Original Article

Role of epidemiological risk factors in improving the clinical diagnosis of streptococcal sore throat in pediatric clinical practice

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Abstract

Background and Aims: Antibiotics are frequently prescribed for sore throat in developing countries, that in turn leads to huge healthcare expenditure and their irrational use may lead to antimicrobial resistance in the community. The aim of this study is to investigate the effect of environmental factors on the frequency of occurrence of group A beta hemolytic streptococcus (GABHS) sore throat and to work out enhancing effect on the sensitivity and specificity and positive predictive value of the signs and symptoms of GABHS sore throat for facilitation of rational antibiotic use. **Settings and Design:** This was a prospective, cross sectional study conducted over period of one year in Pediatric Outpatient Department (OPD) of a Tertiary care teaching hospital. **Methods:** All the children between the age of 5 years and 15 years of age presenting in OPD with the signs and symptoms of sore throat were included in the study. **Statistical Analysis Used:** Statistical analysis was carried out by using Statistical Package for Social Sciences software and statistical tests of Pearson's Coefficient, Chi-square Test, Fischer's Test, Likelihood Ratio, Odds Ratio, and ROC Curve were applied. **Results:** Out of 225 children of the study group, 153 (68%) of the children were in the 5-10 years' age group. Positive throat swab culture was found to be positively associated with high grade fever, pain in throat while swallowing, severely enlarged tonsils, tender lymphadenopathy, poor housing condition, fuel used for cooking, and presence of smoker in house. **Conclusions:** The study stresses on the need of carefully evaluating children presenting with the symptoms of sore throat as majority of the cases may be viral and thus, self-limiting. Poor housing conditions and indoor pollution contribute to the increased prevalence of sore throat.

Keywords: Child, environment, epidemiology, pharyngitis, smoking, streptococcus

Introduction

Acute pharyngitis is a very common illness among children caused by viruses and is benign and self-limited.[1,2] Antibiotics are frequently prescribed for sore throat in developing countries, that in turn lead to huge healthcare expenditure and their irrational use may lead to antimicrobial resistance in the community.[3,4]

It is estimated that approximately 7 episodes of sore throat occur per child per year, with 13.5% of these being caused by group A beta hemolytic streptococcus (GABHS).[5] Community studies in India among symptomatic children with clinical evidence of pharyngitis show that only 4-13.5% have group A streptococcus isolated from their throat.[6,7] However, group A streptococcus is the most common bacterial as well as treatable cause of bacterial pharyngitis.[5,8,9]

Complications of GABHS pharyngitis include both suppurative and Nonsuppurative.[10,11] Suppurative complications are

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peritonsillar abscess (PTA) and retropharyngeal abscess (RPA), of which former is the most common complication of acute tonsillitis. PTA occurs as a direct communication and progression of acute exudative tonsillitis and the incidence is high mainly in adolescents whereas RPA is more common in children under 3 years of age with history of upper respiratory illness.[10,12]

Nonsuppurative complications include acute post streptococcal glomerulonephritis, reactive arthritis, and acute rheumatic fever of which the latter is most important.[10] The epidemiology of acute rheumatic fever (RF)[6,13,14] is linked with that of group-A beta hemolytic streptococcal pharyngitis; both have a maximum incidence in the age group of 5-15 years and an important cause of mortality and morbidity.[15]

The objectives of therapy[16] for group A streptococcal pharyngitis are to prevent suppurative complications, prevent rheumatic fever, decrease infectivity so that the patient can return to school and decrease the clinical duration of the disease which requires early treatment as in great majority of patients the symptoms improve within three to four days even without therapy.

Primary Care Physicians/Pediatricians need to identify those patients with acute pharyngitis who require specific antimicrobial therapy,[2,17] and to avoid unnecessary and potentially deleterious treatment in the large majority of patients who have a benign, self-limited infection that is usually viral. Attempts have been made to develop a clinical tool[18] with high sensitivity and specificity to differentiate the GABHS sore throat from other etiologies of sore throat. Few studies have been conducted in the developing countries to investigate and establish sensitivity and specificity of each symptom and sign of GABHS sore throat in an effort to provide the guidelines to primary care physicians/pediatricians to facilitate the rational drug use in sore throat.

Prescribing antibiotics for children have been discouraged in evidence-based guidelines but non adherence to these guidelines is still present even in developed countries.[19] Antibiotic prescriptions were dispensed for 45% of physicians' visits for viral respiratory tract infections in children. In the developing countries, there is hardly any study on the prescription habits of pediatricians/physicians for acute pharyngitis in daily practice.[20]

A child's health is associated closely with the environment in which he or she lives. Child's health can be adversely affected by unfavorable exposure to environmental pollutants. A number of studies[21] have shown that indoor air pollution concentration can greatly exceed out door concentration and there is sufficient evidence to suggest a causal relationship between exposure to environmental tobacco smoke and asthma, increased airway inflammation, pneumonia etc., there is likelihood that children exposed to tobacco smoke have increased proneness for GABHS sore throat. There is hardly any study available on causal relationship between environmental tobacco smoke exposure and GABHS sore throat.

In the background of the facts as stated, the present study was designed to investigate the effect of environmental factors on the frequency of occurrence of GABHS sore throat and to work out enhancing effect on the sensitivity and specificity and positive predictive value of the signs and symptoms of GABHS sore throat for facilitation of rational antibiotic use.

Methods

This was a prospective observational study conducted over period of one year in Pediatric Outpatient Department (OPD) of a tertiary care teaching hospital in Northern India.

All the children between the age of 5 and 15 of mixed socioeconomic status presenting in OPD with the signs and symptoms of sore throat constituted the study material. Every child enrolled in the study was examined and measured for body dimensions along with signs and symptoms of fever, pain in throat on deglutition, nausea, abdominal pain, erythema of pharynx, tonsillar size, lymphadenopathy, etc., Patients were also enquired for tobacco smoker in house, fuel used for cooking and housing condition. Each of these characteristics was studied. Based on the above mentioned criteria, patient was investigated by taking throat swab culture over both tonsils and across the posterior pharyngeal wall under direct vision with the aid of a light and without touching any other part of throat. Any visible exudate was made to dislodge with the swab. It was then put back into the tube.

Specimen was transported by Filter strip method and sent to the laboratory in a dry box. Specimens were processed on a plate of blood agar containing 5% defibrinated sheep blood and then incubated for 4 hours at 370C in the presence of 5-10% carbon dioxide, following which the strip was lifted with sterile forceps and laid on the same plate away from the previous site. Plate was incubated again overnight at 370°C in the presence of 5-10% carbon-dioxide. After 24 hours, the paper strip was discarded and growth was read. Plates not showing any growth at the end of 24 hours incubation were incubated for another 24 hours.

All plates showing beta hemolytic colonies resembling morphologically to streptococci were further processed. Preliminary tests to identify streptococci were done. These were catalase test, Gram stain and demonstration of long chains in liquid medium.

Screening Test was performed with Bacitracin Disc and incubated at 370°C overnight. Presence of a clear zone of inhibition with a diameter of 14 mm or more around the disc was taken as suggestive of presence of Group A streptococcus. Diameter less than 14 mm were non-Group A strains.

Serogrouping of isolated streptococci was done with latex agglutination kit. A positive result is indicated by the development of an agglutinated pattern showing clearly visible clumping of latex particles.

All Clinical symptoms and signs were studied by using above mentioned criteria and the results of throat swab culture were compared with each of them.

Children presenting with presence of rhinorrhea, coryza, conjunctivitis, cough, sneezing or showing features suggestive of any active heart lesion or with duration of symptoms more than 7 days were excluded from the study.

Statistical analysis was carried out by using Statistical Package for Social Sciences software and statistical tests of Pearson's Coefficient (r), Chi-square Test (CST), Fischer's Test (FT), Likelihood Ratio (LR), Odds Ratio (OR), and ROC Curve were applied according to the nature of the data.

Results

Out of 225 children of the study group, 153 (68%) of the children were in the 5-10 years age group and there was a male children preponderance (58.2%). Majority of the children (56.4%) belonged to the low socio-economic status and the housing conditions of the study group were poor i.e. damp and shady in most (76.4%) of the children. In 52.4% of the children of the study group, the fuel used for cooking was biomass and chullah used was smoke filled and 32.4% of the children were exposed to passive smoke in the house. 56% of the children reported in the OPD for the health advice with fever of more than 3 days duration. The frequency of occurrence of various signs and symptoms varied from 53% to 81% [Table 1].

Out of the 225 patients in the study group, 64 (28.4%) had positive throat swab culture results and 161 children (71.6%) were tested negative for throat swab culture. Out of these 64, 43 (67.2%) were in the age group of 5-10 years and 21 (32.8%).

Of all the patients with positive throat swab culture results i.e. 64, 8 children (12.5%) had Rapid antigen test positive and 28 children (43.75%) had Rapid antigen test negative. Group A beta hemolytic streptococcus was isolated in 36 children out of total 225 children (16%).

High grade fever was present in 210 children (93.3%) with positive association with throat swab culture results (OR = 9.36, $P < 0.007$).

Likewise, positive association of throat swab cultures was also found with pain in throat while swallowing (LR = 35.631, $P < 0.0002$), severely enlarged tonsils ($p = 0.009$), tender lymphadenopathy (CST = 12.163, LR = 13.017, $P < 0.002$), poor housing condition ($p < 0.004$), fuel used for cooking ($p < 0.0001$), and presence of smoker in house (LR = 78.29, OR = 18.647, $P < 0.0001$).

Table 1: Demographic Profile, Environmental Factors and Clinical Features

Patients		5-10 years (*n*=153)	11-15 years (*n*=72)	Total (*n*=225)
Residence	Rural	31 (20.2%)	18 (25%)	49 (21.7%)
	urban	122 (79.8%)	54 (75%)	176 (78.3%)
Gender	Male	101 (66%)	30 (41.7%)	131 (58.2%)
	Female	52 (34%)	42 (58.3%)	94 (41.8%)
Fever	< 3 days	56 (36.6%)	28 (38.8%)	84 (37.3%)
	> 3 days	88 (57.5%)	38 (52.8%)	126 (56%)
Pain in throat		91 (59.5%)	44 (61.1%)	135 (60%)
Nausea and abdominal pain		96 (62.7%)	45 (62.5%)	141 (62.7%)
Erythema of pharynx	No	32 (20.9%)	9 (12.5%)	41 (18.2%)
	Mild	56 (36.6%)	30 (41.7%)	86 (38.2%)
	Severe	65 (42.5%)	33 (45.8%)	98 (43.6%)
Size of tonsil	Normal	42 (28.8%)	23 (31.9%)	67 (29.8%)
	Moderately enlarged	52 (34%)	28 (38.9%)	80 (35.6%)
	Enlarged	57 (37.3%)	21 (29.2%)	78 (34.7%)
Lymphadenopathy	No	56 (36.6%)	26 (36.1%)	82 (36.4%)
	Without tenderness	48 (31.4%)	20 (27.8%)	68 (30.2%)
	With tenderness	49 (32%)	26 (36.1%)	75 (33.3%)
Per capita income per month	< INR 1000/-	89 (58.2%)	38 (52.8%)	127 (56.4%)
	> INR 1000/-	64 (41.8%)	34 (47.2%)	98 (43.6%)
Housing condition	Damp	47 (30.7%)	25 (34.7%)	72 (32%)
	Shady	68 (44.4%)	32 (44.4%)	100 (44.4%)
	Sunny	38 (24.8%)	15 (20.8%)	53 (23.6%)
Fuel used for cooking	Gas	48 (31.4%)	24 (33.3%)	72 (32%)
	Smoke Chullah	82 (53.6%)	36 (50%)	118 (52.4%)
	Smokeless Chullah	23 (15%)	12 (16.7%)	35 (15.6%)
Smoker in house		51 (33.3%)	22 (29.2%)	73 (32.4%)
Positive throat swab culture		43 (28.1%)	21 (29.2%)	64 (28.4%)
Positive latex agglutination kit test		24 (15.7%)	12 (16.7%)	36 (16%)

No association was found with nausea and abdominal pain, duration of fever less than three days, mild erythema of pharynx, mild enlargement of tonsils, and income of the household.

Discussion

High grade fever was found to be associated with positive throat swab culture results which is consistent with studies done by Breese *et al.*[22], Wald *et al.*[23] and Nandi *et al.*[6], but duration of fever at the time of presentation had no bearing with throat swab culture positivity (p-value = 1.00). This observation is supported by Steinhoff *et al.*[24], Nandi *et al.*[6] and Wong *et al.*[25]

Patients having pain in throat have an almost 8 times chance of having a positive throat swab culture than patients who don't have pain in throat. This finding has been consistent with the study done by Nandi *et al.*[6] where this symptom has a sensitivity of 86.2% and specificity of 84.7%.

Nausea and Abdominal Pain does not have any clinical significance on positivity rate of test results (p-value = 0.285) and is supported by McIsaac *et al.*[26], Attia *et al.*[27] in their studies.

Similarly, if only pharyngeal erythema is taken into account it was statistically significant ($p < 0.05$), but grading of erythema of pharynx had no bearing on test result (p-value = 0.374). This observation is supported by Santos *et al.*[28] and Nandi *et al.*[6]

The size of the tonsil had no relationship with positivity rate. Various studies have concurred on the tonsillar size being an important clinical feature like Nandi *et al.*[6] found in their study, this feature has a sensitivity of 86.9% and specificity of 69.1%, and Santos *et al.*[28] found sensitivity of 46% and specificity of 57%. Similar results have been found by Wald *et al.*[23] in their study.

Lymphadenopathy as presenting feature manifested as non-tender and tender lymphadenopathy. Tender lymphadenopathy was found to be highly specific for beta hemolytic streptococcus sore throat (p-value = 0.002) and specificity of around 85%-90%. This finding is consistent with Nandi *et al.*[6] and Santos *et al.*[28]

Poor living conditions had a positive bearing on the positivity rate of test results as throat swab positivity rate was as high as 86.5% in the children living in shady and damp houses.

On analysis of the data, it was found that indoor pollution had a positive effect on positivity of test results (p-value < 0.0005) and child having presence of smoker in the house had an 18 times more chance of having a positive throat swab result. The ROC curve measuring sensitivity and specificity in our study has shown the similar result with these factors having a larger area under the curve. Nandi *et al.*[6] found this similar finding in his study where fuel used for cooking had a relation with sore throat in children.

The per capita income had no statistically significant effect on the positivity rate of throat swab culture results as supported by Nandi *et al.*[6]

Various studies have tried to incorporate different clinical features in devising algorithms for streptococcal sore throat.[22,26,29,30] The performance of these algorithms was similar. They were effective in identifying low-risk patients, that is, those whose chance of having a positive culture result approximated the anticipated asymptomatic carriage rate in the population studied. In contrast, the algorithms were only modestly successful in differentiating streptococcal from non-streptococcal pharyngitis in adults with more-prominent clinical signs and symptoms [Table 2].

Present study has tried to include environmental factors in addition to the clinical signs and symptoms in making diagnosis of streptococcal sore throat easier through Pediatric OPD. Indoor pollution, high grade fever, pain in throat on swallowing, tender lymphadenopathy as factors in this study have shown a very good effect on the positivity rate of throat swab test results with area under the ROC curve being more, and, in particular indoor pollution has a very high sensitivity (95%) and a high specificity (70-85%) [Figures 1 and 2]. Indoor pollution makes a very strong point for inclusion in any further algorithm devised for diagnosing streptococcal sore throat. Though, throat swab culture remains the gold standard, the use of scoring system incorporating above features will reduce

Table 2: Table showing various studies that have tried to incorporate different clinical features in devising algorithms for streptococcal sore throat

Reference	Description	Population	Accuracy	Comment
Centor *et al.*[27]	Simple 4 variable additive score	236 Adults/OPD	Good	Successfully validated in three new populations
Breese *et al.*[19]	9-item additive score	670 Children	Positive Likelihood Ratio=2	Lowest Risk group has 6-16% risk of strep. pharyngitis
Walsh *et al.*[26]	Algorithm based on 5 signs and symptoms	418/Adult/OPD	High Risk=28% streptococcal Moderate Risk=15% streptococcal Low Risk=4% streptococcal	Good Prospective Validation
McIsaac *et al.*[23]	Algorithm based on 4 signs and symptoms and patient age	621 Canadian children>3 years and adults	Risk stratified into 5 levels, from 1%-51%	Good Prospective Validation
Present study	Environmental, clinical signs and symptoms	225 children/OPD	Individual Signs and Symptoms studied	

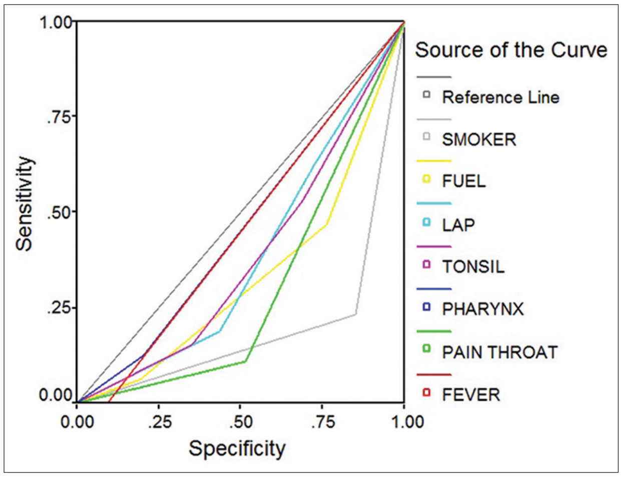

Figure 1: ROC curve illustrating diagnostic ability of different clinical factors

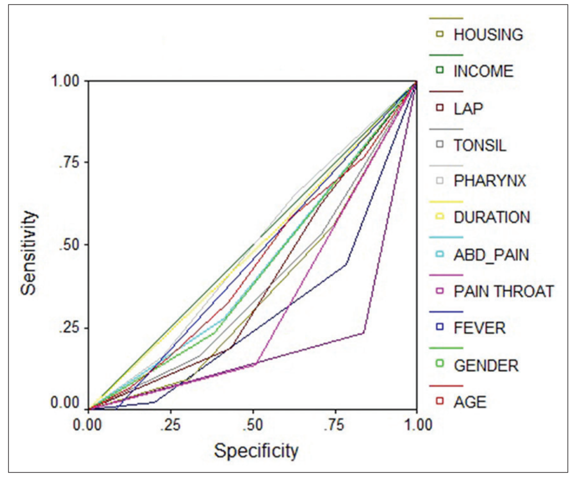

Figure 2: ROC curve illustrating diagnostic ability of different clinical factors

the need to treat all cases of sore throat with antibiotics and thus will reduce the treatment cost. In health centers where laboratory facilities exist, clinical scoring system can be used to select cases for confirmation of diagnosis either by culture or by rapid diagnostic kits, thus reducing the cost of diagnosing the group A beta hemolytic streptococcal pharyngitis. There is therefore a need of development of algorithms for diagnosis and treatment of sore throat, especially in primary care settings so as to prevent misuse of antibiotics, and also antibiotic stewardship programs shall be undertaken by hospitals to spread awareness about antibiotic resistance.

Conclusion

The study stresses on the need of carefully evaluating children presenting with the symptoms of sore throat as majority of the cases may be viral and thus, self-limiting. Some clinical features that may aid clinical diagnosis include high grade fever, pain in throat on swallowing, tender lymphadenopathy, tonsillar enlargement and absence of cough.

Poor housing conditions and indoor pollution contribute to the increased prevalence of sore throat. Presence of tobacco smoker in the house has a major role in causing the indoor pollution and children are the innocent sufferers of this malady. People need to be educated about the harmful effects of the smoking on the health of their children.

Laboratory diagnosis may not be possible everywhere in developing countries where prevalence of sore throat and its complications is high; an algorithm containing clinical signs and symptoms as well as epidemiological factors including indoor pollution is needed for diagnosing group A beta hemolytic sore throat in routine pediatric practice.

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Conflicts of interest

There are no conflicts of interest.

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