCs. Thus, in the assessment of cases of pharyngitis with antibiotic prescriptions, the modified Centor score was applied using the Saudi Acute Respiratory Infections guidelines, where a score of 3 or more was considered justifiable for prescribing antibiotics. Though this score was applied, it has been shown that even with a modified Centor score of 4, the likelihood of GAS pharyngitis is approximately 50% [20].

In our study, the results revealed that a total of 104 patients had pharyngitis, of whom 79% were prescribed antibiotics. This rate of antibiotic prescription for pharyngitis is higher than that reported in other studies in the UK (30.1%) [21] and Taiwan (16.8%) [22] but similar to neighbouring countries as reported in Israel (71%) [23], and the United Arab Emirates (88%) [24]. This finding is unfortunate as most cases of pharyngitis are viral infections [3]. It was no surprise that out of those cases who were prescribed antibiotics in our study, 72% had nonsupporting evidence for antibiotic prescriptions, i.e., they received antibiotics for a modified Centor score of less than 3.

The high rate of antibiotic prescription despite nonsupporting evidence might suggest that physicians are not calculating the modified Centor score for each pharyngitis case; perhaps due to the limited time allotted for each patient. Calculating the modified Centor score has been shown to reduce the number of throat cultures sent for pharyngitis cases [25]. Another factor is the unavailability of RADTs or throat cultures

Figure 1. Physicians' responses to when pharyngitis cases should receive antibiotics using the modified Centor score (physicians' knowledge) versus the modified Centor score of pharyngitis cases actually receiving antibiotics (physicians' practice).



at the MoH's PCCs to help physicians in cases of uncertainty of viral versus bacterial infections. In this study, 34% of the physicians indicated that lack of diagnostic tests, such as RADTs and throat cultures, is a factor for increased antibiotic prescription. Following the guidelines and using diagnostic tests has significantly decreased the rate of antibiotic prescriptions, as reported in other studies [2,26,27].

The types of prescribed antibiotics were assessed in the study. In cases of pharyngitis caused by GAS, the CDC recommends the use of first-line antibiotics of penicillin such as amoxicillin and penicillin V [3]. Unfortunately, the results showed a trend (51%) towards prescribing second-line antibiotics; mainly amoxicillin/clavulanate (a broad-spectrum antibiotic). This trend has been observed in other studies [28,29]. Worldwide, there have been no cases reported of GAS resistant to first-line antibiotics in which broad-spectrum antibiotics would have been needed [3]. Broad-spectrum antibiotics for the treatment of pharyngitis are not superior and have comparable effectiveness to penicillin [30]. Such high rate of broad-

Table 3. Responses of physicians to the modified Centor score criteria to predict the need for antibiotics in patients with pharyngitis.

Criteria	Correct answer	Incorrect answer
	n (%)	n (%)
Age 3-14 years	21 (72)	8 (28)
Age 15-44 years	17 (59)	12 (41)
Age > 44 years	11 (38)	18 (62)
Exudate on tonsils	25 (86)	4 (14)
Tender anterior cervical lymph nodes	25 (86)	4 (14)
Fever > 38°C	25 (86)	4 (14)
Cough is present	11 (38)	18 (62)

spectrum antibiotic use might lead to an increased bacterial resistance rate, health care costs, morbidity, and mortality [28,31]. Although the physicians' motives for prescribing broad-spectrum antibiotics were not investigated, it is assumed that their low knowledge of the effectiveness of first-line antibiotics in managing pharyngitis influenced their practice.

Another antibiotic class that was prescribed to our patients is macrolides; namely azithromycin, which is used only in patients with penicillin allergy. However, there was no documentation of penicillin allergy in which azithromycin would have been necessary. It is not recommended to use macrolide antibiotics as first-line therapy for GAS pharyngitis as it has high resistance rate [3,4]. In Saudi Arabia, GAS resistance to macrolide antibiotics has doubled in recent years to reach 23.4% [4]. Unfortunately, the use of macrolides is commonly observed [28]. The reason why azithromycin is being unnecessarily prescribed may be due to antibiotic dosing. Whereas the recommended antibiotics, amoxicillin and penicillin V, are taken twice daily for an average of 10 days, azithromycin is taken once daily for 3 to 5 days, which makes it easier to adhere to; hence a more favorable option.

Incorporating the Antimicrobial stewardship program would promote a more appropriate antibiotic use [28]. The Saudi Antimicrobial Stewardship Program was initiated at the inpatient units of the MoH hospitals, and is aimed to expand to outpatient departments and the PCCs [13]. Although the program is still in its early stages, the hospitals that implemented the program reported reduction in broad-spectrum antibiotics use, less hospital acquired infections, and a decrease in inappropriate antibiotic prescriptions [32,33]. In a previous study, some of the interventions that demonstrated success in outpatient antibiotics stewardship programs were point-of-care testing (such as the use of RADTs in cases of pharyngitis), delayed antibiotics prescribing strategies, evidence based guidelines, patient education, provider education, and audit and feedback [34]. It is proposed to implement these interventions in outpatient settings and the PCCs in Saudi Arabia and measure its effectiveness.

One of the key elements in the study was the assessment of the physicians' Knowledge about the modified Centor score. Although the physicians had adequate knowledge of the modified Centor score, responses to the criterion 'patient's age' were mostly inaccurate. The same misconception was noted in a local earlier study [35]. The modified Centor score was first introduced in 1998, when the criterion 'patient's age' was added [20]. However, the Saudi National

Protocol for Diagnosis and Treatment of Acute Respiratory Infections, published in 2008, still relies on the Centor score rather than the modified Centor score. Therefore, it was expected that physicians would lack knowledge of the criterion 'patient's age'. Another criterion in which there was discrepancy in the physicians' knowledge of the modified Centor score was the presence of cough. According to the modified Centor criteria, the presence of cough is likely a suggestion of viral infection and should be scored zero, while the absence of cough is scored as one. Surprisingly, one-third of the physicians scored the presence of cough as -1. It is not clear why such finding was observed, whereas most studies have indicated accurate knowledge regarding the cough criterion [35,36].

The relation between physicians' knowledge of the modified Centor score and their practice was evaluated. Physicians were asked at what modified Centor score antibiotics should be prescribed; 7%, 38%, and 41% indicated a score of 2, 3, and 4, respectively. This is contradictory to when patients were actually prescribed antibiotics; the majority (40% and 31%) received antibiotics with modified Centor scores of 1 and 2, respectively. Despite the physicians' appropriate knowledge of the modified Centor score, this was not translated into their practice. A possible explanation is that consultation time is limited due to the low ratio of physicians to patients. The Saudi MoH statistics (2012) show that the ratio of total physicians per 10,000 members of the population is 24.3, while governmental physicians have a ratio of 11.6 physicians per 10,000 members of the population [37]. Increasing the ratio of physicians to patients would allow more time to be spent with patients and, hopefully, yielding better guideline adherence.

It is foreseen that the interventions to reduce antibiotic use in the PCCs should incorporate expanding the Saudi Antimicrobial Stewardship Program, providing them with diagnostic tools, and enabling pharmacists to audit prescriptions and give feedback. Further education, audits and lectures to physicians about the modified Centor criteria and appropriate choice of antibiotics would be of great impact on the appropriate use of antibiotics in the management of pharyngitis.

There are several limitations to our study. First, only accredited centers were included. Accredited centers have better levels of teaching and auditing, which may indicate better management of patients and proper guideline adherence compared to non-accredited centers. Second, the private sector was not included in

this study; it is not clear how this would affect the results. Third, the modified Centor score was not recorded in the patients' files; calculating it without assessing the patient clinically is not deemed optimum. Finally, the sample size for the study was relatively small.

Conclusions

The present study shows that antibiotics are overprescribed, and the majority of prescriptions were second-line (broad-spectrum) antibiotics. Despite this, physicians had adequate knowledge of the modified Centor score criteria and the recommended management of pharyngitis. Unfortunately, this was not translated into their practice. While this study highlights the gaps in antibiotic use in pharyngitis and inappropriate antibiotics use for low Centor score, further studies may require policy makers to implement the Saudi Antimicrobial Stewardship Program in the outpatient department and evaluate its effective strategies in the PCCs.

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Authors' Contributions

RO designed the study, collected the data, and drafted the manuscript. DO analyzed and interpreted the data, and revised the manuscript. All authors have read and approved the final manuscript.

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Corresponding author

Rawaa Ibrahim Olwi, MBBS
 Department of Family and Community Medicine, University of Toronto, 500 University Ave, Toronto, ON M5G 1V7, Canada.
 Tel. +1(647)992-9616,
 E-mail. r.olwi@mail.utoronto.ca

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