



# **Role of Echocardiography in Detection of Subclinical Valvulitis in Patients with Rheumatic Fever**

## **Thesis Proposal**

**Submitted for fulfillment of PhD in Childhood Studies**

**(Child Health and Nutrition)**

**Department of Medical Studies**

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**2013**

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## **List of Abbreviations**

**ACE:** Angiotensin Converting Enzyme

**AHA:** American Heart Association

**AN:** Aschoff Nodules

**AO:** Aorta

**AR:** Aortic Regurge

**ARF:** Acute Rheumatic Fever

**ASOT:** AntiStretolysin O Titre

**AV:** Aortic Valve

**AVB:** AtrioVentricular Block

**CHF:** Congestive Heart Failure

**CRP:** C Reactive Protein

**CSANZ:** Cardiac Society of Australia and NewZealand

**DNase:** Deoxyribonuclease

**ECG:** Electrocardiogram

**ESR:** Erythrocyte Sedimentation Rate

**GABHS:** Group A $\beta$  Hemolytic Streptococci

**GAS:** Group A Streptococcus

**GI:** Gastro-Intestinal

**GU:** Genito-Urinary

**HLA:** Human Leucocytic Antigen

**HRQoL:** Health Related Quality of Life

**IE:** Infective Endocarditis

**IU:** International Unit

**IVIG:** Intravenous Immunoglobulin

**IVR:** Initiative for Vaccine Research

**LA:** Left Atrium

**LAP:** Long Acting Penicillin

**LV:** Left Ventricle

**LVOT:** Left Ventricular Outflow Tract

**MR:** Mitral Regurge

**MV:** Mitral Valve

**NHFA:** National Heart Foundation of Australia

**NSAID:** Non-Steroidal Anti-Inflammatory Drugs

**RA:** Right Atrium

**RADT:** Rapid Antigen Detection Test

**RF:** Rheumatic Fever

**RHD:** Rheumatic Heart Disease

**RV:** Right Ventricle

**RVOT:** Right Ventricular Outflow Tract

**TSS:** Toxic Shock Syndrome

**ULN:** Upper Limit of Normal

**URTI:** Upper Respiratory Tract Infection

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## *Acknowledgement*

*First of all praise is to **ALLAH** the most beneficial and the most merciful for helping me in every single step in this work and in my life.*

*It is a great honour to express my gratitude and respect to **Prof. Dr. Mohamed Salah Eldin Mostapha** Professor of Preventive Medicine and Epidemiology Institute of Post Graduate Childhood Studies Ain Shams University, for exerting a great effort in supporting me in this work. I would like to thank him for his kindness and guidance and his fatherly attitude. Really, I have benefited a lot from his experience and I am really grateful to him for supplying me with scientific books and guiding me in the field of statistics and in my life aspects.*

*I am deeply indebted and really grateful to **Prof. Dr. Hala Salah Eldin Hamza** Professor of pediatrics-Head of "Rheumatic Fever" clinic — Center for Social Preventive Medicine — Cairo University Hospitals, for being keen and sincere in establishing of the clinic for the sake of the patients, providing me with scientific guidelines in weekly conferences, teaching me echocardiography and supplying the with medical and electronic needs and establishing a database system for registry of rheumatic fever patients. I would like to thank her again for her continuous support and guidance.*

## *Dedication*

*I would like to dedicate this work to my family; my mother who suffered a lot caring for me and supporting me with her continuous encouragement and prayers despite her illness, my father Zakareya for his continuous support and care, and for helping me with his valuable advice, my sister Fatemah assistant professor in Faculty of Women's College for Arts, Sciences and Education, for helping me with her experience and knowledge, and my brother engineer Fahya for his care and help, and for technical support of my devices. Thanks for my family for their continuous care, support and guidance in every single aspect of my life, without them my life would be a mess.*

## **Abstract**

**Background:** Echocardiography is an important tool in detecting subclinical valvulitis, thus allowing early diagnosis, treatment, prophylaxis, and preventing complications of rheumatic heart disease (RHD).

**Aims and Objectives:** This study aims to identify the role of echocardiography in detection of subclinical valvulitis in patients with rheumatic fever with no clinical evidence of RHD.

**Methodology:** This is a cross sectional study where patients coming to "Rheumatic Fever" clinic in Cairo University Hospitals with different complaints were examined and those with acute rheumatic arthritis and rheumatic chorea without clinical evidence of carditis were subjected to 2D Doppler echocardiography to detect subclinical valve affection according to WHO echocardiographic criteria during the period from the beginning of September 2011 to the end of December 2012.

**Results:** A total of 1096 patients with different presentations were examined and 50 patients fulfilled the study inclusion and exclusion criteria, where 26 patients (16 females and 14 males) representing 52 % of study patients had subclinical valvulitis by 2 D Doppler echocardiography. The majority of cases presented with acute arthritis (44 patients representing 88 % of study population); of those 21 patients representing 42% of total study population had subclinical valvulitis. On the other hand 6 patients presented with chorea constituting 12% of study patients where 5 patients representing 10% of total patients had subclinical valve affection. Most patients were from Giza governorate followed by Cairo governorate.

**In conclusion:** Echocardiography should be performed in patients with rheumatic fever with no clinical carditis and should be included in Jone's criteria for diagnosis of rheumatic heart disease.

**Key Words:**

**Rheumatic Fever - Subclinical Valvulitis - Echocardiography**

## Introduction

Acute rheumatic fever (ARF) and rheumatic heart disease (RHD) are global health problems affecting mainly children of developing countries and indigenous populations of developed countries (**Pandey et al., 2012**).

It is a postinfectious, nonsuppurative sequela of pharyngeal Group A  $\beta$  hemolytic *Streptococcus* (GABHS). All manifestations of rheumatic fever can resolve except valve damage which can become a chronic condition leading to congestive heart failure, strokes, endocarditis, and death (**Carapetis et al., 2005**).

Worldwide, incidence of RF is 19/100,000 (range, 5 to 51/100,000) (**Pessler and Sherry, 2010**). In Egypt, the prevalence of RHD was reported to be 7 per 10,000 in school children (**El-Aroussy et al., 2013**). In 2005, **Carapetis and colleagues** estimated a world burden of 2.4 million children aged 5-14 years affected and that a total population of 15-20 million was living with rheumatic heart disease at that time and that 233 thousand people per year died of RHD.

Studies show that individuals who have had an attack of rheumatic fever are at very high risk of developing recurrences after subsequent infection by group A streptococcal pharyngitis (**Gerber et al., 2009**).

According to revised Jones criteria, the diagnosis of rheumatic fever can be made when two of the major criteria, or one major criterion plus two minor criteria are present along with evidence of streptococcal infection. Exceptions are chorea and indolent carditis, each of which by itself can indicate RF (**Saxena, 2000**).

The Major criteria are migratory polyarthrititis, carditis, Sydenham chorea, erythema marginatum, and subcutaneous nodules. While the Minor criteria are arthralgia, fever, elevated acute-phase reactants, and first degree heart block (*Special Writing Group of the AHA, 1992*).

Due to subclinical or atypical presentations of rheumatic fever, lack of seeking medical advice, or under reporting, up to 10 times the current number of known sufferers remain undiagnosed in these countries (*Farrar and Butcher, 2012*).

Subclinical valvulitis is defined as pathological valvular regurgitation detected on echocardiography that is not evident clinically (*Turbidy-Clark and Carapetis, 2007*).

A national study of ARF in children in Australia showed that the reasons why patients do not fulfill the RF criteria include:(1) atypical presentations of RF, (2) the high incidence of delayed presentation (more than 20% of cases in one study) (3) and incomplete investigation, commonly resulting in the absence of results for the erythrocyte sedimentation rate (ESR), C reactive protein (CRP), electrocardiogram (ECG) or streptococcal serology (*Noonan et al., 2013*).

Subclinical valvulitis occurs in 8-75% of first episode of ARF (*Ekici et al., 2012*). A systematic review done in 2007 from 23 different studies estimated the prevalence of subclinical valvulitis was 17% among those with ARF (*Tubridy-Clark, and Carapetis, 2007*).

The diagnosis of patients with subclinical valvulitis may be overlooked unless echocardiography is used. Thus, because they will receive secondary preventive treatment inadequately or will not receive at all, these patients may experience more severe and early RHD with recurring episodes (*Carapetes et al., 2007*).

It was previously claimed that subclinical carditis was caused by examination performed by inexperienced people but this view was not supported in later studies (*De Sanctis et al., 2003*).

To avoid over-diagnosis or under diagnosis or misdiagnosis of valve regurge, the World Health Organization (WHO) developed echocardiographic criteria which are widely used by practitioners for the diagnosis of subclinical RHD, and are based only on Doppler characteristics of the valvular regurgitation, defined by the association of a regurgitant jet >1 cm in length, seen in at least 2 planes, a mosaic color jet with a peak velocity >2.5 m/s, persisting throughout systole or diastole. Only the aortic and mitral valves were considered in this setting because mild pulmonary or tricuspid regurgitation is frequent and seldom rheumatic in origin without addressing any morphological criteria (*WHO, 2004*).

Echocardiography is important for assessing the prognosis of patients with acute rheumatic fever and subclinical valvulitis and is critical in determining the duration of antibiotic prophylaxis (*Ozkutlu et al., 2001*).

## **Aim of the Study**

This study aims to identify the role of echocardiography in detection of subclinical valvulitis in patients with rheumatic fever. This allows proper classification of these patients as having rheumatic heart disease, for effective prevention of recurrence of rheumatic heart attacks by effective prophylaxis, early intervention, effective treatment, and prevention of complications including cardiac damage, disability, and even death.

# Chapter I

## Streptococcal Pharyngitis

### **Definition:**

Group A  $\beta$  hemolytic streptococci (GABHS) is the first event in the natural history of acute rheumatic fever. It should be diagnosed, differentiated from non-streptococcal pharyngitis, and treated. *Streptococcus pyogenes* (group A streptococcus, GAS) is a Gram-positive extracellular bacterial pathogen which colonizes the throat or skin and is responsible for a broad spectrum of diseases that range from simple pharyngitis and skin infections (impetigo, erysipelas, and cellulitis) to scarlet fever and life-threatening invasive illnesses(*Cunningham,2000*)(*Pfoh et al.,2008*).

### **Prevalence:**

GAS is the most common bacterial cause of acute pharyngitis and it is responsible for 5%–15% of sore throat visits in adults and 20%–30% in children with an estimated 7.3 million outpatient physician visits each year among children in the USA (*Ebell et al., 2000*) (*Linder et al., 2006*) . A study in Alexandria showed that the prevalence of Streptococcal tonsillopharyngitis was 17% with the highest isolation rates detected in children aged 10-15 years and in early spring (*Bassili et al., 2002*).

### **Clinical Picture of Streptococcal Pharyngitis:**

The signs and symptoms of GAS and non-streptococcal pharyngitis overlap so broadly that accurate diagnosis based on clinical grounds alone is usually impossible. The vast majorities of children and adults with acute pharyngitis have a viral etiology and do not need antibiotic treatment, even