



## Acute Rheumatic Fever in the North East of Iran: A Study of 80 Cases

Eftekhar Mahmudi, MD\*, Farah Ashrafzadeh, MD, Saeed Talebi, MD, Fatemeh Ghaneh, MD, Vahid Jafari, MD

Ghaem Hospital Medical Center, Mashad University of Medical Sciences (MUMS), Mashad, Iran.

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### Abstract

**Background:** To evaluate the frequency, clinical presentation and cardiac involvement of children with RF in the North-East of Iran.

**Methods:** A case series analysis was conducted on 80 patients with acute rheumatic fever (ARF), who were hospitalized at Ghaem hospital in Mashad between 1994 and 2000, were studied. Laboratory tests and results from echocardiographic examinations, and clinical findings were analyzed. All patients received standard care for children with ARF. The  $X^2$  test was used for comparison of binary data.

**Results:** When compared to similar studies from developed countries, our study demonstrates a decreased frequency of RF in North-East Iran over the past few years. However, it is still a major health problem and the most common cause of acquired heart disease in childhood. The distribution of the major modified Jones criteria in our study is slightly different from that described in the literature, with a higher incidence of carditis.

**Conclusion:** It appears that carditis is endemic in this region. Considering the high morbidity and complications involved in this disease, there is an immediate need for effective preventive programs for the initiating cause streptococcal infections, especially since it is treatable.

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### Introduction

In 1994, WHO estimated the annual incidence of Rheumatic Fever/Rheumatic Heart Disease (RF/RHD) as approximately 10 million individuals throughout the world, accounting for 400 000 deaths per year; the majority are from the Asia-Oceania region. It also estimated that the carrier rates of Group A Beta hemolytic streptococcal infection (GABHS) in different regions is 7.5-39% among school age children. This global issue has been the subject of many international studies and has prompted WHO to reintensify its RF/RHD program with the participation of 16 countries from five regions, namely Africa, the Americas, Eastern

Mediterranean, South-East Asia and Western Pacific. The long-term objective of this program is to reduce the morbidity and mortality associated with RF/RHD through primary health care efforts.<sup>1</sup>

Rheumatic fever (RF) is the most common cause of acquired heart disease in children and young adults in developing countries.<sup>2</sup> Although the incidence of ARF has declined in the United States and Western Europe, it has remained high in developing countries.<sup>3-6</sup> Known suspected contributing factors include low socio-economic status, overcrowding, malnutrition,

\*Corresponding Author: Eftekhar Mahmudi, Associate Professor of Pediatric Cardiology, Ghaem Hospital, Mashad, Iran.  
Tel: +98 511 8417451. Fax: +98 511 8417451. E-mail: E-mahmoudi@mums.ac.ir.

and low government health subsidy.<sup>1</sup>

Carditis is the most important and serious manifestation of the disease because it can be lethal or lead to the development of permanent heart disease.<sup>6-9</sup> In order to evaluate the clinical presentation and cardiac involvement of children with RF, we conducted a case series study in children admitted to our hospital with the diagnosis of acute RF from 1994 to 2000.

## Methods

This was a case series analysis conducted on patients less than 16 years of age with the discharge diagnosis of ARF. These patients were admitted to Ghaem hospital, the largest tertiary referral center and a major teaching hospital in Mashad.

All patients were admitted with the diagnosis of ARF. Diagnostic criteria was based on the modified Jones criteria.<sup>2</sup> 63 of the patients (79%) were experiencing their first attack and the remaining 9 cases (11%) were admitted due to disease recurrence.

Eight cases (10%) were suspected to be recurrences, but there was no scientific proof.

Information on sex, age, preceding history of pharyngitis, family history of RF, and demographic distribution of the patients was collected. An initial diagnostic evaluation consisted of a full blood count, erythrocyte sedimentation rate (ESR), C-reactive protein, streptococcal serology, throat and blood cultures, midstream urine, ECG and chest x-ray. M-mode, two-dimensional and color Doppler echocardiography was done for all of patients.

Initial clinical assessment consisted of daily measurements of heart rate (awake and asleep), temperature, joint involvement, and presence or absence of rash, chorea, or nodules. The blood parameters assessed weekly, included: ESR, C-reactive protein, and streptococcal serology. Quiescence of disease activity was ascertained when ESR was below 30 mm/h, joint symptoms disappeared clinically and relief of cardiac disease was assured at serial evaluations. Cardiac evaluation consisted of standard clinical and echocardiograph assessment.

Valvular regurgitation was graded as mild, moderate and severe. Mild regurgitation was considered subclinical but pathological regurgitation. A massive holodiastolic (aortic regurgitation) or holosystolic (mitral regurgitation) color jet in Doppler echocardiography was the criterion for pathological regurgitation. Mitral regurgitation was considered moderate if the jet filled half or less of the left atrium; any amount greater than that accounted as severe. A jet diameter less than 30% of the diameter of the left ventricular outflow was considered moderate while greater amounts were classified as severe aortic insufficiency. On the basis of this grading, about one fourth of the patients had mild, one half had moderate and another one fourth had severe valvular regurgitation.

All patients received standard care for children with ARF. The  $\chi^2$  test was used for comparison of binary data.

## Results

### Population

In this article we have studied Clinical data from 80 patients with ARF, who were hospitalized at Ghaem hospital in Mashad between 1994 and 2000.

There was a slight male predominance (56% of the patients were males). The mean age on hospitalization was  $10.29 \pm 2.55$  years (mean  $\pm$  SD), and ranged from 5 to 16 years. Twenty percent of patients were less than 8 and 80% were less than 12 years of age.

There was a positive family history of RF in 14% of patients. A preceding history of pharyngitis was reported in 78% of the patients.

### Laboratory Findings

The most common laboratory findings were as follows; leukocytosis in 84% of the patients, anemia in 62%, elevated erythrocyte sedimentation rate (ESR) ( $>40$  mm/hr) in 90% and positive C-reactive protein (CRP) in 85% of patients. Anti-streptolysin O (ASO) titers were elevated in 87% of patients. Positive Throat cultures for GABHS infection, scarlet fever and both raised ASOT and positive throat culture was 3.5%, 3.5% and 90.5% respectively.

### Demographic Distribution

Sixty-one percent of the hospitalized patients were from Mashad's urban areas, and the rest were from rural areas. The socioeconomic status of 78 patients (86%) was low. Eighty one percent of patients were in families with 4 to 8 members. Most of our patients (63%) were admitted in winter and spring (figure 1).

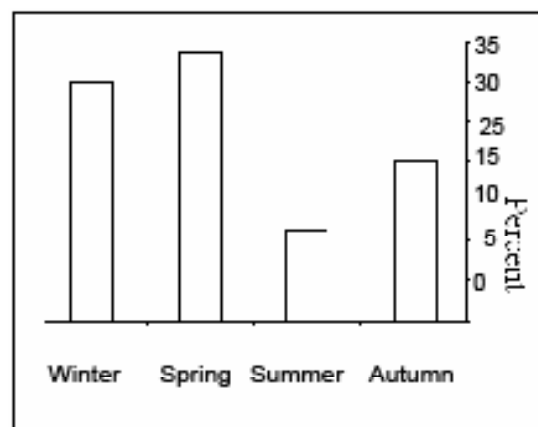


Figure 1: Frequency of patients with acute rheumatic fever in each season

Incubation period was less than 30 days in 85% of patients. The frequency of ARF declined from 19 patients in 1994 to 5 patients in the year 2000 (figure 2).

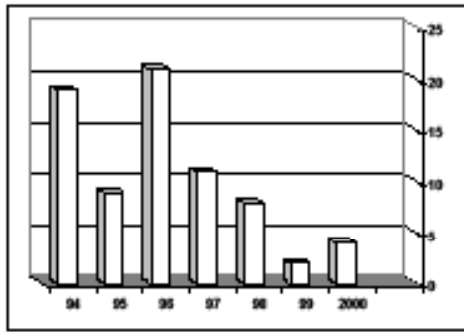


Figure 2: Frequency of acute rheumatic fever in mashad between 1994-2000

### **Jones Criteria**

Carditis occurred in 81%, Arthritis in 69%, Sydenham's chorea in 8%, and erythema marginatum in 3% of patients. Subcutaneous nodules were present only in one patient. Fever occurred in 71% and arthralgia in 76% of patients.

### **Cardiac Manifestations**

Valvulitis occurred in 80% of patients with cardiac involvement. MR was the most common presentation of valvulitis (75%). Aortic insufficiency was seen in 13% of patients. Tricuspid insufficiency and Mitral stenosis developed in 1.3% and 5% of patients respectively. Carditis, valvulitis and cardiomegaly was significantly more common in female patients ( $p=0.03$ ,  $p=0.01$ ,  $p=0.02$  and  $p=0.04$  respectively). Pericardial effusion occurred in 2.5% of patients. Acute congestive heart failure (CHF) on first presentation occurred in 5% of patients.

### **ECG & X-Ray findings**

The least prevalent minor criteria was prolonged P-R interval which was seen in 15% of the studied population; the most common ECG finding was sinus tachycardia (50%). ST and T changes were seen in 2.5% and 1.3% of patients respectively. The most common X-Ray findings were cardiomegaly (37%). Atrial enlargement was seen in 16.5% of patients.

### **Medical Treatment**

Non-steroidal anti-inflammatory therapy was used in 86% of cases. Steroid was used for 42% and digoxin for 11% of patients with carditis.

### **Discussion**

Ironically, in many instances, the first attack of RF is highly treatable with primary prophylaxis and the recurrences with

valvular damage are highly preventable by adherence to secondary prophylaxis.

Unfortunately, preventive programs for eradicating GABHS are beyond the realm of many healthcare systems. In underdeveloped countries, the prevalence rate of RF/RHD remains an unacceptably high 12.6 cases per 1000 school children in Zambia, 10.2 cases per 1000 school children in Sudan, and 7.9 cases per 1000 school children in Bolivia.<sup>10</sup>

WHO estimation reveals that therapy of 1000 sore throats prevents a single case of RF. In Asia, with the exception of industrialized countries like Japan and Singapore, RF and RHD continues to drain human and government resources with millions of dollars in secondary prevention. Thus RF/RHD continues to be one of the health priorities in countries with limited resources.<sup>1</sup>

When our study was compared to the reported series of RF in the literature, there were both similarities and differences.<sup>3,6-8,11-13</sup> When compared to similar studies from developed countries, our study showed that the frequency of RF has decreased in recent years in North East of IRAN probably due to earlier diagnosis and treatment of streptococcal pharyngitis. The age of hospitalized patients (10.3+2.5 years) was similar to the Lebanon study (11.1+2.9 years).<sup>14</sup> The gender predominance was also the same (slight male predominance). The majority of our patients came from large low-income families. 81% of patients belonged to large families with 4-8 members. Most of our patients were from Mashad and its peripheral areas (that are relatively urban areas), which is probably a referral bias. About 50% of our patients were from poor socio-economic conditions (workers and farmers). This finding highlights the need for an urgent control program and early detection and treatment of streptococcal infections in this group. Most of our patients (63%) were admitted in winter and spring, probably due to higher streptococcal infections of upper respiratory tract. About 44% of our patients had a history of antibiotic therapy for pharyngitis before admission.

The incidence of arthritis and carditis were 69% and 81% respectively. Comparison of this study with similarly designed studies<sup>5,15-18</sup> shows that in our study the incidence of carditis is more frequent than arthritis. It seems that carditis may be endemic to the east of Iran, thus rheumatic heart disease prevention programs should remain the central goal. The mitral and aortic valve involvement in this study (MR in 75% and AI in 13%) were comparable to that reported in the literature.<sup>5,15,17,19,20</sup> MR, valvulitis and increased PR interval were significantly and indefensibly more common in female gender ( $p$  value < 0.05).

### **Conclusion**

Due to the established high morbidity and severe complications of ARF, this study reaffirms the need for



effective preventive programs for streptococcal infections, especially since this cause is treatable. Public health education by all available media especially through video films is also recommended. Although the incidence of ARF is declining in comparison to previous years, this study showed that ARF is endemic in this area. This study confirmed that the incidence of ARF is high in low socio-economic groups and highlights the need for an urgent control program. Greater effort should be made in the early detection and treatment of streptococcal infections.

## References

1. Asuncion AR. Rheumatic fever and rheumatic heart disease in Asia: a global concern. *Prog Pediatr Cardiol* 1998;9:53-54.
2. Dajani AS, Ayoub E, Bierman FZ, Bisno AL, Denny FW, Durack DT, Ferrieri P, Freed M, Gerber M, Kaplan EL, Karchner AW, Markowitz M, Rahimtoola SH, Shulman ST, Stollerman G, Takahashi M, Taranta A, Taubert KA, Wilson W. Guidelines for the diagnosis of rheumatic fever: Jones criteria updates 1992. *Circulation* 1993;87:302-8.
3. Grover A, Dhawan A, Iyengar SD, Anand IS, Wahi PL, Ganguly NK. Epidemiology of rheumatic fever and rheumatic heart disease in a rural community in northern India. *Bull World Health Organ* 1993;71:59-66.
4. Ibrahim Khalil S, Elhag M, Ali E, Mahgoub F, Hakiem S, Omer N, Shafie S, Mahgoub E. An epidemiological survey of rheumatic fever and rheumatic heart disease in Sahafa Town, Sudan. *J Epidemiol Community Health* 1992;46:477-479.
5. Karademir S, Demircen F, Atalay S, Atalay S, Demircin G, Sipahi T, Tezic T. Acute rheumatic fever in children in the Ankara area in 1990-1992 and comparison with a previous study in 1980-1989. *Acta Pediatr* 1994;83:862-865.
6. Majeed HA, Batnager S, Yousof AM, Khuffash F, Yusuf AR. Acute rheumatic fever and the evolution of rheumatic heart disease: a prospective 12 years follow-up report. *J Clin Epidemiol* 1992;45:871-875.
7. Barlow JB, Marcus RH, Pocock WA, Barlow CW, Essop R, Sareli P. Mechanisms and management of heart failure in active rheumatic carditis. *S Afr Med J* 1990;78:181-186.
8. Marcus RH, Sareli P, Pocock WA, Barlow JB. The spectrum of severe rheumatic mitral valve disease in a developing country. Correlation among clinical presentation, surgical pathologic, and hemodynamic sequelae. *Ann Intern Med* 1994;120:177-183.
9. Wu MH, Lue HC, Wang JK, Wu JM. Implication of mitral valve prolapse in children with rheumatic mitral regurgitation. *J Am Coll Cardiol* 1994;23:1199-1203.
10. Hasab AA, Jaffer A, Riyami AM. Rheumatic heart disease among Omani schoolchildren. *Eastern Med Health J* 1997;3:17-23.
11. Ayoub EM. Resurgence of rheumatic fever in the United States. The changing picture of a preventable illness. *Postgrad Med* 1992;92:133-136.
12. Ferguson GW, Shultz JM, Bisno AL. Epidemiology of acute rheumatic fever in a multiethnic, multiracial urban community: the Miami-Dade county experience. *J Infect Dis* 1991;164:720-725.
13. Veasy LG, Tani LY, Hill HR. Persistence of acute rheumatic fever in the inter mountain area of the United States. *J Pediatr* 1994;124:9-16.
14. Bitar F, Hayek P, Obeid M., Gharzeddine W, Mikati M, Dbaibo GS. Rheumatic Fever in Children: A 15-Year Experience in a Developing Country. *Pediatr Cardiol* 2000;21:119-122.
15. al-Eissa YA, al-Zamil FA, al Fadley FA, Al Herbish AS, Al-Mofada SM, Al-Omair AO. Acute rheumatic fever in Saudi Arabia: mild pattern of initial attack. *Pediatr Cardiol* 1993 Mar;14:89-92.
16. Eltohami EA, Hajar HA, Folger GM Jr. Acute rheumatic fever in an Arabian Gulf country--effect of climate, advantageous socioeconomic conditions, and access to medical care. *Angiology*. 1997 Jun;48:481-9.
17. Habib GS, Saliba WR, Mader R. Rheumatic fever in the Nazareth area during the last decade. *Isr Med Assoc J* 2000;2:433-437.
18. Majeed HA, Khan N, Dabbagh M, Najdi K, Khateeb N. Acute rheumatic fever during childhood in Kuwait: the mild nature of the initial attack. *Ann Trop Paediatr* 1981;1:13-20.
19. Vazquez-Antona C, Calderon-Colmenero J, Attie F, Zabal C, Buendia-Hernandez A, Diaz-Medina LH, Bialkowski J, Garcia Arenal F. Rheumatic cardiopathy in children younger than 6 years of age. *Arch Inst Cardiol Mex* 1991;61:143-147.
20. Woo KS, Kong SM, Wai KH. The changing prevalence and pattern of acute rheumatic fever and rheumatic heart disease in Hong Kong (1968-1978). *Aust N Z J Med* 1983;13:151-156.