

# Acute rheumatic fever in Jordanian children

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## الحمى الروماتيزمية الحادة في الأطفال الأردنيين

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**الخلاصة:** تعتبر الحمى الروماتيزمية مشكلة صحية هامة في الأردن، وقد استعرضنا بشكل استعادي الملفات الطبية لـ 28 فتى و22 فتاة، عمرهم الوسطي عند مراجعتهم الطبية  $10.5 \pm 2.6$  سنوات، وكان التشخيص المؤكد مبنياً على المعايير المعدلة لجونز، وتمت الدراسة في معهد الملكة علياء للقلب في الفترة بين شباط/فبراير 1999 وشباط/فبراير 2002. وكان أكثر المظاهر التي دفعت المرضى لمراجعة المعهد هو التهاب المفاصل في 88% من الحالات، أو التهاب المفاصل المتنقل في 68% من الحالات، في حين كان المظهر الثاني من حيث الشبوع هو التهاب القلب الذي لوحظ في 48% من الحالات وكان في 8% من الحالات صامتاً، ثم داء الرقص الذي لوحظ في 6% من الحالات. ولم تترافق أي حالة بعقيدات تحت الجلد أو بحمامى هامشية. وكان أكثر صمامات القلب تأثراً هو الصمام المترالي (80%) ثم إصابة مشتركة للصمامين المترالي والأبهر في 25% من الحالات، في حين شوهد التهاب التأمور في 12.5% من الحالات، وفشل القلب الاحتقاني في 4% من الحالات. وعلى هذا فإنه ينبغي على الأطباء الممارسين الانتباه إلى المظاهر السريرية الواسعة الاختلاف مع التأكيد على الالتزام الدقيق بالدلائل الإرشادية الوقائية.

**ABSTRACT** Rheumatic fever remains a significant health problem in Jordan. We retrospectively reviewed medical charts of 28 boys and 22 girls (mean age at presentation  $10.5 \pm 2.6$  years) with confirmed diagnosis based on modified Jones criteria at Queen Alia Heart Institute from February 1999 to February 2002. Arthritis was the commonest major manifestation (88%; 68% migratory), carditis was second commonest (48%; 8% silent carditis) and chorea was seen in 6%. None had subcutaneous nodules or erythema marginatum. The mitral valve was most commonly affected (80%); both mitral and aortic valves were affected in 25%. Pericarditis was seen in 12.5% and acute congestive heart failure in 4%. Practitioners should be aware of diverse clinical presentations and emphasize strict adherence to prophylaxis guidelines.

## Le rhumatisme articulaire aigu chez des enfants jordaniens

**RESUME** Le rhumatisme articulaire demeure un important problème de santé en Jordanie. Nous avons procédé à une étude rétrospective des dossiers médicaux de 28 garçons et 22 filles (âge moyen lors de la survenue  $10,5 \pm 2,6$  ans), chez lesquels le diagnostic avait été confirmé sur la base des critères de Jones révisés, à l'Institut cardiologique de la reine Alia de février 1999 à février 2002. L'arthrite était la manifestation majeure la plus fréquente (88 % ; 68 % migratrice) suivie par la cardite (48 % ; 8 % cardite silencieuse) et la chorée était observée chez 6 % des patients. Aucun n'avait de nodules sous-cutanés ou d'érythème marginé. La valve mitrale était le plus fréquemment atteinte (80 %) ; les valves mitrales et aortiques étaient toutes deux atteintes chez 25 % des sujets. Une péricardite était observée chez 12,5 % et une insuffisance cardiaque congestive aiguë chez 4 % des sujets. Les praticiens devraient connaître les diverses présentations cliniques et souligner l'importance du respect strict des directives pour la prophylaxie.

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## Introduction

Acute rheumatic fever is a common and serious public health problem in developing countries [1,2]. At the end of the 20th century, after an apparent decline, acute rheumatic fever constitutes a great challenge to industrialized and developing countries [3–6]. In the 1980s and early 1990s when many clinicians were hoping that it was a disease of the past, anxieties were renewed when outbreaks were reported in several areas around the United States [7].

Rheumatic valvular heart disease, an important sequel to rheumatic fever, is the most common acquired heart disease worldwide and is the major cause of cardiovascular death during the first 5 decades of life in developing countries [2,8,9].

Rheumatic valvular heart diseases are associated with severe, incapacitating haemodynamic disturbances in young adults and children [1,10]. Many patients are seen with established rheumatic heart disease at their first visit [10]. Acute rheumatic fever can mimic many other diseases and because the diagnosis is based on clinical criteria, it is still under-diagnosed or over-diagnosed in different settings [3]. Prevention of chronic rheumatic heart disease is feasible and cost effective if secondary prophylaxis is started and maintained regularly [11,12].

These facts emphasize the importance of accurate diagnosis, prompt treatment and secondary prophylaxis. In the present study we retrospectively describe the clinical profile of acute rheumatic fever in Jordanian children to increase the awareness of practitioners involved in the health care of young children.

## Methods

Medical charts of children with acute rheumatic fever seen at Queen Alia Heart Insti-

tute between February 1999 and February 2002 were retrospectively reviewed. Data were obtained and where further information was needed the patient was clinically reviewed and/or echocardiography was performed. The age of the study population ranged from 6 to 15 years. Diagnosis of acute rheumatic fever was based on the 1992 update of the Jones criteria [4].

Data obtained included clinical profile and standard laboratory investigations including complete blood count, sedimentation rate, C reactive protein level, antistreptolysin O titre, throat swab culture, chest radiography and electrocardiography.

Cross-section echocardiography and colour Doppler evaluation were performed within 2–3 days of presentation and after 2–3 weeks. Multiple cross-section views were usually taken from parasternal apical and subcostal positions according to the recommendations of the American Society of Echocardiography. Criteria for pathological valvular regurgitation agreed upon by the operators included:

- colour jet seen in at least 2 planes
- mosaic colour jet
- length of the colour jet  $\geq 1$  cm.

## Results

Of the 50 patients in the study, 28 were male and 22 were female (male to female ratio 1.3:1).

The mean age of the study population was  $10.5 \pm 2.6$  years. Arthritis was the most common presenting feature (88% of total) and was migratory in 30 and monoarticular in 14 (68% and 32% respectively of those with arthritis). Carditis with both auscultatory and echo evidence was seen in 24 (48% of total) and silent carditis with no auscultatory findings was seen in 4 (8% of

total). Chorea was seen in 3 patients, with evidence of carditis in 2 patients (Table 1). Cardiac features at presentation and 2–3 weeks later are shown in Table 2.

Table 3 shows results of laboratory investigations. Throat swabs were requested for 20 patients and were positive for group A streptococcus in only 8%. Antistreptolysin O titres ranged from 350–1250 IU with mean (standard deviation) of 520 (320). Erythrocyte sedimentation rate was elevated in 74% with a range of 65–125 mm in the first hour and C reactive protein was positive in 75% with a titre range of 74–104 IU.

## Discussion

Rheumatic fever continues to be a major health problem in developing and industrialized countries, especially since the recent outbreaks that emphasized the need for practitioners to remain vigilant and to maintain prevention efforts [13]. Although the

criteria for diagnosis are well known, the clinical symptoms needed to diagnose do not always appear concurrently and the initial illness may be mild or short-lived and diagnosis may be missed.

The Jones criteria were introduced in 1944 as a set of clinical guidelines for the diagnosis of rheumatic fever [4,14]. The manifestations of rheumatic fever were divided into major and minor categories in the Jones criteria. Major manifestations were least likely to lead to an improper diagnosis and included carditis, joint symptoms, subcutaneous nodules and chorea. History of rheumatic fever or rheumatic heart disease was also a major manifestation. Minor manifestations were suggestive of rheumatic fever, but were not sufficient for diagnosis and included clinical signs such as fever and erythema marginatum and laboratory markers of inflammation. The presence of 2 major or 1 major and 2 minor manifestations provided reasonable evidence of rheumatic activity. However, because previous history of definite rheumatic fever or rheumatic heart disease was a major criterion, the presence of a minor manifestation was sufficient to establish the diagnosis of rheumatic fever recurrence.

To improve specificity, these guidelines have been periodically modified [15–18]. In the first modification [17], objectively identifiable arthritis replaced joint symptoms as a major manifestation and arthralgia was assigned to the category of minor manifestations. History of previous rheumatic fever or rheumatic heart disease was downgraded to the minor category, and therefore, documentation of a major manifestation became necessary for the diagnosis of recurrence of rheumatic fever. Meanwhile, erythema marginatum was recommended as a major criterion. Most importantly, the evidence of preceding

**Table 1 Clinical features of the 28 boys and 22 girls aged 6–15 years with diagnosed acute rheumatic fever**

Features	No.	%
Sex		
Male	28	56
Female	22	44
Arthritis	44	88
Migratory	30	68
Monoarthritis	14	32
Carditis	24	48
Chorea	3	6
Erythema marginatum	0	0
Subcutaneous nodules	0	0

Mean age  $\pm$  standard deviation of the patients = 10.5  $\pm$  2.6 years.

Table 2 **Clinical and echo-Doppler cardiac findings**

Cardiac findings	At presentation		After 2–3 weeks	
	Clinical	2D echo-Doppler	Clinical	2D echo-Doppler
Mitral	18 (75.0)	18 (75.0)	18 (75.0)	18 (75.0)
Mitral and/or aortic	3 (12.5)	5 (21.0)	4 (16.5)	5 (21.0)
Pericarditis	3 (12.5)	3 (12.5)	2 (8.0)	3 (12.5)
Congestive heart failure	1 (4.0)	1 (4.0)	0 (0)	0 (0)

Values given are No. (%) of patients.

group A streptococcal pharyngitis was added to the list of minor manifestations in the modified Jones criteria [17]. Evidence of a prior streptococcal infection was essential for the diagnosis of rheumatic fever in the 1965 revision of Jones criteria and it was suggested that exclusion of clinical syndromes of non-streptococcal origin would further increase the accuracy of the criteria [15]. The increased specificity adversely affected the sensitivity and 25% of the rheumatic fever cases diagnosed by modified criteria could not be diagnosed by revised Jones criteria [15–17]. Such cases usually presented in relatively late phases of the disease or with delayed manifestations of rheumatic fever, when anti-streptococcal antibody titres suggestive of preceding

streptococcal infection had already normalized. Therefore, late manifestations of rheumatic fever were subsequently exempted from the requirement of elevated anti-streptococcal antibody titre [18].

In our study, all patients fulfilled the diagnostic modified Jones criteria [4]. Arthritis was the most frequent manifestation (88%) as has been reported in many studies [13,19]. Migratory arthritis typical of rheumatic arthritis was seen in 68% and monoarticular arthritis was seen in 32% of those with arthritis. The possibility of rheumatic fever should be considered for any patient with monoarticular arthritis; it is not necessary for arthritis to be migratory to consider this diagnostic possibility. Diagnosis of a primary episode of rheumatic cardi-

Table 3 **Laboratory investigations**

Laboratory test	No. (%)	Mean (s)	Range
Positive throat swab culture	2/20 (8)	NA	NA
Elevated antistreptolysin O titre (IU)	41/50 (82)	520 (320)	350–1250
Elevated erythrocyte sedimentation rate (mm/h)	37/50 (74)	55 (43.8)	65–125
Positive C reactive protein (IU)	30/40 (75)	39 (35.5)	74–104

s = standard deviation.

NA = not applicable.

tis is based on presence of significant apical systolic and/or basal diastolic murmurs, clinical presence of pericarditis or unexplained congestive heart failure. With sub-optimal auscultation skills, an echo-Doppler study will quickly determine the presence or absence of a clinically detectable murmur [20,21].

Clinically manifest mitral or aortic regurgitation is still the diagnostic hallmark of acute rheumatic carditis [5,22]. Our findings confirm previous reports that echo-Doppler can detect significant valvular incompetence in the absence of auscultatory finding [23,24]. In our study, 4 patients had silent carditis (8% of total); 2 of the silent carditis cases were evident at presentation and 2 became clinically evident at 2–3 weeks follow-up. The incidence of subclinical carditis was low compared with previous reports in which silent carditis accounted for 30%–50% of cases. Patients may seek medical advice late in the course of the disease when clinical valvular involvement is evident. This agrees with a report from New Zealand where all patients with silent carditis developed an audible murmur within 2 weeks of onset [23,24].

There is a great disparity in the proportion of cases of acute rheumatic fever with chorea between different populations from many industrialized and developing countries [5,25–27]. Chorea manifested in only 6% of our patients, in agreement with reports from Africa, South and East Asia, the Pacific and the Arabian Peninsula, where chorea was reported in less than 15% of all cases of acute rheumatic fever [26]. In studies from the United States of America, Pakistan and Turkey, chorea manifested in higher proportions, i.e. up to 52% of cases [27].

Our patients had neither subcutaneous nodules nor erythema marginatum, similar

to a report from Saudi Arabia where erythema marginatum and subcutaneous nodules were infrequent [19].

Sibling studies have suggested an inherited susceptibility to patterns of acute rheumatic fever [28]. Studies from the USA and the Caribbean have identified a B cell alloantigen (D8/17), present in high percentage of B cells from patients with acute rheumatic fever and their family members [29]. This however was not found among an Indian population with acute rheumatic fever [30]. This may give a clue to the pathogenesis of acute rheumatic fever and may explain how populations may differ in their immune responses to group A streptococcal infections and develop different rates of certain clinical manifestations of acute rheumatic fever.

Laboratory investigations are of great support to the diagnosis, including evidence of streptococcal infection. In our patients, antistreptolysin O titre was substantially higher, as has been reported in another study [31].

Acute phase reactants were significantly elevated in approximately three-quarters of patients with acute rheumatic fever [32].

Increased susceptibility to recurrences of rheumatic fever appears to last into adulthood, therefore, we must optimize the clinical diagnosis procedure and ensure long-term adherence to secondary prophylaxis [33].

Acute rheumatic fever continues to be a major public health problem in Jordan and results in economic burdens and serious health sequelae. Practitioners should be more aware of this health problem, should consider this diagnostic possibility when appropriate and should ensure strict and long-term adherence to secondary prophylaxis.

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