DEVELOPMENT OF A CLINICAL PREDICTION INSTRUMENT FOR GROUP (A) BETA HEMOLYTIC STREPTOCOCCAL PHARYNGITIS IN CHILDREN

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In Pediatrics

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بسم الله الرحمن الرحيم

" و علمك ما لم تكن تعلم و كان فضل الله عليك عظيما"

صدق الله العظيم

النساء(١١٣)

Abstract

The study included 1626 children, 26.4%(N:430) of the children had a positive throat culture for group A B-hemolytic streptococci , 42.3% were girls, 45.5% were above 5 years of age. The highest rate of positive cultures was in children above 5 years of age (51.7%,p-value =0.002).Each presenting sign and symptom was evaluated in terms of its frequency and association with GABHS pharyngitis. The sensitivity, specificity, PPV, NPV, LR+ve,and LR-ve were calculated for each sign and symptom that was positively associated with GABHS Pharyngitis. Multiple logistic regression analysis was used to develop our final clinical prediction model.

Key Words :

Rheumatic heart disease - Epstein-Barr virus - Herpes simplex virus .

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List of abbreviations

GABHS	Group (A) beta hemolytic streptococcus
GAS	Group (A) streptococcus
RF	Rheumatic fever
RHD	Rheumatic heart disease
CN	Cranial nerve
EBV	Epstein-Barr virus
CMV	Cytomegalovirus
HSV	Herpes simplex virus
HIV	Human immunodeficiency virus
RPR	Rapid plasma reagin
ASO	Anti-streptolysin O
ADB test	Anti –DNAse tests
OIA	Optical Immunoassay
PANDAS	Pediatric Autoimmune Neuropsychiatric Disorder Associated with Group A Streptococci
CUSPH	Cairo University Specialized Pediatric Hospital
MLR	Multiple logistic regression
ROC	Receiver Operating Characteristic curves
AUC	Area under the curve
SPSS	Statistical Package for Social Science
PPV	Positive predictive value
NRV	Negative predictive value
LK+ve	Likelihood ratio positive
LK-ve	Likelihood ratio negative
OR	Odds ratio
WHO	World Health Organization

Introduction

Pharyngitis due to group (A) beta hemolytic streptococcus (GABHS) assumes a special significance because of the risk of subsequent rheumatic fever (RF) and chronic rheumatic heart disease (RHD) in the infected child. Pharyngitis or sore throat is a common ailment the world over, and is especially common in children. About 10%-30% of acute pharyngitis is caused by (GABHS); (Pichichero ME,1995) [1] viral infection accounts for the majority of the others. About 0.3-3% of patients of untreated (GABHS) pharyngitis go on to develop (RF) (WHO/ISFC meeting, 1995). [2] Carditis occurs in about 70% of children with (RF) and about a fourth of these go on to develop chronic (RHD).

In wealthy countries, (RF) and (RHD) have been largely controlled since the 1950s. (Pichichero ME,1995) [1] This dramatic decline is attributed partly to antibiotic treatment of streptococcal pharyngitis and partly to improvement in living standards. In developing countries, these same problems exist and are compound by other issues. The prevalence of (GABHS) pharyngitis in these countries is largely unknown due to paucity of studies. Secondly, facilities for performing throat cultures and agglutination tests as well as determining antibody titers are not generally available. Lastly, because of lack of awareness, many patients don't seek medical care(WHO/ISFC meeting, 1995).[2]

The pathogenesis of (RF) is still not fully understood but is known to be related to group A beta hemolytic streptococcal infection of the upper respiratory tract and a specific susceptibility of the individual host. Thus the most efficient strategy for the primary prevention of (RF),

besides improvement in living standards, lies in the antibiotic management of streptococcal pharyngitis.

Diagnosis of (GABHS) pharyngitis is traditionally made by throat culture in wealthy countries, however not all patients positive for throat culture represent true infection. More than 50% of such patients may be carriers (Wannamaker LW,1972).[3] Demonstration of rise in antibody titers to (GABHS) in paired sera is only a mean of retrospective diagnosis. Recently, rapid streptococcal agglutination tests have become available and are highly specific, though they lack sensitivity.(McIssac WJ et al ,1997)[4]

Penicillin has been used to treat pharyngitis since 1952. Despite the availability of many alternative antibiotics, it is still the form of therapy recommended by the American Heart Association, the American Academy of Pediatrics, the World Health Organization (WHO) (Gerber MA et al, 1999) (WHO program for the prevention of rheumatic fever/ rheumatic heart disease, 1992)[5,6] Penicillin has a narrow spectrum of antimicrobial activity, proven efficacy and safety, and is the least expensive form of treatment. Penicillin may be administered intramusculary or orally (Bass JW,1986).[7] For Penicillin allergic patients, erythromycin is recommended. Recent studies have shown oral cephalosporins, to be effective in the treatment of (GABHS) pharyngitis. These drugs are not practical for use in developing countries because they are very expensive and are not widely available in these countries. Additionally, use of these broad spectrum antibiotics can lead to increased antimicrobial resistance of other bacteria.

Improved care for streptococcal pharyngitis in children in less developed regions will have two major impacts 1) It will reduce the large burden of preventable cardiac disease in these regions, and 2) has the potential to reduce indiscriminate antibiotic use which is increasing the frequency of antimicrobial-resistant bacteria.

Since it is not desirable to treat all pharyngitis with antibiotics and laboratory facilities for culture and serology are not generally available, it would be useful to have guidelines for clinical identification of (GABHS) pharyngitis in less wealthy regions. Although there are a fairly large number of studies on (GABHS) pharyngitis in the literature, there are only a few which deal with clinical prediction rules for (GABHS) pharyngitis in children .There are some studies in adults describing clinical prediction rules for (GABHS) pharyngitis (Walsh et al, 1975) (Centor et al, 1981) (Komaroff et al, 1986).[8,9,10] Decision analyses for the illness in adults suggests that clinical prediction instruments are accurate enough to predict over the threshold treatment probability (Dippel DW et al, 1992) (Tompkins RK et al, 1997) [11,12] In children, there are few studies of this type.

Aim of work

This study aims to improve clinical diagnosis of group (A) beta hemolytic streptococcal (GABHS) pharyngitis and to develop clinical criteria for the presumptive diagnosis of streptococcal pharyngitis. The guideline will allow clinicians to provide antibiotic therapy only for those children with a high probability of streptococcal pharyngitis, and will therefore reduce antibiotic use in the majority of pharyngitis cases which are not streptococcal. Improved clinical care of children in less developed regions and the reduction of indiscriminate antibiotic use will improve health states of children, aiding economic development.

Primary objective:

To identify the optimal set of clinical findings in children between 24 months and 12 years of age that are predictive of (GABHS) pharyngitis as documented by positive throat culture and/or serology.

Secondary objectives;

To describe the prevalence of (GABHS) pharyngitis in children seeking care for the complaint of sore throat under different conditions.

To describe the variation in (GABHS) strains and association with clinical manifestations of streptococcal pharyngitis.

To describe the prevalence of (GABHS) carrier state in patients with acute respiratory infections (ARI).