



**Institute of Postgraduate Childhood Studies  
Medical Studies Department**

# **Recurrence Of Rheumatic Fever During Prophylaxis And Postoperative Valve Procedures And Some Of Its Psychological Effects**

**THESIS**

Submitted for Fulfillment of Ph.D. Degree In Medical  
Childhood Studies

**BY**

**Mohammed Atef Abdel-Ghany Negm**

*(M.B., B.Ch., M.Sc.) (Pediatrics)*

**Supervised By**

**Prof.Dr. RABHA EL-SHENNAWY**

Prof. Of Pediatric Cardiology,  
Faculty of Medicine,  
**Cairo University.**

**Prof.Dr. MAGDY KARM EL-DEEN**

Prof. Of Public Health in Medical  
Department  
Institute of Postgraduate Childhood Studies  
**Ain Shams University**

**Prof.Dr. EHAB M. EID**

Prof. of Public Health in Medical Department,  
Childhood Studies,  
**Ain Shams University.**

**2005-2006**



معهد الدراسات العليا للطفولة

قسم الدراسات الطبية

## تكرار الحمى الروماتيزمية أثناء الوقاية منها وبعد الإجراءات الجراحية العلاجية فى صمامات القلب وانعكاسها على بعض الجوانب النفسية

توطئة للحصول على درجة دكتوراه الفلسفة فى دراسات الطفولة الطبية

قسم الدراسات الطبية - صحة وتغذية الطفل

### رسالة مقدمة من

الطبيب/ محمد عاطف عبد الغنى نجم

بكالوريوس الطب والجراحة - ماجستير طب الأطفال - جامعة القاهرة

### تحت إشراف

أ.د/ مجدى كرم الدين

أستاذ الصحة العامة بقسم الدراسات الطبية

معهد الدراسات العليا للطفولة - جامعة عين شمس

أ.د/ رابحة الشناوى

أستاذ أمراض القلب فى الأطفال

كلية الطب - جامعة القاهرة

أ.د/ ايهاب محمد عيد

أستاذ الصحة العامة بقسم الدراسات الطبية

معهد الدراسات العليا للطفولة - جامعة عين شمس

2006 - 2005

## ACKNOWLEDGEMENTS

“Thanks to God before and after”

*Without the aid of GOD, this work would have not been finished.*

*I would like to express my deep gratitude to Prof. Dr. RABHA EL-SHENNAWY, Professor of Pediatric Cardiology, Cairo University for her generous and kind supervision.*

*I wish to express my deep thanks and sincere gratitude to Prof. Dr. Magdy Karm El-Din, Professor of Public Health Institute of PostGraduate Shildhood Studies, Ain Shams University, for his great patience, valuable suggestions, instructive supervision and precious advice.*

*I also extend my deepest thanks to Prof. Dr. EHAB M. EID, Professor of Public Health, in Medical Department, Institute of PostGradiue Childhood Studies, Ain Shams University, who offered valuable guidance and support.*

*I would like to express my gratitude to Prof. Dr. Atef Awad; Assistant Prof. of Public Health, Faculty of Medicine, Menoufia University; for his continuous help during the statistical part of this work.*



---

---

## ***ABSTRACT***

Rheumatic fever is a multi-system-non-suppurative, inflammatory disease triggered by GA $\beta$ HS infection of the upper respiratory tract. Patients in whom RF develops have a marked tendency to suffer from recurrent attack after subsequent GA $\beta$ HS infection of the upper respiratory tract. **Aim of the study:** Determining the risk factors causing the recurrence of RF during prophylaxis with LAP and post operative valve procedures and identifying the possible associating social and psychological repercussion. Patients and methods: 128 pediatric patients had RHD were followed for one year. These patients were divided into 2 groups. Group 1 included 64 patients under medical treatment and the second group included 64 patients whom had surgical procedures. Full clinical examination, plain x-ray of chest and heart, complete blood picture, ESR, CRP, ASOT, ECG, & echo-Doppler were performed. **Results:** The recurrence of RF is a dangerous problem which affects the Egyptian children .Recurrence was present in 47% of cases under medical treatment versus to 31% of cases with surgical procedures. Most of the clinical manifestations, major and minor were presented in these patients. Family history and the compliance of patients for restricted program of LAP prophylaxis were very important factors affecting the recurrence of RF .Different statistical tests were applied like Student test &  $\chi^2$ . **In conclusion**, the study ended with the following conclusions. Recurrence of RF should be considered and should be managed perfectly in addition



---

---

to the secondary prophylaxis to avoid squeale of RF. The following factors or variables were associated with increase or more likely occurrence of recurrence of RF age less than 12 yrs., family history, in addition to male sex, tonsillectomy, psychiatric troubles and patients being under medical treatment were associated with slightly but not significantly increase of recurrence. Middle and high SEL were associated with decrease of recurrence. Also, regular and irregular LAP prophylaxis were associated significant decrease of recurrence

**Key words:**

1. Rheumatic fever
2. Recurrence of RF.
3. Psychology
4. Prophylaxis
5. Valves



## **LIST OF ABBREVIATIONS**

|                |   |
|----------------|---|
| <b>βHGAS</b>   | Beta hemolytic group A streptococci         |
| <b>a PL</b>    | Antiphospholipid                            |
| <b>A.S.O.T</b> | Antistreptolysin O titre                    |
| <b>Ao.R</b>    | Aortic Regurgitation.                       |
| <b>Ao.S</b>    | Aortic stenosis                             |
| <b>APSGN</b>   | Acute post-streptococcal glomerulonephritis |
| <b>ARF</b>     | Acute rheumatic fever                       |
| <b>CHF</b>     | Congestive heart failure                    |
| <b>CI</b>      | Confidence interval                         |
| <b>C.R.P.</b>  | C. reactive protein                         |
| <b>CLp</b>     | Cardiolipin                                 |
| <b>CRHD</b>    | Chronic rheumatic heart disease             |
| <b>E.S.R</b>   | Erythrocyte sedimentation rate              |
| <b>GAS</b>     | Group A streptococci                        |
| <b>G.C.S</b>   | Group C streptococci                        |
| <b>G.G.S</b>   | Group G streptococci                        |
| <b>IL</b>      | Interleukin                                 |
| <b>LA</b>      | Left atrium                                 |



---

---

|             |                          |
|-------------|--------------------------|
| <b>LAP</b>  | Long acting penicillin   |
| <b>LV</b>   | Left ventricle           |
| <b>M.R.</b> | Mitral Regurgitation.    |
| <b>M.S.</b> | Mitral stenosis          |
| <b>MPA</b>  | Main pulmonary artery    |
| <b>NK</b>   | Natural killer cells     |
| <b>OR</b>   | Odd's ratio              |
| <b>OS</b>   | Opening snap             |
| <b>RF</b>   | Rheumatic fever          |
| <b>RHD</b>  | Rheumatic heart disease  |
| <b>RV</b>   | Right ventricle          |
| <b>SEL</b>  | Socioeconomic Level      |
| <b>T.R.</b> | Tricusped Regurgitation. |



## **LIST OF TABLES**

| <b>No.</b>         | <b>Title</b>  | <b>Page</b> |
|--------------------|---|-------------|
| <b>Table (1):</b>  | Cross reactions between streptococcal and cardiac antigens.   |             |
| <b>Table (2):</b>  | Cross-Reactivity in ARF: Human Tissues and its Respective Group A Streptococcal GAS Component Sharing Common Epitopes |             |
| <b>Table (3):</b>  | Reported prevalence of RHD in Egypt, 1956-1994.   |             |
| <b>Table (4):</b>  | Possible reasons for variability in reporting RHD prevalence in Egypt.  |             |
| <b>Table (5):</b>  | Selected indicators reflecting RF/RHD estimated magnitude in Egypt (1990s).   |             |
| <b>Table (6):</b>  | Estimated costs of RHD management (in L.E.).  |             |
| <b>Table (7):</b>  | Pathogenesis of RF, GAS.  |             |
| <b>Table (8):</b>  | Extracellular products of streptococci.   |             |
| <b>Table (9):</b>  | Immunologic phases in the pathogenesis of RF and RHD.   |             |
| <b>Table (10):</b> | Guidelines for diagnosis of initial attack of RF.   |             |
| <b>Table (11):</b> | The many faces of ARF: Possible features.   |             |
| <b>Table (12):</b> | Clinical manifestations of carditis in ARF.   |             |
| <b>Table (13):</b> | Simplified schema for the diagnosis of acute rheumatic carditis.  |             |
| <b>Table (14):</b> | Differential diagnosis of ARF.  |             |
| <b>Table (15):</b> | Clinical diseases associated with antiphospholipid protein antibodies.  |             |
| <b>Table (!6):</b> | Controlling GAS infections for primary prevention of RF.  |             |
| <b>Table (17):</b> | Requirements for the implementation nation wide penicillin prophylaxis programs.                                      |             |





|                    |  |  |
|--------------------|--|--|
| <b>Table (18):</b> | Secondary prevention of RF.  |  |
| <b>Table (19)</b>  | Duration of secondary RF prophylaxis.  |  |
| <b>Table (20):</b> | Mortality rate of RHD.   |  |
| <b>Table (21):</b> | Characteristics of the studied patients  |  |
| <b>Table (22)</b>  | Comparison of medical and surgical patients regarding their characteristics  |  |
| <b>Table (23):</b> | Incidence of recurrence of RF fever in the studied patients  |  |
| <b>Table (24):</b> | Factors associated with recurrence of RF   |  |
| <b>Table (25):</b> | Multivariate logistic regression of predictor factors for RF recurrence  |  |
| <b>Table (26):</b> | Clinical presentation of recurrence of RF according to Jones criteria  |  |
| <b>Table (27):</b> | Correlation between recurrence of RF and valvular lesions laboratory investigation echocardiography and LAP  |  |
| <b>Table (28):</b> | Comparison between recurrent rheumatic fever patients and non-recurrent patients in relation to psychological troubles and normal behavior and psychosocial stress |  |



## **LIST OF FIGURES**

| <b>No.</b>        | <b>Title</b>   | <b>Page</b> |
|-------------------|--|-------------|
| <b>Fig. (1):</b>  | The components of streptococcal cell and its cross reactions with various mammalian tissue components. |             |
| <b>Fig. (2):</b>  | Streptococcal cell structure.  |             |
| <b>Fig. (3):</b>  | Normal structure of the valve.   |             |
| <b>Fig. (4):</b>  | Structure of M-protein.  |             |
| <b>Fig. (5):</b>  | Factors implicated in RF incidence.  |             |
| <b>Fig. (6):</b>  | The pathogenic sequence and key morphologic features of rheumatic heart disease.                       |             |
| <b>Fig. (7):</b>  | Immunopathogenesis of RF and rheumatic carditis.   |             |
| <b>Fig. (8):</b>  | The immunological effectors in RHD.  |             |
| <b>Fig. (9):</b>  | Outlines of the pathogenesis of ARF.   |             |
| <b>Fig. (10):</b> | Simplified Schematic of the pathogenesis of RF & RHD   |             |
| <b>Fig. (11):</b> | Typical Aschoff nodule.  |             |
| <b>Fig. (12):</b> | Rheumatic vegetations.   |             |
| <b>Fig. (13):</b> | Acute rheumatic endocarditis   |             |
| <b>Fig. (14):</b> | Acute and CRHD.  |             |
| <b>Fig. (15):</b> | Forms of vegetative endocarditis.  |             |
| <b>Fig. (16):</b> | Rheumatic fever arthritis.   |             |
| <b>Fig. (17):</b> | The clinical association among the major feature of GABHS pharyngitis.                                 |             |
| <b>Fig. (18):</b> | The occurrence of each of the major manifestations.  |             |
| <b>Fig. (19):</b> | Rheumatic chorea   |             |
| <b>Fig. (20):</b> | Basal ganglia  |             |
| <b>Fig. (21):</b> | Stratum  |             |
| <b>Fig. (22):</b> | Erythema marginatum  |             |



|                   |  |  |
|-------------------|--|--|
| <b>Fig. (23):</b> | The subcutaneous nodules.  |  |
| <b>Fig. (24):</b> | Cardiac size by chest X-ray.   |  |
| <b>Fig. (25):</b> | The diastolic frame shows a normal aortic valve (closed).                  |  |
| <b>Fig. (26):</b> | Apical 4 chamber view by echocardiography                                  |  |
| <b>Fig. (27):</b> | Production of interleukin 2.   |  |
| <b>Fig. (28):</b> | Age distribution of rheumatic fever patients by recurrence                 |  |
| <b>Fig.(29):</b>  | Sex distribution of rheumatic fever patients by recurrence                 |  |
| <b>Fig. (30):</b> | Socioeconomic level of rheumatic fever patients by recurrence              |  |
| <b>Fig. (31):</b> | Family history of rheumatic fever by recurrence                            |  |
| <b>Fig. (32):</b> | History of tonsillectomy by recurrence                                     |  |
| <b>Fig. (33):</b> | Long acting penicillin intake among rheumatic fever patients by recurrence |  |
| <b>Fig. (34):</b> | Psychiatric troubles among rheumatic fever patients by recurrence          |  |
| <b>Fig. (35):</b> | Type of treatment of rheumatic fever patients and recurrence               |  |
| <b>Fjg. (36):</b> | Agglutination Test of CRP  |  |



# CONTENTS

| Title  | Page       |
|--|------------|
| <b>LIST of ABBREVIATIONS.....</b>            | <b>I</b>   |
| <b>LIST of TABLES &amp; FIGURES.....</b>     | <b>III</b> |
| <b>INTRODUCTION.....</b>                     | <b>1</b>   |
| <b>AIM OF THE STUDY.....</b>                 | <b>5</b>   |
| <b>REVIEW OF LITERATURE.....</b>             | <b>7</b>   |
| A) ARF.....                                  | 7          |
| - Definition.....                            | 7          |
| - Etiology.....                              | 7          |
| - Epidemiology.....                          | 21         |
| - Pathogenesis.....                          | 36         |
| - Pathology.....                             | 53         |
| - Clinical Manifestations and Diagnosis..... | 61         |
| - Differential Diagnosis.....                | 99         |
| - Treatment.....                             | 112        |
| - Prevention.....                            | 118        |
| - Recurrence of RF .....                     | 128        |
| - Surgery of RHD.....                        | 134        |
| - Psychosocial effect of RF.....             | 136        |
| - Complications.....                         | 139        |



|                                     |     |
|-------------------------------------|-----|
| - Course and prognosis.....         | 146 |
| - B) CRHD:.....                     | 150 |
| - Mitral Regurgitation.....         | 151 |
| - Mitral Stenosis.....              | 158 |
| - Aortic Regurgitation.....         | 167 |
| - Aortic Stenosis.....              | 172 |
| - Tricusped Valve Disease.....      | 178 |
| - Pulmonary Valve Disease.....      | 178 |
| - <b>PATIENTS AND METHODS</b> ..... | 179 |
| - <b>RESULTS</b> .....              | 191 |
| - <b>DISCUSSION</b> .....           | 215 |
| - <b>CONCLUSIONS</b> .....          | 245 |
| - <b>RECOMMENDATIONS</b> .....      | 247 |
| - <b>SUMMARY</b> .....              | 249 |
| - <b>REFERENCES</b> .....           | 253 |
| - <b>APPENDIX</b> .....             | 279 |
| - <b>ARABIC SUMMARY</b> .....       | 1   |



### **AIM OF THE STUDY**

The aims of this study are as follows:

1. Determining the risk factors causing the recurrence of rheumatic fever during prophylaxis with benzathine penicillin G and postoperative valve procedure.
2. Identifying the possible associating social and psychological repercussions of such conditions.



## **INTRODUCTION**

The first step in the sequence leading to RF is streptococcal pharyngitis. The association of a sore throat with RF was described by Cheadle over 100 years ago. In 1900 Poynton and Payne reported that RF was caused by "a dispiostreptococcus that entered the body by way of the tonsils." Combs in 1924, also attributed RF to this streptococcus rheumatics" of Poynton, noting that, the reaction was proliferative and not "suppurative". Clinicians recognized for years that RF, followed epidemics of scarlet fever. The etiology became better defined during the early 1930s when Dr. Rebecca Lancefield defined, the subgroups of streptococci based on the carbohydrate moieties in the cell wall. GAS was then recognized as the most significant human pathogen, (*McCarty and Lanceflele, 1955*). Epidemiological studies by Collis, in England, and Coburn, in the United States, during the 1930s confirmed the close relationship between streptococcal pharyngitis and the development of RF. During World War II studies by (*Rammelkamp et al 1952*), demonstrated that RF could be prevented by treating streptococcal pharyngitis with penicillin. These investigations provided the final