Prevalence and risk factors associated with rheumatic fever and rheumatic heart disease among Egyptian school age children living in Qualioub, Qualioubia Governorate

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Abstract

Rheumatic fever and rheumatic heart disease remain major health problems in most countries of the developing world, including Egypt. In these countries ,RHD is estimated to be responsible for 30-60% of all cardiac patients admitted to hospital **(Nordet p., 1994)** .

The aim of this study to find out the prevalence of rheumatic fever and rheumatic heart disease among school children living in Qualiob, Qalioubia Governorate, in Egypt and Risk factors associated with rheumatic fever and rheumatic heart disease.

Key words;

rheumatic fever
rheumatic heart disease
Thickened mitral valve

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AHA……. ……	American Heart Association
Anti-Dnase B..... …… …	Anti deoxyribonuclease B
AR……	Aortic Regurgitation
ASOT…….....	Antistreptolysin O titre
CABHS…….. …	Group A B hemolytic streptococci
CRP……	.C-reactive protein
DNases……..	Deoxyribonucleases
ESR……	Erythrocyte sedimentation rate
HIV……	Human immunodeficiency virus
HLA ……	Human leukocyte antigen
IL…….	Interleukin
INF……	Interferon
LAP ……	Long acting penicillin
MF……	Mitogenic factor
MHC……	Major histocomptability complex
MHC……	Major histocomaptabilty complex
MR……	Mitral Regurgitation
MS……	Mitral Stenosis
NABG……	N-acetyl Beta-D-glucosamine
NADase……	Nicotine-adenine-dinucleotidase
OF……	Opacity factor
PCR……	Polymerase Chain reaction
PMN……	Polymorphic nuclearcytes
PSRA…… .	post streptococcal reactive arthritis
RF……	Rheumatic Fever
RH……	Rheumatic heart disease
RHD……	Rheumatic heart disease
S.pyogenes……	Streptococcal pyogenes
SIC……	Streptococcal inhibitor complement
SPE……	Streptococcal pyrogenic exotoxin
SPYCPE……	S.pyogenes cell envelope proteinase
SSA……	Streptococcal super antigen
TNF……..	Tumor necrosis factor
TR……..	Tricuspid regurgitation
TSS……	Toxic shock syndrome

WHO……..World health organization

INTRODUCTION

The incidence of Rheumatic Fever (RF) and prevalence of Rheumatic Heart Disease are markedly variable in different countries **(Narula et al, 1999).** At the beginning of the 20th century, the incidence of RF in the United States exceeded 100 per 100,000 populations, ranged between 40 and 65 per 100,000 between 1935 and 1960, and is currently estimated at less than 2 per 100,000. Beginning in 1984, several outbreaks of acute RF were reported from a number of geographically distinct areas in the United States **(world health organization, 1998).** These Focal outbreaks were not associated with a national increase in the incidence of RF **(Dajani AS, 1991).** The decline in the incidence of RF in industrialized countries is in sharp contrast to the persistent high incidence of the disease in non industrialized countries.

In many developing countries, the incidence of acute RF approaches or exceeds 100 per 100,000 **(Narula et al, 1999).** In keeping with the falling incidence of RF in industrialized countries, the prevalence of Rheumatic Heart Disease has also declined in developing countries **(Jose VJ et al, 2003).**

The decline in incidence of RF and prevalence of Rheumatic Heart Disease has been attributed to several factors (improved economic standards, better housing conditions, decreased crowding, and access to medical care) although the decline preceded the introduction of antimicrobial agents for the treatment of streptococcal pharyngitis, some reports suggests that the use of these agents may have enhanced the rate of this decline **(Taubert KA et al, 1994)**. Improved economic standards, better housing conditions, decreased crowding in homes and schools , and access to medical care are often credited, at least in part, for the marked decline in RF **(Narula et al, 1999).** Epidemiological observations in the United States **(Massell BF et al, 1988)** and the United Kingdom **(Schwartz B et al, 1990)** show periodic shifts in the appearance and disappearance of specific M types in a particular geographical location. Such shifts may be another reason for the decline and resurgence of RF in some parts of the world.

Because of the causal relationship between RF and Group A streptococcus (GAS) pharyngitis, the epidemiologies of the two illnesses are very similar. Initial attacks of RF occur most commonly between the ages of 6 and 15 years, and RF rarely occurs before the age of 5 years **(Colman G et al, 1993).** The risk of RF is increased in populations at high risk for

streptococcal pharyngitis, such as military recruits, persons living in crowded conditions, and those in close contact with school-age children. The incidence of RF is equal in male and female patients. The seasonal incidence of RF also parallels that of streptococcal pharyngitis. The peak incidence of RF in Europe and the United States is in spring. Although RF used to be considered a disease of temperate climates, it is now more common in warm tropical climates, particularly in developing countries.

The incidence of Rheumatic fever and Rheumatic Heart Disease is still high in Egypt, which represent a great social and economic burden. The reasons for this observation may be due to a) Improper treatment of children with Rheumatic Fever, b) Environmental and social factors, c) Patient compliance with the prescribed medications, d) Genetic factors and /or type of streptococcal strain present in Egypt. So, it is of great importance to know the prevalence of Rheumatic Fever and Rheumatic Heart Disease in Egypt, Moreover, it is important to know in which social class (es) in the community is the disease prevalent and the risk factors associated with its occurrence. This information will be most valuable and will aid in planning and intervening in the disease spread, treatment, and eradication.

This study aims at describing the magnitude of Rheumatic Fever and Rheumatic Heart Disease as major health problems among Egyptian school age children.

AIM OF THE WORK

This study aims at describing the magnitude of Rheumatic Fever and Rheumatic Heart Disease as major health problems among Egyptian school age children.

OBJECTIVES

1. To find out the prevalence of rheumatic fever and rheumatic heart disease among school children living in Qualiob, Qalioubia Governorate, in Egypt.
2. Risk factors associated with rheumatic fever and rheumatic heart disease.

Epidemiology and pathogenesis of rheumatic fever

Rheumatic fever (ARF) is a delayed, nonsuppurative sequela of a pharyngeal infection with the group A streptococcus (GAS). Following the initial pharyngitis, a latent period of two to three weeks occurs before the first signs or symptoms of ARF appear (***Rammelkamp and Stolzer, 1961).*** The disease presents with various manifestations that may include arthritis, carditis, chorea, subcutaneous nodules, and erythema marginatum.

EPIDEMIOLOGY:

Worldwide, there are 470,000 new cases of rheumatic fever and 233,000 deaths attributable to rheumatic fever or rheumatic heart disease each year; most occur in developing countries .Among indigenous groups and developing nations, over 15 million people are estimated to have rheumatic heart disease (***Carapetis, 2007)***

In the United States and other developed countries, the incidence of ARF is much lower at 2 to 14 cases per 100,000; this is probably due to improved hygienic standards and routine use of antibiotics for acute pharyngitis. Many cases that do occur are part of localized outbreaks ***(Stollerman, 1997).***

Rheumatogenic strains:

The observation in some studies that only a few M serotypes (types 3, 5, 6, 14, 18, 19, 24, and 29) were implicated in outbreaks of rheumatic fever in the United States suggested a particular "rheumatogenic" potential of certain strains of GAS ***(Johnson et al, 1992).***

To address the "rheumatogenic" potential of GAS, a serologic surveillance study compared the M types of GAS recovered from children in Chicago with acute pharyngitis during the time period 1961 to 1968 to the GAS strains recovered from Chicago children and children from across the United States in the time period 2000 to 2004. Rheumatogenic strains (eg, types 3, 5, 6, 14, 18, 19, and 29) were less prevalent among the latter isolates (10.6 versus 49.7 percent in the earlier time period) ***(Shulman et al,2006).***

The authors hypothesized that the marked decrease in the incidence of acute rheumatic fever in the United States correlates with the

replacement of rheumatogenic types by nonrheumatogenic types. However, an accompanying editorial noted that although the prevalence of rheumatogenic strains decreased two- to fivefold, the reduction in the incidence of ARF over the same period was ≥20-fold (***Lee and wessels ,2006)***. Thus, a shift in the prevalence of rheumatogenic M type GAS strains is not solely responsible for the decrease in ARF.

Our own series, gathered over a 20-year period, has produced different results. We isolated a large number of different M serotypes, including six strains that were nontypable. In addition, several different M types were isolated from the patients seen during a mid-1980s outbreak of ARF in Utah; these strains were both mucoid and non-mucoid in character. In addition, M serotypes different from those in the United States have been associated with ARF in Trinidad and Hawaii ***(Erdem et al, 2007)***

Thus, the issue of potential "rheumatogenic" strains remains unresolved. A streptococcal strain capable of causing a well-documented pharyngitis almost always is potentially capable of causing rheumatic fever, although some exceptions have been recorded. The lack of specific rheumatogenic strains also can explain the relatively high risk of recurrent disease with new streptococcal infections, in contrast to poststreptococcal glomerulonephritis, in which only a few "nephritogenic" strains appear to be capable of inducing the disease (eg, type 12 with pharyngitis and type 49 with impetigo), and recurrent disease is uncommon ***(Erdem et al ,1969)***.

PATHOGENESIS:

The pathogenic mechanisms that lead to the development of acute rheumatic fever remain incompletely understood. Clearly streptococcal pharyngeal infection is required, and genetic susceptibility may be present. On the other hand, evidence is sparse that toxins produced by the streptococcus are important.

Within this framework, molecular mimicry is thought to play an important role in the initiation of the tissue injury. However, the factors responsible for maintenance of the process remain unclear.

Role of the streptococcus:

Despite the lack of evidence for the direct involvement of GAS in the affected tissues of patients with ARF, significant epidemiologic and immunologic evidence indirectly implicates the GAS in the initiation of disease.

- Outbreaks of rheumatic fever closely follow epidemics of streptococcal pharyngitis or scarlet fever with associated pharyngitis ***(Kaplan and bison,2006)***.
- Adequate treatment of a documented streptococcal pharyngitis markedly reduces the incidence of subsequent rheumatic fever ***(*Denny et al 1959)**.
- Appropriate antimicrobial prophylaxis prevents the recurrence of disease in patients who have had ARF ***(Shulman et al ,1994)***.
- Most patients with ARF have elevated antibody titers to at least one of (if not all) three antistreptococcal antibodies (streptolysin "O", hyaluronidase, and streptokinase), whether or not they recall an antecedent sore throat ***(Stollerman et al,1956)***.

In contrast to the high sensitivity of antistreptococcal antibodies for the documentation of streptococcal infection, the rate of isolation of GAS from the oropharynx of patients with ARF is extremely low, even in populations that generally do not have access to microbial antibiotics. The clinical documentation of an antecedent pharyngitis also appears to have an age-related discrepancy. One study, for example, noted that the recollection of pharyngitis approached 70 percent in older children and young adults versus only 20 percent in younger children. Thus, a high index of suspicion of ARF is important, particularly in children or young adults presenting with signs of arthritis and/or carditis, even in the absence of a documented episode of pharyngitis ***(Veasy et al,1987).***

In certain areas, it has been suggested that ARF might be due to non-group A streptococcal strains (eg, group C and group G) that inherited certain group A streptococcal antigens or enzymes that are important for initiating ARF ***(McDonald et al,2004)***