# Validation of Different Clinical Prediction Scores to Guide Management of Children with Acute Sore Throat in Primary Care Practice

Thesis

*Submitted for Partial Fulfillment of Medical Doctorate in Family Medicine*

By

**Shereen Nabil Hamza El Boray**
*M.Sc. 2013*
*Faculty of Medicine - Ain Shams University*

Under Supervision of

**Prof. Dr. Nehal Mohamed El Raggal**
*Professor of Pediatrics*
*Faculty of Medicine - Ain Shams University*

**Prof. Dr. Diaa Marzouk Abd El Hameed**
*Professor of Community Medicine, Head of Family Medicine Department*
*Faculty of Medicine - Ain Shams University*

**Assist. Prof. Dr. Reda Mohamed Sabra**
*Assistant professor of Otorhinolaryngology*
*Faculty of Medicine - Ain Shams University*

**Assist. Prof. Dr. Sherin Ahmed ElMasry**
*Assistant professor of Clinical Pathology*
*Faculty of Medicine - Ain Shams University*

**Prof. Dr. Paul Little**
*Professor of Primary Care*
*Faculty of Medicine - Southampton University*

Faculty of Medicine – Ain Shams University
2017

# List of Contents

# List of Tables

# List of Tables (Cont...)

# List of Tables (Cont...)

# List of Figures

# List of Abbreviations

| Abb. | Full term |
|---|---|
| ***ARF*** | *Acute Rheumatic Fever* |
| ***AUC*** | *Area under the Curve* |
| ***BAPs*** | *Blood Agar Plates* |
| ***CI*** | *Confidence Interval* |
| ***CPR*** | *Clinical Prediction Rule* |
| ***GAS*** | *Group A Streptococcus* |
| ***GBD*** | *Global Burden of Disease* |
| ***LN*** | *Lymph Node* |
| ***LR-*** | *Likelihood Ratio Negative* |
| ***LR+*** | *Likelihood Ratio Positive* |
| ***NPV*** | *Negative Predictive Value* |
| ***OTC*** | *Over the Counter* |
| ***PPV*** | *Positive Predictive Value* |
| ***RADT*** | *Rapid Antigen Detection Test* |
| ***RBCs*** | *Red Blood Cells* |
| ***RCT*** | *Randomized Controlled Trial* |
| ***RHD*** | *Rheumatic Heart Disease* |
| ***SD*** | *Standard Deviation* |
| ***UK PHE*** | *United Kingdom Public Health England* |
| ***WHO*** | *World Health Organization* |

# Abstract

The area under the curve (AUC) for the three clinical scores (FeverPAIN, Adapted Centor and Steinhoff) was around 0.50. FeverPAIN Score had the highest sensitivity of 100% followed by Adapted Centor Score 91.9%, then Steinhoff Score (72.8%). On the contrary, Steinhoff Score had the highest specificity (31.3%).

A theoretical testing of FeverPAIN and Adapted Centor scores after application of RADT have resulted in dramatic improvement in their validity. Both scores had sensitivity of 100%. FeverPAIN and Adapted centor scores had specificity of 77.1% and 70.1%, respectively.



**Keywords:** Acute Sore Throat - Clinical Prediction Scores - Epidemiology and Complications - GAS Infection

# INTRODUCTION

Acute sore throat, termed pharyngitis by clinicians, is a common and frequent presentation to primary care practice. In primary care, roughly, third of the patients with respiratory tract infections presents with sore throat and almost third of the antibiotics are prescribed for these infections ***(Petersen et al., 2007 & Little et al., 2014a).*** Although viruses are the most common cause of sore throat, Group A β-haemolytic streptococcus (GAS), known as Streptococcus pyogenes, is the most frequently identified bacterial cause of sore throat, with over a half-billion people affected annually worldwide ***(Carapetis et al., 2005).*** The pooled prevalence of GAS sore throat among children of all ages is 37% and in Egypt the prevalence is 24 % among children aged 2-5 years and 33% among 5-12 years age group ***(Nader et al., 2010).***

Streptococcus pyogenes (GAS) infection has a great burden on school-aged children ***(Dunne et al., 2013).*** This agent can also cause severe life-threatening conditions and non-suppurative sequelae. Accurate diagnosis and proper treatment are recommended in US guidance to prevent postinfectious suppurative and non suppurative complications, such as peritonsillar abscesses, acute rheumatic fever (ARF), and poststreptococcal glomerulonephritis ***(Shulman et al., 2012).*** Antibiotic treatment of acute streptococcal sore throat can prevent acute rheumatic fever ***(Abd El-Ghany et al., 2015),*** however,

presumptive antibiotic prescriptions to patients with streptococcal pharyngitis without relying on a valid clinical guidance or a diagnostic test can predispose to upsurge in the carrier state and in the rate of antibiotic-resistant strains of GAS ***(Devi et al., 2011 & Abd El-Ghany et al., 2015).*** Antibiotic-resistant bacterial infections increase the costs of healthcare and associated with increased mortality and morbidity ***(Borg et al., 2009).***

The gold standard microbiological method for establishing the diagnosis of GAS pharyngitis is throat culture with a blood agar plate (BAP) ***(Gerber and Shulman, 2004);*** however the availability and feasibility of bacterial culture in clinical settings cannot be guaranteed, especially in regions with limited resources and higher incidences of post-infectious cardiac complications, as in many developing countries ***(McIsaac et al., 2004; Steinhoff et al., 2005 & Rimoin et al., 2008).*** In these regions, the use of clinical scoring systems can predict streptococcal throat infections and guide clinicians' decisions on prescribing antibiotic for these infections ***(Steinhoff et al., 2005).***

The relevance of clinical prediction scores for determining which children with sore throat should undergo a lab detection test remains questionable ***(Jérémie et al., 2015).*** A formal comparisons of clinical prediction rules performance is needed to provide an informative evaluation and standardization of clinical outcomes ***(Steinhoff et al., 2005).*** Our study aims at measuring the validity of three of clinical

prediction scores (Fever/Pain, Adapted centor score (McIsaac) and Steinhoff scores) for identification of Group A Streptococcal throat infections in children with acute sore throat compared with throat culture results as a gold standard, in order to improve clinical practice and to target antibiotic use more effectively.

## Research Question

Are the clinical prediction scores (FeverPAIN, Adapted Centor and Steinhoff scores) valid for predicting Group A Streptococcal throat infections in children with acute sore throat?

# AIM OF THE WORK

1- To measure the validity of three clinical prediction scores (FeverPAIN, Adapted Centor and Steinhoff scores) in order to find out how well clinical examination performs in diagnosing group A beta-hemolytic streptococcal (GAS) pharyngitis in children with acute sore throat, attending primary care clinics in Cairo, Egypt.

2- To assess different clinical variables which could potentially guide antibiotic prescription for patients with group A streptococcal sore throat.

## Ultimate objectives

1- To improve clinical practice by targeting antibiotics for treatment of children with GAS sore throat.

2- To decrease the morbidity and mortality from GAS infection and reducing antibiotic resistance rates.

# Chapter 1
# ACUTE SORE THROAT AND GAS INFECTION: EPIDEMIOLOGY AND COMPLICATIONS

## 1.1 Acute Sore Throat:

Acute sore throat (pharyngitis) is a common symptom that occurs as a result of an inflammation of the pharynx, nasopharynx or tonsils ***(Pelucchi et al., 2012).*** There are a variety of infectious and non infectious aetiology of sore throat. Most of the pharyngitis cases are due to infectious causes such as viral, bacterial and fungal, however the most common cause is viral infection, and accounts for 80% of infectious pharyngitis ***(Bertold et al., 2012 & Khaled Sorour., 2014).*** Approximately 40% of the cases are caused by rhinovirus and adenovirus. In addition, influenza, parainfluenza, coronavirus, Epstein Barr, and herpes simplex can also cause viral sore throat ***(Middleton, 1996 & Bertold et al., 2012).*** This condition is usually associated with cold symptoms such as cough, conjunctivits, runny nose, and sneezing. It is usually a self-limiting condition that does not require any specific treatment.

Of the bacterial causes of sore throat, group A β-haemolytic streptococcus (GAS) also known as Streptococcus pyogenes (S. pyogenes), belongs to Lancefield serogroup A, and is the most frequently identified (5-36%) ***(SIGN, 2010 &***

***Cohen et al., 2013).*** GAS throat infection has more severe and persistent symptoms and signs than viral infections. Other bacteria that occasionally cause sore throat include non-group A β-haemolytic streptococcus (groups C and G streptococci), Mycoplasma pneumoniae, Chlamydia pneumoniae and Neisseria gonorrhoeae ***(Pichichero et al., 1998).*** Candidal infection and other fungi are rare causes of sore throat ***(Bertold et al., 2012).***

On the other hand, there are a various non-infections causes of sore throat. This includes physico- chemical causes such as smoking, snoring, shouting and some medications (for example, Angiotensin converting enzyme inhibitors (ACEIs) and Chemotherapy), and environmental factors including air pollution, humidity, temperature and air conditioning). Other factors include allergies, gastro-oesophageal reflux disease, and Stevens-Johnson syndrome. Diagnosis of non infectious sore throat is based on the persistence of sore throat with absence of infectious symptoms and signs e.g. rhinitis or sinusitis ***(Bertold et al., 2012).***

## 1.2 Epidemiology of GAS pharyngitis:

GAS was first isolated from human suppurative lesions in 1884 by Rosenbach and has been considered as a significant human pathogen for centuries ***(Sugumari and Mahesh, 2016).*** Humans are the only known reservoir for Streptococcus pyogenes and infection spreads mainly by respiratory droplets

as nasopharynx and oropharynx are the usual carriage sites for the pathogen. GAS causes a wide variety of human diseases that include pharyngitis, scarlet fever, pneumonia, meningitis pyoderma, cellulitis, erysipelas, necrotizing fasciitis, toxic streptococcal syndrome and sepsis ***(Ferretti, 2016).***

In general, GAS pharyngitis is more common during the winter and spring seasons ***(Hugh et al., 2013).*** It occurs in all age groups, with a peak prevalence in children 5-10 years old. Both gender and all races can equally be affected with GAS sore throat ***(Harold, 2016).*** GAS accounts for 20% to 40% of sore throat cases in children and 5% to 15% in adults ***(Ebell et al., 2000; Shaikh et al., 2010 & Wessels, 2011).***

The incubation period of GAS pharyngitis is 1 to 4 days and the disease lasts for 3 to 5 days with a variable degree of symptoms and signs. Typical presentation includes fever and sore throat. Headache, abdominal pain, nausea, vomiting and malaise are frequent, however other symptoms such as cough, rhinorrhea, conjunctivitis, hoarseness and diarrhoea are unusual ***(Pechère and Kaplan, 2004).*** GAS are gram positive bacteria that give a specific morphology as pairs or chains of variable length when cultured in blood agar. The pathogen causes complete hemolysis of red blood cells (RBCs) on sheep blood agar and grow as round and small colonies. A variety of factors have mediated the pathogenesis of GAS, including streptolysins O and S; steptokinase; proteases; pyrogenic exotoxins A, B,