



Pattern of Rheumatic Fever in Egyptian Children Younger Than 5 Years

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Authors' contributions

This work was carried out in collaboration between all authors. Author LAI designed the study, wrote the protocol, and wrote the first draft of the manuscript, managed the analyses of the study. Author s AMF and HSH managed the analyses of the study, review the manuscript. Author HSH and Author WAA managed the literature searches. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aims: Acute rheumatic fever (ARF) is common between 5-15 years, uncommon with different presentation 25 in children below 5 years. The aim of this study is to assess the frequency and characterize the pattern of 26 presentation of rheumatic fever (RF) in Egyptian children younger than 5 years.

Study Design: Retrospective study.

Place and Duration of the Study: Pediatric department, cardiology division, Cairo University Children's Hospital, 5 years follow up.

Methodology: We retrospectively reviewed the pre-completed data of 766 patients following up in the rheumatic fever clinic. Those with incomplete medical records were excluded. We compared between children younger than 5 years and those who are 5 years or older as regards their demographic data, clinical presentations, laboratory findings and echocardiographic findings.

Results: We enrolled 667 patients; 17 of them (2.5%) were younger than 5 years (mean age $3.82 \pm$ SD 0.393 years). The group of patients younger than 5 years old; included 10 females (58.8%) and 7 males (41.2%). Positive family history was encountered in 6 patients (37.7%). The most common presentations of the younger age group of patients were arthritis in 12 patients (70.5%), followed by carditis in 5 patients (29.4%), chorea in 3 patients (17.6%), and skin manifestations in 2 patients in the form of erythema marginatum (11.7%). Subclinical carditis was more common in younger children than the

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older group, with more severe valve affection. None of the patients in the younger age group had recurrence of the RF during a period of 5 years follow up while recurrences were encountered in 16 patients (2.5%) of the older age group.

Conclusion: ARF can occur in children younger than 5 years. The possibility of rheumatic fever should be adequately investigated in those young children presenting with arthritis, chorea, or skin rash especially in developing countries like Egypt. Echocardiography is an essential tool to diagnose cases with subclinical carditis.

Keywords: Rheumatic fever; pattern; children; <5 years.

1. INTRODUCTION

Rheumatic fever (RF) which is considered to be a delayed autoimmune reaction in genetically predisposed individuals to group A beta hemolytic streptococci remains a major health problem especially in developing countries like Egypt [1]. Acute rheumatic fever (ARF) is still an important cause of death in childhood, and chronic cardiac disease is the major cause of acquired heart disease in adolescents and young adults, besides being an important cause for valvular surgery [2]. ARF is common between 5-15 years, and reported to be uncommon with a different presentation in children below 5 years [3,4,5]. The aim of this study was to detect the frequency and to characterize the pattern of RF presentation in Egyptian children younger than 5 years.

2. PATIENTS AND METHODS

2.1 Patients

We conducted a retrospective study on the patients diagnosed with ARF/RHD and following up in the RF clinic at Cairo University Children's Hospital. We included the data of 667 patients diagnosed with RHD according to the WHO guidelines [6]. Patients included either initially presented to the clinic between 2007 and 2012 during an attack of ARF or were referred for follow up in the clinic after resolution of the acute attack.

A case of acute rheumatic fever was diagnosed based on recognition of major and minor criteria supported by evidence of preceding streptococcal infection according to modified Jones criteria. Acute carditis usually presents clinically by disproportionate sinus tachycardia, diminished 1st heart sound, prolonged PR interval, and there may possibly be an apical holosystolic murmur with or without a mid-diastolic flow murmur (Carey Coombs murmur), or an early diastolic murmur at the base of the heart (aortic regurgitation), there may also be chest pain and pericardial rub due to underlying pericarditis [7]. Patients presenting with insidious onset carditis were diagnosed to have rheumatic fever, after exclusion of other causes of carditis, even in the absence of preceding evidence of group A streptococcal infection according to WHO guidelines [6], cases presenting for the first time with chronic valve lesions of RHD do not require any other criteria to be diagnosed as having RHD depending on the WHO guidelines [6].

Patients with incomplete medical records (109 patients), concerning the demographic data, clinical presentation or the echocardiographic examination, were excluded. The institutional research committee approval was obtained.

2.2 Methods

We manually reviewed the pre-completed files of all the included patients in order to record the demographic data (age, age at presentation, sex, residence according to the governorates and family history of rheumatic fever in a first degree relative), the results of history taking and clinical examination on admission or initial presentation, the laboratory investigations in the form of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and antistreptolysin O titer (ASOT) as well as the echocardiographic findings.

Echocardiographic examination was performed using Siemens' Acuson Cypress echo machine with a 3VC2 probe for all the patients on their initial presentation to the RF clinic as well as on the follow up visits to assess valve lesions, the systolic function of the ventricles, to detect chamber enlargement and the presence of a pericardial effusion. This was done even in the absence of clinical manifestations of carditis. For a diagnosis of abnormal regurgitation, both the color and Doppler signals must be holodiastolic for aortic regurgitation, or holosystolic for mitral regurgitation. The Doppler signal must be of high velocity, either from a pulsed or continuous wave (a mosaic color jet with a peak velocity ≥ 2.5 m/s) [8]. Some authors have suggested that a minimal jet length of 1cm seen in at least two planes supports pathological regurgitation [9].

MR jet was considered pathological if: regurgitate jet extends in the left atrium more than 1 cm, posterolateral color jet with mosaic pattern, identification of the jet in at least 2 planes, holosystolic regurgitate jet, with velocity > 2.5 mm/sec by pulsed wave or continuous Doppler, pathological AR jet is identified if: it appears in 2 planes, holodiastolic regurgitate jet, with peak velocity > 2.5 mm/sec [2]. Sub clinical carditis was diagnosed when clinical examination is normal but echocardiogram is abnormal [10].

Based on color flow Doppler mapping, it has been suggested that the severity of mitral and aortic valvular regurgitation may be classified into a six-point scale as follows [9]:

- 0 : Nil, including physiological or trivial regurgitation jet < 1.0 cm, narrow, small, of 98 short duration, early systolic at mitral valve or early diastolic at aortic valve.
- 0+ : Very mild regurgitation jet, more than 1.0 cm, wider, localized immediately above or below the valve, throughout systole at the mitral valve or diastole at the aortic valve (clinically, no murmur audible).
- 1+ : Mild regurgitation jet.
- 2+ : Moderate regurgitation jet, longer and at a wider area.
- 3+ : Moderately severe regurgitation jet, reaching the entire left Atrium (mitral regurgitation) or left ventricle (aortic regurgitation).
- 4+ : Severe regurgitation jet, diffusely into the enlarged left atrium, with systolic backward flow into pulmonary veins (mitral valve); markedly enlarged left ventricle filled with regurgitation jets (aortic valve).

The medical records were also reviewed for the type of secondary prophylaxis taken by the patients (whether long acting penicillin or oral erythromycin), compliance with secondary prophylaxis (missing one dose was defined as poor compliance), and the incidence of recurrence of rheumatic fever attacks. Patients were classified into 2 groups according to their age of presentation; group (1) younger than 5 years and group (2) who were 5 years and older.

3. STATISTICAL ANALYSIS

Data were statistically described in terms of mean standard deviation (SD), and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student *t* test for independent samples. For comparing categorical data, Chi square [2] test was performed. Exact test was used instead when the expected frequency is less than 5. Correlation between various variables was done using Spearman rank correlation equation. *P* values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

4. RESULTS

The total number of reviewed patients' records was 776. After exclusion of those with incomplete medical records (109 patients), the total number of enrolled patients was 667. Those who were younger than 5 years at the age of presentation were 17 patients (2.5%) with a mean \pm SD of 3.82 ± 0.393 125 years. The youngest child was 2 years old at presentation, they were 7 males (41.2%) and 10 females (58.8%). The age range of the older age group was 5-19 years. The sex distribution was similar in the older age group where females were more predisposed 354 (54.5%). The positive family history in first degree relatives was detected in 6 patients (37.7%) while in the older age group it was found in 154 patients (25%). Those who were diagnosed with ARF/RHD in our hospital were 11 patients (64.7%) in the younger group and 358 patients (55.9%) in the older age group. The remaining patients were referred to us from other hospitals.

The differences in the presentation between the two groups as regards the major and minor Jones criteria are shown in Table 1. The most common presentations of the younger age group of patients were arthritis in 12 patients (75%), followed by carditis in 5 patients (31.3%), chorea in 3 patients (18.8%), and erythema marginatum in 2 patients (12.5%). Although arthritis, chorea, and skin manifestation were more common among younger children, while clinical carditis was more common among older children, yet these differences were statistically insignificant.

Table 1. Major and minor Jones criteria in 2 groups of patients

	Children<5 years	Children>5 years	<i>p</i> value
Arthritis	12 (70.5%)	405 (62.4%)	.58
Carditis	5 (29.4%)	268 (41.2%)	.29
Chorea	3 (17.6%)	50 (7.7%)	.12
Erythema marginatum	2 (11.7%)	7 (1.1%)	.02
Fever	13 (76.5%)	383 (58.9%)	.34
Arthralgia	5 (29.4%)	300 (46.2%)	.38
High ESR,CRP	8 (47.1%)	247 (38.1%)	.30
High ASOT	6 (35.3%)	305 (46.9%)	.62

The differences in echocardiographic findings between the 2 groups are shown in Table 2. Mitral valve lesions were the only valve affections detected in the younger age group. Although moderate to severe mitral regurgitation (MR) was more common in the younger

age group than the older group still it was statistically insignificant. No aortic valve affection was detected in this group.

Table 2. Echocardiographic data of 2 groups of patients

	Children<5 years	Children>5 years	<i>p value</i>
Mitral valve prolapse	3 (20%)	187(63.3%)	.42
Mild MR	5 (33.3%)	276 (53.3%)	.24
Moderate to severe MR	3 (20%)	78 (15.1%)	.23
Mitral stenosis	0	17 (3.3%)	.002
Aortic stenosis	0	3 (0.6%)	.77
Aortic regurge	0	165 (31%)	.14

In our study, subclinical carditis was found in 6 patients (35.5%) of the younger 159 group but in 127 patients (19.7%) in the older group, those patients were presenting to the clinic by either by rheumatic arthritis, chorea, or minor criteria of ARF with evidence of preceding streptococcal infection.

Most of the younger age group patients, 15 children (93.8%) were on long acting penicillin for secondary prophylaxis, with good compliance in 12 patients (70.5%). None of the patients in the younger age group had recurrence while in the older group 16 patients (2.5%) patients had recurrence.

5. DISCUSSION

In developing countries (like Egypt), ARF and RHD are still leading causes of cardiovascular morbidity and mortality [1]. Although the disease is more frequent between 5-15 years, still it can occur in the younger age < 5 years [2]. In our study, we found that 2.5% of the children with rheumatic fever were less than 5 years old. Other studies reported a similar percent [11] while others reported more cases [4], probably due to the longer duration of their study. The variability in the reported incidence may be as well attributed to the difference in the geographical distribution and socioeconomic level. The high positive family history in the younger age group compared to the older children supports the role of genetic predisposition in the pathogenesis of rheumatic fever. The positive family history or sharing the same environmental variables might add to the increase number of affected persons in family members. In this study, the younger children presented more with arthritis, chorea and skin manifestations (erythema marginatum) than the older group which was in accordance with other studies [4]. Others reported that none of their patients below 5 years presented with chorea [11]. The difference in clinical presentations between the different studies can be explained by the varied awareness of the populations to seek medical advice especially where the disease is endemic and the increased alertness of the pediatricians to suspect disease in children < 5 years. The higher presentation with skin manifestations may be due to the higher probability of detecting the rash by the parents during bathing or dressing the younger children as compared to older children, who are independent, since the rash is asymptomatic. Carditis with moderate to severe mitral valve affection was more common in the younger children compared to older group, this was similar to previous studies [4,12] that reported a greater severity of cardiac affection in younger children, this is particularly important since the severity of the cardiac involvement initially, is a risk factor for the development of chronic heart disease [13] however it was statistically insignificant in our study probably due to small number of patients. Echocardiographic evidence of subclinical

carditis was common in younger children. The same was reported in other studies [10,14,15] underlying the importance of echocardiography in the diagnosis of ARF in children < 5years as many cases may pass unnoticed in childhood with development of chronic valvular affection later on [16].

In this study, there was no recurrence in the younger children compared to 2.5% recurrences in the children > 5years. This is unlike others stating increased risk of RF recurrence in younger children [4]. This is probably due to the adequate secondary prophylaxis among our patients. Our study was limited by the short duration of follow up which was around 5 years. The other limitation was the incomplete medical records of many patients which forced us to exclude their data from the study.

6. CONCLUSION

Acute rheumatic fever although common between 5 and 15 years, still it can occur in children younger than 5 years. Carditis if present is associated with more severe valve affection mostly the mitral valve. So, in developing countries like Egypt where rheumatic fever is endemic, the possibility of rheumatic fever should be adequately investigated in children younger than 5 years presenting with arthritis, carditis, chorea, or skin rash utilizing as well echocardiography to detect subclinical cases which may progress to chronic heart disease later on. It is as well an essential tool to diagnose cases with subclinical carditis.

An accurate, complete registry of patients diagnosed with ARF/RHD and their follow up is essential. Long term follow-up is necessary to determine the outcome for young children with subclinical echocardiographic evidence of valvular disease.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

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COMPETING INTERESTS

The authors have no competing interests of sources of funding to disclose.

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