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Evaluation of Rapid Antigen Detection Test for Group A Streptococci Pharyngitis among Children in an Out-Patient Clinic in Malaysia

(Penilaian Ujian Antigen Pantas untuk Pengesanan Keradangan Farinks oleh Streptokokus Kumpulan A dalam Kalangan Kanak-Kanak di Klinik Pesakit Luar di Malaysia)

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ABSTRACT

One of the most common conditions encountered in the out-patient setting is acute pharyngitis. Group A Streptococcus (GAS) accounts for 15%-30% of cases of sore throat particularly in children under 15 years old. Rapid antigen testing (RADT) is an alternative diagnostic method to detect GAS pharyngitis. This study was done to evaluate the agreement between RADT whereby BIONEXIA® Strep A Plus (BioMérieux, France) kit was used and throat culture in the diagnosis of GAS pharyngitis in children presented with a sore throat. One hundred and ten children from a primary health care clinic with sore throat were included in this study. All children were evaluated based on McIsaac scoring and throat swab samples were taken for both throat culture and RADT testing. The prevalence of GAS pharyngitis by RADT in this study was 7.3% over one year. A higher incidence of GAS pharyngitis was noted in the school-aged children than the preschool-age children. There was no correlation between cough, lymph node enlargement, and tonsillar enlargement in predicting GAS pharyngitis. The sensitivity and specificity of RADT were 100% and 98%, respectively, when taking throat culture as a gold standard. A good agreement between RADT and throat culture was achieved (k=0.848). McIsaac scoring was noted to have good predictability for GAS pharyngitis with AUC=0.82. In conclusion, the rapid streptococcal antigen detection test showed excellent sensitivity and specificity and detecting GAS from the throat swab samples. Thus, it can be used to aid in the diagnosis of group A Streptococcal pharyngitis and could reduce the overuse of antibiotics. McIsaac score has also proven to be useful as a screening tool for bacterial pharyngitis.

Keywords: Group A Streptococcal pharyngitis; McIsaac score; rapid antigen detection test

ABSTRAK

Keradangan farinks akut adalah salah satu keadaan yang biasa dijumpai di klinik pesakit luar. Antara 15 hingga 30 peratus daripada kesakitan tekak terutamanya dalam kalangan kanak-kanak di bawah umur 15 tahun ini adalah disebabkan oleh jangkitan Streptokokus Kumpulan A. Ujian antigen pantas adalah ujian alternatif yang boleh dilakukan bagi mengesan jangkitan Streptokokus Kumpulan A ini. Kajian ini dijalankan dengan objektif untuk menilai persamaan antara ujian antigen pantas (BIONEXIA® Strep A Plus kit) dan kultur bakteria dalam pengenalpastian radang farinks yang disebabkan oleh Streptokokus kumpulan A ini. Seramai 110 pesakit kanak-kanak yang mengalami sakit tekak telah dilibatkan dalam kajian ini. Sistem Pemarkahan McIsaac dan sapuan tekak telah dilakukan ke atas semua kanak-kanak tersebut. Ujian antigen pantas dan kultur bakteria dibuat untuk semua sampel sapuan tekak tersebut. Berdasarkan kepada keputusan ujian tersebut, didapati prevalens Streptokokus kumpulan A melalui ujian antigen pantas sebagai penyebab radang farinks adalah pada kadar 7.3 peratus. Didapati juga, prevalens ini lebih tinggi dalam kalangan kanak-kanak yang bersekolah berbanding dengan mereka di bawah umur persekolahan. Kajian ini tidak menunjukkan sebarang hubung kait antara batuk, bengkak kelenjar dan bengkak tonsil sebagai simptom penentu untuk radang farinks Streptokokus kumpulan A. Kesensitifan dan kekhususan ujian antigen pantas ini pula didapati pada kadar 100 peratus dan 98 peratus. Kepatuhan antara ujian antigen pantas dan kultur bakteria juga didapati pada kadar yang sangat baik (k=0.848). Sistem Pemarkahan McIsaac pula menunjukkan prestasi yang baik untuk digunakan sebagai penentu kepada radang farinks Streptokokus kumpulan A ini dengan AUC=0.82. Kesimpulannya, ujian antigen pantas ini telah menunjukkan ujian ini mempunyai kesensitifan dan kekhususan yang sangat baik apabila kaedah kultur bakteria dijadikan sebagai ujian piawai. Oleh tu, kaedah ujian ini boleh digunakan untuk membantu mengesan penyakit ini dan dapat mengurangkan salah guna antibiotik dalam perawatan pesakit. Selain itu, Sistem Pemarkahan McIsaac juga telah didapati sangat berguna untuk diguna pakai sebagai alat saringan untuk radang farinks yang disebabkan oleh bakteria.

Kata kunci: Sistem pemarkahan McIsaac; Streptokokus Kumpulan A radang farinks; ujian antigen pantas

Introduction

One of the most common conditions encountered in an outpatient setting is acute pharyngitis. It is commonly caused by a virus but occasionally can be caused by bacteria. *Streptococcus pyogenes* or Group A Streptococcus (GAS) was the most predominant bacteria found in the case of bacterial pharyngitis. GAS accounted for between 15 and 30 percentages of sore throat particularly in children under 15 years old (Alcaide & Bisno 2007; Wessels 2011). The incidence decreased with increasing age and less than 10% of acute pharyngitis in adults were bacterial causes (Hildreth et al. 2015). Globally, over 600 million cases of GAS pharyngitis are estimated each year (Carapetis et al. 2005).

Patients with GAS pharyngitis typically present with a sore throat, enlarged tonsils, enlarged cervical lymph nodes, and fever. The presentation of streptococcal pharyngitis can be overlapped broadly thus clinical examination alone is not sufficient to prove streptococcal pharyngitis (Bisno et al. 2002). Only half of the children with GAS pharyngitis had tonsillar or pharyngeal exudates (Alcaide & Bisno 2007). The importance of GAS pharyngitis diagnosis is to prevent complications by providing immediate appropriate treatment. Acute rheumatic fever is the devastating complication of the infection and is still one of the significant causes of child morbidity and mortality especially in low-income countries around the world. The estimated number of deaths from rheumatic heart disease is 233,000 per year worldwide (Carapetis et al. 2005).

The throat culture is considered as a gold standard for the diagnosis of GAS. *Streptococcus pyogenes* grow well on the sheep blood agar characteristically produced beta-hemolytic colonies. Identification of *Streptococcus pyogenes* can be done by the biochemical reaction, a serological procedure that detects the Lancefield group antigen, and susceptibility testing for bacitracin. Commercial biochemical tests such as API System (API 20 Strep) and Vitek 2 are available for the identification of *Streptococcus pyogenes*. Matrix-assisted Laser-Desorption/Ionization Time of Flight Mass Spectrometry (MALDI-TOF) has been evaluated in several studies for the identification of *Streptococcus pyogenes*. It has been proven to correctly identify this organism when compared to API 20 Strep (Wang et al. 2012). However, the throat culture method can only produce the final result after 48 h. Thus, a faster detection method is required to help the clinician determine if the sore throat is due to GAS. Furthermore, most guidelines for the management of acute pharyngitis are in favour of testing for GAS before an antibiotic is prescribed. This can be done either by sending the throat swab sample for bacterial culture or by performing a rapid antigen detection test (Cooper et al. 2001). As the throat culture is time-consuming, some studies indicated that the use of this rapid detection method is adequate for the diagnosis of GAS pharyngitis (Lean et al. 2014).

As a fast and reliable method for the detection of Group A Streptococcus as the causative agent of acute pharyngitis is crucial, this study was carried out to evaluate the performance of a RADT in terms of sensitivity, specificity, positive predictive value, and negative predictive value in GAS pharyngitis in a primary care setting.

Materials and Methods

Study Design and Population

A prospective cross-sectional study was conducted in a primary care clinic over one year from 1st August 2018 until 31st July 2019. As the previous prevalence of GAS pharyngitis among children was stated to be between 15% and 30%, we calculated the sample size based on the 15% prevalence. Based on the prevalence formula published by Kish (1965), the calculated sample size was 196. However, due to time limitations, the desired sample size was unachievable. A total of 110 children aged between 3 and 15 years' old who presented with sore throat or clinically have inflamed pharynx or enlarged tonsils were included. Informed consent was taken from each parent. Those who were uncooperative or refused for throat swabs to be taken and who received antibiotic therapy in the previous two weeks before the current presentation were excluded from this study. Throat swabs samples were subjected to RADT testing and bacterial culture on the sheep blood agar. The children were classified according to the different age groups based on typical Malaysia's school-age; 3-6 years as preschool, 7-12 years as primary school, and more than 12 years as a secondary school.

Rapid Streptococcal Antigen Detection

Rapid Streptococcal antigen detection (RADT) was performed using BIONEXIA® Strep A Plus kit (BioMérieux, France). This kit was chosen because of its easy accessibility in the local market. Furthermore, previous studies demonstrated an excellent specificity achieving 100% using the same kit (Altun et al. 2015; Plainvert et al. 2015). The test was done using a lateral flow assay principle. The antigen from the throat swab sample was extracted using sodium nitrate and acetic acid solution that is available in the kit. At the initial stage,

four drops of sodium nitrate and acetic acid solutions were mixed in the extraction tube. Subsequently, the throat swab specimen placed into the extraction tube and swirled for at least 10 times and maintained in the tube for one minute. Three drops of the solution were then dropped into the test cassette. During the test, the GAS antigen in the sample reacts with the antibodies to GAS. The result was read after 5 min and stable for another 5 min. The antigen-antibody complex migrates up to the membrane test line (T) by capillary action. The presence of a colored line on the test line (T) and control line (C) of the kits indicates positive results. The procedure was performed according to the manufacturer's description.

THROAT CULTURE

The throat swabs were gently rolled onto the sheep blood agar and later streaked by using a sterile loop. The plate was then incubated at 37 ºC with 5% carbon dioxide for 24 h. After incubation, the plate was reviewed for the presence of beta-hemolytic colonies. When there were no beta-hemolytic colonies were found, the plate will be re-incubated for another 18-24 h. Subsequently, if there were still no beta-hemolytic colonies observed, the culture will be classified as no GAS isolated. When the beta-hemolytic colonies were observed on the sheep blood agar, the Gram-stain was performed to confirm the presence of Gram-positive cocci in the chain. A catalase test was also done to screen for *Streptococcus* species which are catalase-negative, and further identification of GAS was done using susceptibility testing to bacitracin disc (0.04 µg) and grouping by a commercial latex agglutination test (Pulse Streptococcus Grouping Latex Test, Pulse Scientific Inc, Canada). GAS was identified when they were sensitive to bacitracin and agglutinate with Lancefield group A.

ANTIBIOTIC SUSCEPTIBILITY TESTING

The isolated GAS was tested against the following antibiotics; ampicillin, clindamycin, ceftriaxone, erythromycin, and penicillin. The antibiotic susceptibility testing was performed using the disc diffusion method. The protocol was done as per the 29th edition M100 document of the Clinical and Laboratory Standard Institute. The interpretation of the zone of inhibition for each antibiotic was done according to a similar guideline for the ß-hemolytic *Streptococci* spp. (Clinical and Laboratory Standard Institute (CLSI) 2019).

McISAAC SCORING

All patients were assessed clinically and were given a score using McIsaac scoring (McIsaac et al. 2004). Regardless of the score given, all patients will be subjected to throat swab sampling for culture and RADT. The score is shown as follows:

Criteria	Points
Temperature > 38 ºC	1
Cough	-1
Swollen, tender anterior cervical lymph node	1
Tonsillar swelling or exudates	1
Age	
3-14 years old	1
15-44 years old	0
45 years or older	-1
Score	Suggested Management
≤1	No further testing. No antibiotics.
2-3	Culture all. Antibiotics only to a positive culture
≥4	Empirical antibiotics with or without culture

ETHICAL CONSIDERATION

This study was approved by the local research and ethical committee (JEP-2018-179). Informed consent from the parents was taken before the child is included in this study.

DATA COLLECTION AND STATISTICAL ANALYSIS

Demographic data including age, and gender were collected. RADT results were collected as positive or negative and throat culture as GAS or no GAS isolated. All the data were analyzed using SPSS version 24. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for RADT with throat culture as the laboratory reference. Pearson's Chi-square test (2) and Fisher's exact test were used when analyzing the association between the parameters with positive GAS either by culture or RADT or both. Cohen kappa analysis was used to evaluate the agreement between the RADT test and throat culture. A p-value of < 0.05 was taken as significant.

RESULTS

DEMOGRAPHIC, CLINICAL PRESENTATION AND MCISAAC SCORING ACCORDING TO DIFFERENT AGE GROUPS

One hundred and ten children were included during the study period. Sixty-six children were male and 44 were female. Fifty percent of the patients were aged less than 7 years old (pre-school age) followed by 37.3% aged between 7 and 12 years old (primary school) and 12.7% aged more than 12 years old (secondary school). All children had a sore throat, but the sore throat was not the main complaint in some of the children when they visited the clinic. Majority of the children mainly presented with fever (n=59) followed by the sore throat (n=45), and non-specific complaints in six patients. According to the different age groups, fever and non-specific complaints were more prominent in pre-school children (41%), while sore throat more notable in primary school age (51.2%) and secondary school age (71.4%).

Throat examination showed that enlarged tonsils were prominent in all age groups. In children less than 7 years old, 52.7% had enlarged tonsils while 14.5% had enlarged tonsils with exudates. Among the primary school children, 53.7% had enlarged tonsils and 19.5% had enlarged tonsils with exudates. Subsequently, in secondary school children, 42.7% had enlarged tonsils and 14.3% had enlarged tonsils with exudates. Only one child had a normal throat examination. Seventy-three (66.4%) of the children complaint of cough; 52 among pre-school, 24 among primary school, and 7 among secondary school. The majority of the children were noted to have no lymph node enlargement. McIsaac scoring was performed on all children. The McIsaac score was categorized as less than 3 and at least 3 (<3 or ≥ 3). There was a statistically significant difference between age group with those pre-school children were more likely to have a McIsaac score of <3 (p=0.029). Primary school children were noted to be more likely to score at least 3. The data were as shown in Table 1.

RADT AND THROAT CULTURE FOR GAS

From 110 samples collected, 8 samples (7.3%) were positive for RADT for GAS. However, two of these 8 samples were negative by culture. Thus, the calculated sensitivity and specificity was 100% (95% confidence interval [CI]: 54-100%) and 98.07% (95% CI:93.2-99.8%), respectively. The positive likelihood ratio for the test is 51.5 (95% CI:13.06-203.16) as shown in Table 2. Further analysis according to the different age groups showed that GAS was more common in the primary school age group based on the positive RADT (p=0.047) and culture (p=0.021) as shown in Table 1.

In terms of the agreement between RADT and the culture method for GAS detection, a good correlation was achieved between the two tests. Cohen's kappa analysis was done to determine this agreement. The strong agreement was found between the two tests with κ = 0.848 (95% CI, 0.640 to 1.055), $p < 0.001$.

All GAS isolates were subjected to antibiotic susceptibility testing and all were susceptible to penicillin, ampicillin, and ceftriaxone except for one isolate which was noted to be intermediate to erythromycin and resistant to clindamycin.

CLINICAL FINDINGS AND ITS ASSOCIATION WITH GAS PHARYNGITIS

Considering patients with McIsaac score of 3 and above as more likely to have GAS pharyngitis, the children were categorized accordingly. Using this categorical variable, we found a statistically significant association between McIsaac score with the positive GAS isolated in throat culture. Inpatient with a McIsaac score of less than 3, the isolation of GAS from the throat culture was unlikely (2 = 4.870, p=0.038), an odds ratio of 8.205 (95% CI, 0.924 to 72.8). When we adjusted the McIsaac score to less than 4 or at least 4, it showed a similar finding with p=0.007 (Fischer's exact test). Similarly, when the RADT was used instead of culture, at the McIsaac score of at least 3, it was more likely to be associated with positive RADT (2=8.11, p=0.004, Cramer's V=0.272), as shown in Table 3.

Receiver-operator curve (ROC) analysis was subsequently performed for the use of McIsaac scoring in detecting GAS (positive throat culture/RADT). It showed that McIsaac Score had a good predictive ability for GAS with the area under the curve (AUC) of 0.82 (95% CI, 0.64-1.00). We noted that the cut-off points of the McIsaac Score of at least 3 had sensitivity and specificity of 83.3% and 62.1%, respectively. The positive predictive value and negative predictive values were 15.27% (95% CI, 0.11-0.20) and 98.42% (95% CI, 0.90-0.99) respectively as shown in Figure 1.

ANTIBIOTIC PRESCRIPTION

We observed that majority of the patients were not prescribed antibiotics (80.9%). Among those that received antibiotics had a McIsaac Score of at least 3. Importantly, those that had a McIsaac Score of 2 and below were not prescribed antibiotics. There was a significant association between McIsaac Score with antibiotic prescription whereby antibiotic was more likely to be prescribed in those with higher McIsaac score (Fisher's exact = 30.94, $p<0.001$).

DISCUSSION

This present study showed that rapid streptococcal antigen testing (RADT) had an almost perfect agreement with the throat culture method for the detection of GAS from the throat swab samples. It had good sensitivity and specificity when throat culture was used as the reference method for the detection of GAS. Theoretically, this test is easy to be performed in the clinical setting, particularly in the primary care clinic. The ability to provide the result during the same clinic session when compared to the traditional culture method which required between 42 and 72 h can help to reduce the time to result for the clinician to decide on giving appropriate antibiotics. This study also showed that the McIsaac score had good predictability for Group A *Streptococcus* (GAS) pharyngitis particularly for ruling out the diagnosis of GAS with its excellent negative predictive value of 98%. Otherwise, we also observed that there were no specific signs and symptoms which could predict GAS pharyngitis clinically.

The prevalence of GAS pharyngitis in this study was 7.3% and 5.5% based on the positive RADT and throat culture, respectively. This prevalence was noticeably lower compared to previously published studies. In a review, it was noted the overall prevalence of GAS was reported between 15 and 30% in children aged less than 15 years (Alcaide & Bisno 2007). A systematic review and meta-analysis study demonstrated the prevalence of 29.7% when GAS was detected by immunochromatography method among the paediatric groups (Stewart et al. 2014). Generally, the prevalence of GAS pharyngitis varies from one country to another. The difference in GAS prevalence was also found between the high and low/middle-income countries which were 24.3% and 17.6%, respectively (Oliver et al. 2018).

The laboratory techniques used for the detection of GAS can contribute to the difference in GAS prevalence. We observed that the prevalence of GAS was higher by RADT than throat culture (7.3% versus 5.5%). In one study, it was shown that the prevalence of GAS was between 24.5 to 39.4% and 23.9 to 41.8% based on culture and RADT methods, respectively (Rimoin et al. 2010). It was clear that the prevalence of GAS by RADT was higher than by using the culture method as found in this current report. There were two possible false-positive RADT in this study. The first patient presented with a sore throat, fever, enlarged tonsils with exudates, enlarged anterior cervical lymph node, and no cough or McIsaac Score of 4. Clinical features of this patient were highly suggestive for GAS pharyngitis however, throat culture showed no isolation of GAS but group B streptococci (GBS). The role of GBS in pharyngitis is controversial and data are limited and conflicting on whether this bacterium was a true pathogen of pharyngitis (Tiemstra & Miranda 2009).

The second false-positive result came from a 4-year-old child who presented with a high-grade fever, no cough, inflamed pharyngeal area but no tonsil enlargement, and enlarged lymph node (McIsaac score = 3). For this patient, the throat culture was negative. We did not perform Gram-staining from the initial clinical sample to observe if there were any Gram-positive cocci in the chain indicating the possibility of GAS but was not able to be cultured due to its unviability. We also noticed that a previous study had reported false-positive RADT results (Kose et al. 2016). The reason for this false positive was not clearly explained.

We showed excellent sensitivity and acceptable specificity for GAS RADT. The sensitivity and specificity of RADT were 100% and 98%, respectively, while the positive and negative predictive values were at 75% and 100%, respectively. Generally, RADT was shown to have good sensitivity of more than 85% and specificity of more than 90% (Cohen et al. 2012; Kose et al. 2016; Orda et al. 2016; Rimoin et al. 2010). A higher sensitivity means that the test is a suitable point of care test to be used as a screening method in a primary setting.

McIsaac score or Centor score had been developed as a standardized tool for the primary clinician in classifying the

risk and managing GAS pharyngitis (McIsaac et al. 2004). These scores have been validated and widely used in the primary care setting. Alas, it is important to note that the clinical features of viral infection and bacterial infection can sometimes be overlapped. In this study, we did not show any clinical features to be significantly associated with GAS. However, cervical lymphadenopathy was previously reported as the only clinical feature to be associated with GAS (Rimoin et al. 2010). For children age less than 9 years old, the absence of cough and the presence of fever were found to be commonly associated with GAS in another report (Cohen et al. 2012). When the clinical features were used collectively such as by using the McIsaac score, the cut-off of the score can be used to differentiate between the bacterial or viral cause of acute pharyngitis. We noted that there was a significant statistical association between McIsaac score and positive RADT or throat culture for GAS. McIsaac score of less than 3 appeared to be more unlikely to be related to GAS. This was similar to McIsaac's findings in their validation study (McIsaac et al. 2004). We found that the score of 3 was more likely to have GAS and this increased for those who had a score of 4 and above. This finding was consistent with the previously reported study which showed that a higher McIsaac score was more likely to have GAS pharyngitis (Cohen et al. 2012; Fine et al. 2012). Overall, we showed a better McIsaac score with an area under the curve (AUC) of 0.82 for the diagnosis of GAS compared to previously published studies (Fine et al. 2012; Orda et al. 2016). This was possibly due to our age-specific sampling method which excludes those aged less than 3 years and more than 15 years old as previously reported that GAS pharyngitis was perhaps more common among children aged between 5 and 19 years (Oliver et al. 2018).

Acute pharyngitis is commonly caused by viruses and requires no antibiotic treatment. Bacterial pharyngitis is also a self-limiting disease and rarely causes complications. The main concern in the treatment of GAS pharyngitis is the risk of developing suppurative and non-suppurative complications especially acute rheumatic fever if left untreated. However, overprescribing antibiotics can contribute to resistance issues. In our study, we noted that 19.1% of the patients had been given antibiotics despite GAS was only detected in 7.3%. However, when the data was further analyzed, the antibiotic prescription was considered appropriate based on clinical assessment and judgement of the treating clinician based on the McIsaac score. Most of the patients who had been given antibiotics were those who had a McIsaac score of 3 in comparison with those who had a score of £ 2 (Fisher's =30.94, $p<0.001$). This showed that McIsaac score together with RADT could further reduce the rate of unnecessary antibiotic usage in acute pharyngitis. The implementation of RADT in acute pharyngitis was shown to reduce antibiotic prescription by 42.6% (Kose et al. 2016). Another study had shown that adherence to antibiotic prescription occurred more readily when RADT was performed than not (Llor et al. 2010).

In this study, all GAS that was subjected to antibiotic susceptibility testing were susceptible to penicillin, ampicillin, and ceftriaxone except for one isolate that was resistant to clindamycin and intermediate to erythromycin. In the U.S., macrolide and clindamycin non-susceptible rates were estimated to be 15% (DeMuri et al. 2017). Globally, the macrolide resistance rate in GAS varies depending on geographical area. Surveillance studies have shown rates of resistance of 3.2% in France, 32 % in Spain, and 65% in Taiwan (DeMuri et al. 2017). In Germany, surveillance was conducted in 2006 noted the rate of macrolide resistance was 13.6% and this rate was significantly reduced to 2.6% in 2009 after a reduction in macrolide prescription (Farmand et al. 2012). Hence, the judicious usage of antibiotics is important to prevent the development of resistant patterns in GAS even though the resistant strains are not common.

We acknowledged some limitations in this study including the prevalence reported may not represent the true prevalence of GAS pharyngitis in this country as the study was conducted in a single-center urban primary care clinic. Thus, the demographic of the patients included did not represent the real demographic of the Malaysian population. Otherwise, this study was conducted prospectively, and the children were selected based on the strict criteria that allow us to avoid selection bias during the patient's recruitment. It is important to highlight that only a single RADT kit was used for this study which was BIONEXIA® Strep A Plus. Ideally, other rapid antigen detection for GAS should also be included for comprehensive evaluation. However, this was not feasible in our study due to budget constraints. Otherwise, we were able to perform both RADT and culture on specimens taken from all children to allow us to determine the performance of this RADT kit. We suggested further study with a multicenter design involving urban, semi-urban, and rural areas in this country would give a better prevalence of GAS pharyngitis and similarly different commercially available rapid tests can be evaluated together.

TABLE 1. Clinical presentation and McIsaac score in different age groups

	Preschool age <7 years old) N (%)	Primary school age 7-12 years old N(%)	Secondary school age >12 years old N (%)	*p-value
Chief Complaint				
Fever	38 (69.1%)	18 (43.9%)	3 (21.4%)	
Sore throat	14 (25.5%)	21 (51.2%)	10 (71.4%)	p<0.001
Non-specified	3 (5.4%)	2 (4.9%)	1 (7.1%)	
Temperature				
Above 38 °C	17 (30.9%)	18 (43.9%)	4 (28.6%)	
Below 38 °C	20 (36.4%)	12 (29.3%)	8 (57.1%)	p=0.292
No fever	18 (32.7%)	11 (26.8%)	2 (14.3%)	
Throat examination				
Inflamed pharynx	17 (30.9%)	11 (26.8%)	6 (42.9%)	
Tonsil enlarged	29 (52.7%)	22 (53.7%)	6 (42.9%)	p=0.867
Tonsil enlarged with exudates	8 (14.5%)	8 (19.5%)	2 (14.3%)	
Normal	1 (1.8%)	0 (0.0%)	0 (0.0%)	
Cough				
Cough	42 (76.4%)	24 (58.5%)	7 (50.0%)	p=0.72
No Cough	13 (23.6%)	17 (41.5%)	7 (50.0%)	
Lymph Node Enlargement				
Present	7 (12.7%)	8 (19.5%)	2 (14.3%)	
Absent	48 (87.3%)	33 (80.5%)	12 (85.7%)	p=0.656
McIsaac Score				
< 3	38 (69.2%)	18 (43.9%)	10 (71.4%)	
≥3	17 (30.9%)	23 (56.1%)	4 (28.6%)	p=0.029
RADT				
Positive	1 (12.5%)	6 (75%)	1 (12.5%)	p=0.047
Negative	54 (52.9%)	35 (34.3%)	13 (12.7%)	
GAS isolated				
Yes	0 (0.0%)	5 (83.3%)	1 (16.7%)	p=0.021
No	54 (52.4%)	36 (35%)	13 (13.2%)	

TABLE 2. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for RADT

RADT result	Group A Streptococcus isolated by conventional bacterial culture		
	Isolated	Not isolated	
Positive	6	2	*PPV:* 6 / 8 = 75%
Negative	0	102	*NPV:* 102/102 = 100%
Total	6	104	
	Sensitivity: 6/6 = 100%	*Specificity:* 102/104= 98%	

TABLE 3. Correlation between culture method and RADT for Group A Streptococci with demographic and clinical parameters

Parameters		Culture Method		*p-value*	RADT		*p-value*
Cough	Yes	2	70		3	70	
	No	4	33	0.177	5	32	0.073
Lymph Node	Present	2	15		3	14	
	No	4	88	0.235	5	88	0.073
Fever	Yes	6	72		8	71	
	No	0	31	0.180	0	31	0.066
Tonsil enlargement	Yes	4	70		6	69	
	No	2	33	1.000	2	33	1.000
McIsaac Score	< 3	1	64		1	65	
	≥ 3	5	39	0.038	7	37	0.004

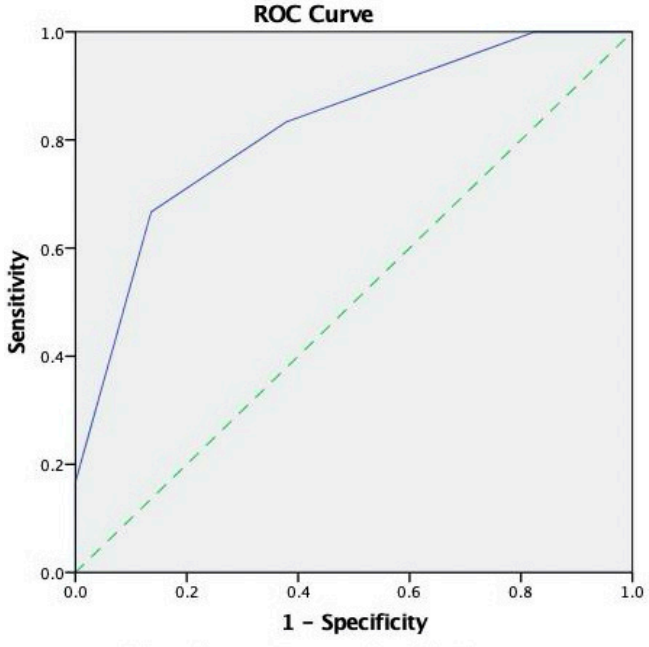

FIGURE 1. Receiver-operator characteristic (ROC) analysis of McIsaac Score and diagnosis of GAS pharyngitis. Area under the curve = 0.82

Conclusion

The non-specific nature of the clinical signs and symptoms for bacterial pharyngitis required additional tools to assist in the diagnosis. Rapid antigen detection test showed a good sensitivity and specificity when evaluated against throat culture as laboratory reference method. Combination of RADT and McIsaac score had been proven to be useful as a screening tool for bacterial pharyngitis. This could reduce the over prescription of antibiotics and help to prevent antimicrobial resistance in the community.

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