

## ORIGINAL ARTICLE

# CHANGES IN THE PREVALENCE OF ACUTE RHEUMATIC FEVER IN SOUTHERN IRAN

Gholam-Reza Rezaian MD\*, Shohreh Beheshti MD\*\*, Ali Fereshtehnejad MD

\*Department of Cardiology, \*\*Department of Clinical Pathology,  
Shiraz University of Medical Sciences, Shiraz, Iran

### Abstract

**Background-**Acute rheumatic fever (ARF) and rheumatic heart disease (RHD) are still two major public health problems in Iran. Our objective was to assess the status of acute rheumatic fever in children and adults admitted to four major teaching hospitals during the last 20 years.

**Methods-**The number of annual hospital admissions of patients coded as ARF from March 1979 to March 1998 was obtained from medical records. The diagnosis of ARF was confirmed only if the patients fulfilled the modified Jones Criteria. The presenting signs and symptoms and the annual in-hospital prevalence were determined and the annual incidence per 100,000 cases hospitalized was calculated.

**Results-**There were 675 cases with ARF of which 585 were initial and 90 were recurrent attacks. Female to male ratio was 3:4. The age of the patients was  $15.4 \pm 7.5$  years (mean  $\pm$  SD) with a range of 4 to 78 years. The groups most at risk were children and young adults aged 6 to 20 years (n=364). The major presenting complaints included polyarthritis (92.44%), carditis (57.48%), chorea (4.6%), erythema marginatum (1.9%) and subcutaneous nodules (0.15%). The attack rate was higher between the years 1979 and 1995 and lower thereafter.

**Conclusion-**The changing pattern of the frequency of ARF during the last few years might be attributed to an improvement in the status of education and awareness in the general population, availability of a larger number of physicians in the primary health care settings, especially in rural areas, and earlier diagnosis and treatment of patients suspected with streptococcal pharyngeal infection.

**Keywords** • Acute rheumatic fever • rheumatic heart disease • Iran

### Introduction

At the turn of the 20th century, rheumatic fever had become rare in most industrialized countries such that many physicians have never encountered a case. However, there is still a high rate of acute rheumatic fever (ARF) and rheumatic heart disease (RHD) in the socially and economically disadvantaged countries worldwide.<sup>1</sup> Neither antimicrobial agents nor other public health measures have been totally effective in the control of rheumatic fever.<sup>2</sup> Starting in the 1980s, unexpected scattered outbreaks of ARF among

both adults and children in North America have confirmed the capacity for this potentially serious illness to re-appear and pose a significant public health problem.<sup>3,4</sup> Current estimates suggest that the incidence of rheumatic fever among children in the USA is 0.5 to 3.1 per 100,000 population.<sup>5-7</sup> A similar incidence has been reported from countries in western Europe.<sup>6-8</sup>

In this report, we have assessed the status of acute rheumatic fever in children and adults admitted to four main teaching hospitals during the last 20 years.

### Patients and Methods

The hospital records of all patients with a final diagnosis of ARF in four major teaching hospitals

•Correspondence: G.R. Rezaian MD, Department of Cardiology, Shiraz University of Medical Sciences, Shiraz, Iran. P.O.Box: 71935-1334, Fax: +98-711-629733.

in Shiraz, southern Iran, were reviewed. This included a 20-year, 13-year and 7-year analysis of patients' medical records admitted to Shahid Faghihi, Namazee, Hafiz and Shahid-Dastgheib Hospitals, respectively.

Patients were included only if they fulfilled two major or one major and two minor criteria for the last updated Jones Criteria<sup>9</sup>, associated with supporting evidence of an antecedent streptococcal infection. Carditis was considered to be present when there was clinical evidence of mitral regurgitation, aortic regurgitation or signs of congestive heart failure with supporting evidence on chest radiography, and whenever available, echocardiographic signs of valvular regurgitation, cardiomegaly or pericardial effusion. Patients with chorea were considered as having ARF only after other etiologies were excluded.

A recurrent attack was defined as a new episode of ARF in a patient with previously documented ARF. Suspected cases of recurrence with only the minor criteria were excluded from the study. The presenting signs and symptoms were determined. In addition, the annual number of ARF cases admitted to each hospital (in-hospital prevalence) was determined and the annual incidence per 100,000 hospitalized cases was calculated and trends in the incidence and in-hospital prevalence of ARF were statistically analyzed.

## Results

There were 675 episodes of ARF during this 20-year period, of which 294 (43.6%) were females and 381 (56.4%) were males. There were 585 new cases and 90 recurrences. The patient's

age at the time of diagnosis was  $15.4 \pm 7.5$  years (mean $\pm$ SD). Table 1 shows the frequency of symptoms and signs of ARF in admitted patients.

A history of sore throat before presentation was documented in 88.3% and scarlet fever in 0.3% of the patients. Increased ASO titer was demonstrated in 91% of patients and group hemolytic streptococci were isolated from 19% of throat cultures.

Recurrent episodes occurred in 90 cases. The time interval from previous attacks ranged from 3 months to more than 30 years (median 6.6 years). Penicillin prophylaxis was regularly used 38 cases, irregularly 29 and not at all the remaining 33 patients.

The overall annual in-hospital prevalence of ARF, admitted to our 4 main teaching hospitals between 1994 to 1998, is shown in Figure 1. These data confirm a steady decline in the number of patients with ARF admitted to our hospitals, especially during the last 3 years of the study.

The average incidence of the disease during two consecutive years (1994 and 1995) was 97.5 per 100,000 total hospital admissions. This figure was 28.3 per 100,000 for 3 consecutive subsequent years (1996-1998), which means a more than four-fold decline in the incidence rate during this period ( $p < 0.005$ ).

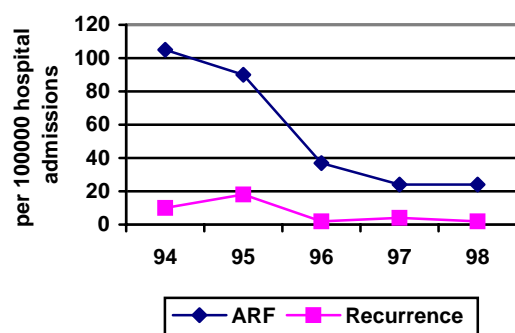
## Discussion

In recent years our medical society has witnessed a significant decline in the annual in-hospital prevalence and incidence of ARF in Fars Province, which includes new as well as recurrent cases. It should be emphasized that although our main teaching hospitals are the major referral

**Table 1.** Clinical manifestations of in-hospital patients with ARF.

	Clinical manifestations	Frequency (%)	Comment
Major criteria	Migratory polyarthritis	642 (92.4)	Mostly involving the knee, hip and wrist
	Carditis	388 (57.5) initial attack	75.6% less frequent in subsequent attacks
	Chorea	31 (4.6)	male/female=1:5
	Erythema marginatum	13 (19)	male/female=3:1
	Subcutaneous nodule	1 (0.15)	----
Minor criteria	Arthralgia	641 (95)	----
	Fever	574 (85)	----
	Elevated ESR*	655 (97)	----
	Positive CPR**	425 (63)	----
	Prolonged P-R interval	108 (16)	----

## Acute Rheumatic Fever in Southern Iran



**Figure 1.** Prevalence of ARF and its recurrence (1994-1998).

centers for acutely ill patients in Fars Province, it is clear that not all patients with ARF had been hospitalized in these centers during the study period. Thus, our data may not represent the actual prevalence and incidence of ARF in this community. Despite this, the decline in the number of patients admitted with ARF during the recent years may be a reflection of a possible decrease in the incidence of the disease in this region.

Several factors can explain the decline in the incidence of ARF. It could be because of a decline in streptococcal infections<sup>10</sup> or a change in the incidence of infections produced by rheumatogenic types in our community. Stollerman<sup>8</sup> suggested that variations in the rheumatogenicity of streptococcal strains could influence the attack rate of ARF.

Current evidence is consistent with a change in the virulence of the streptococcus over time since scarlet fever has become a much milder disease over the last few decades and its incidence has declined.<sup>11</sup> In addition, the incidence of post-streptococcal acute glomerulonephritis has also declined, although not as markedly as that of rheumatic fever.<sup>12</sup> On account of having no adequate epidemiologic data, it is difficult to make such solid statements at present.

Other factors include improved economic standards, enhancement of primary prevention efforts and increased availability of health care. At least part of the decline in ARF must be due to more effective primary health care as well as the increasing number of physicians.<sup>13,14</sup> Primary health care is provided by a network of health centers distributed throughout Iran assuring the availability of health care for a larger number of people especially in rural areas. In addition, the physician to patient ratio has been considerably

increased during the past decade, and more physicians are working in the private sector than before. However, observations derived from recent outbreaks in the USA undermine the significance of these variables. Since most children involved in these outbreaks were from high to middle income families with established access to medical care<sup>15,16</sup>, other causes may have contributed to the decline and resurgence of rheumatic fever in these populations.

It is important to note that host factors have long been recognized as having a role in the risk of rheumatic fever, so the decline in rheumatic fever may be due to some changes in the host.

The in-hospital prevalence of ARF was higher in children and in young adults. The higher risk of rheumatic fever in children has generally been attributed to their greater exposure to streptococcal infections. Streptococci adhere more vigorously to cells of young patients compared with middle-aged subjects.<sup>17</sup> This suggests the possibility that host factors may affect infectivity and rheumatogenicity<sup>18</sup> of this organism.

An important variable that influences the reported incidence of rheumatic fever is the accuracy of diagnosis. There is no specific test to definitely establish the diagnosis of ARF at present. Therefore, it is not unjustified to over-diagnose the present cases of ARF. It is difficult to differentiate a patient with juvenile rheumatoid arthritis from one with ARF without carditis. Only recently, we have come to know that other illnesses such as viral, rickettsial, or mycoplasmal infections can cause myocarditis and that certain types of mitral valve disease can be of congenital and not of rheumatic etiology.<sup>19,20</sup> Use of stricter criteria in the diagnosis of ARF is vital for true assessment of the incidence of this disease.

## References

- 1 Carapetis JR, Currie BJ. Preventing rheumatic heart disease in Australia. *Med J Aust.* 1998; **168**: 428-9.
- 2 Fauci AS, Braunwald E, Isselbacher KJ, et al. *Harrison's Principles of Internal Medicine.* 14th ed. New York: Mc Graw-Hill; 1998.
- 3 Congeni BL. The resurgence of acute rheumatic fever in United States. *Pediatr Ann.* 1992; **21**: 816-20.
- 4 Veasy LG, Tani LY, Hill HR. Persistence of acute rheumatic fever in the intermountain area of the United States. *J Pediatr.* 1994; **124**: 9-16.
- 5 WHO Study Group. Rheumatic fever and rheumatic heart disease. *World Health Organ Tech Rep Ser.* 1988; **764**: 21-5.
- 6 Markowitz M. The decline of rheumatic fever: role

- of medical intervention. *J Pediatr.* 1985; **106**: 545-50.
- 7 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**: 720-5.
  - 8 Stollerman GH. Rheumatogenic group A streptococci and the return of rheumatic fever. *Adv Intern Med.* 1990; **35**: 1-25.
  - 9 Special Writing Group of the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association. Guidelines for the diagnosis of rheumatic fever. Jones criteria, 1992 update. *JAMA.* 1992; **268**: 2069-73.
  - 10 Bisno AL, Pearce IA, Wall HP, et al. Contrasting epidemiology of acute rheumatic fever and acute glomerulonephritis. *N Engl J Med.* 1970; **283**: 561-5.
  - 11 Denny FW. A 45-year perspective on the streptococcus and rheumatic fever: the Edward H Kass Lecture in infectious disease history. *Clin Infect Dis.* 1994; **19**: 1110-22.
  - 12 Gordis L. The virtual disappearance of rheumatic fever in the United States: lessons in the rise and fall of disease. *Circulation.* 1985; **72**: 1155-62.
  - 13 Eltohami EA, Hajar HA, Folger GM. Acute rheumatic fever in an Arabian Gulf country; effect of climate, advantageous socioeconomic conditions, and access to medical care. *Angiology.* 1997; **48**: 481-9.
  - 14 Carapetis JR, Walker AR, Kilburn CJ, et al. Ten year follow-up of a cohort with rheumatic heart disease (RHD). *Aust NZ J Med.* 1997; **27**: 691-7.
  - 15 Veasy LG, Wiedmeier SE, Orsmond GS, et al. Resurgence of acute rheumatic fever in the intermountain area of the United States. *N Engl J Med.* 1987; **316**: 421-7.
  - 16 Ayoub EM. Resurgence of rheumatic fever in the United States. The changing picture of a preventable illness. *Postgrad Med.* 1992; **92**: 133-42.
  - 17 Zaman MM, Rouf MA, Haque S, et al. Does rheumatic fever occur usually between the age 5 and 15 years? *Int J Cardiol.* 1998; **66**: 17-21.
  - 18 Kaur S, Kumar D, Grover A, et al. Ethnic differences in expression of susceptibility markers in rheumatic fever/rheumatic heart disease patients. *Int J Cardiol.* 1998; **64**: 9-14.
  - 19 Davachi F, Moller JH, Edwards JE. Disease of the mitral valve in infancy. An anatomic analysis of 55 cases. *Circulation.* 1971; **43**: 565-79.
  - 20 Chen SU, Tsai CC, Nouri S. Carditis associated with *Mycoplasma pneumoniae* infection. *Am J Dis Child.* 1986; **140**: 471-2.