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## FULL LENGTH ARTICLE

# A dramatic decline in university hospital admissions of acute rheumatic fever in the eastern region of Saudi Arabia

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## KEYWORDS

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Rheumatic heart disease

**Abstract** *Backgrounds:* Acute rheumatic fever (ARF) and its sequel, chronic valvular heart disease are the most important causes for cardiovascular morbidity and mortality worldwide and mainly in developing countries. However, the incidence of ARF has declined in developed countries during the second half of 20th century.

*Material and methods:* The case files of all patients admitted as new cases of ARF over ~11 years and 8 months, both in pediatric and medical departments of a university hospital located in the eastern region of Saudi Arabia were reviewed. The demographic and clinical data and the frequency of the new cases were compared with the data that have been published by us 10 years ago from the same hospital during a similar period of time (11 years and 8 months).

*Results:* In the current study there was a significant decline in the frequency of admission of cases of ARF as compared to our previous study during a similar period of time, with a frequency rate of 12 cases per 100.000 hospitalizations versus 45 cases per 100.000 hospitalizations, respectively,  $P < 0.001$ . Dyspnea and chest pain as clinical features of acute rheumatic carditis (ARC) were less

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frequent in the current study as compared to the previous study (35% versus 44%,  $P = 0.02$  and 10% versus 28.6%,  $P = 0.031$ ). The subgroup analysis revealed also a decreased frequency of the clinical features of ARC in pediatric age group in the current study as compared to our previous study.

**Conclusion:** There is a significant decline in the frequency of new hospital admissions due to ARF. This decline was associated with similar decline in the frequency of the manifestations of ARC especially in pediatric age group (1–12 years).

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## 1. Introduction

Acute Rheumatic Fever (ARF) is a systemic inflammatory disease of childhood affecting mainly connective tissue, in many cases recurrent, that follows a group A beta-hemolytic streptococcal infection. Rheumatic heart disease (RHD) refers to the cardiac manifestations of ARF and includes pancarditis (myocarditis, pericarditis, and endocarditis) during the early acute phase and chronic valvular heart disease later. However, severe pancarditis occasionally produces fatal heart failure during the acute phase (Dajani AS, 2005; World Health Organization, 2004; Miyake et al., 2007). It has been reported that most major outbreaks of ARF occur under conditions of poor overcrowding where access to antibiotic therapy is limited, and RHD accounts for 25–50% of all cardiac admissions international (Chun et al., 1987). Regions of major public health concern include Middle East, Indian subcontinent, some areas of Africa and South America (Tibazarwa et al., 2008; Carapetis et al., 2005; Lee et al., 2009; Shulman and Tanz 2010; Abdul-Mohsen and Lardhi 2000).

Nevertheless, it has been found that ARF and its sequel, chronic valvular heart disease are the most important causes for cardiovascular morbidity and mortality worldwide and especially in developing countries. (Lee et al., 2009; Shulman and Tanz 2010; McDonald et al., 2004; Meira et al., 2005). Carapetis et al had estimated that 95% of the nearly 20 million cases of RHD in the world, and up to ~500,000 annual deaths due to ARF and RHD, occur in developing countries (Carapetis et al., 2005; Carapetis et al., 2006). Vijavkumar et al. found also that the younger age of onset (juvenile RHD) seen in India is a special feature of both public health and clinical importance and they emphasized that these patterns of ARF and RHD, which may be similar to those in other developing countries, underscore the importance of effective public health strategies for prevention and control (Vijay kumar et al., 1994). Several investigators in the Middle East have had the same clinical impression (Abdul-Mohsen and Lardhi, 2000; Hamdan and Manasra, 1988; Majeed et al., 1981; Al-Eissa, 1991; EL-Eissa et al., 1993).

The usefulness of modified Jones criteria for the diagnosis of ARF remained unchanged since it was revisited and reaffirmed in 1992 by the American Heart Association's. Expert Committee on Rheumatic Fever (Jones, 1944; Guidelines for the diagnosis of rheumatic fever. Jones Criteria, 1992; Dagani et al., 1993). The renewed efforts of the World Health Organization (WHO) in collaboration with many governments to combat ARF and RHD through health promotion improved surveillance and the application of effective prevention strategies had a great share in the significant decline in the incidence of ARF worldwide during the last century (Carapetis et al., 2005; Carapetis et al., 2006; Mayosi, 2007 and Robertson

et al., 2006). In a review about the incidence of ARF worldwide, the incidence of the first attack of ARF per annum varied between 5 and 51 cases per 100,000 (the mean for all studies was 19 per 100,000; 95% CI 9–30/100,000) (Miyake et al., 2007).

In our retrospective analytical study we aimed to compare the annual incidence and the clinical profile of 20 new cases of ARF (13 Saudis), admitted to a 500 bedded university hospital (King Fahd Hospital of the University, located in Al-Khobar city, Eastern Province, Saudi Arabia) during two successive similar periods of time, 11 years and 8 months each (1987–1998 and 1999–2010) (Abdul-Mohsen and Lardhi, 2000).

## 2. Material and methods

The hospital files of all ARF cases admitted between September 1st 1998 and April 30th 2010 to our hospital were retrospectively reviewed. Both the demographic and clinical data were analyzed to know the annual frequency of the new cases of ARF in relation to the total hospital admissions during the study period and to compare it with the frequency of cases of ARF during a similar period of time (between January 1st 1987 and August 31st 1998) in the same hospital (Abdul-Mohsen and Lardhi, 2000). The clinical profile of the patients in the current study will be also compared with our published data in year 2000 (Abdul-Mohsen and Lardhi, 2000).

Continuous data were expressed as the mean  $\pm$  SD and were tested for normal distribution using the Kolmogorov–Smirno test. *T*-test was used for comparison of continuous normally distributed data. Dichotomous data were expressed as number and percentage and were analyzed using Chi-square test or Fisher–Exact test as appropriate. A *P* value  $< 0.05$  was considered significant. Analysis was performed using Statistical Software Version 7.0 for windows (Statsoft. Inc).

## 3. Results

There were 162,672 admissions to King Fahd Hospital of the University during the pre-scheduled study period (11 years and 8 months) compared to 169,878 admissions during exactly a similar period of time in our previous study (Abdul-Mohsen and Lardhi, 2000). In this study, there were new 20 cases of ARF with a frequency of 12 cases per 100,000 admissions per year compared with 77 new cases in our previous study with a frequency rate of 45 cases per 100,000 admissions per year,  $P < 0.001$  (Table 1 and Figs. 1 and 2).

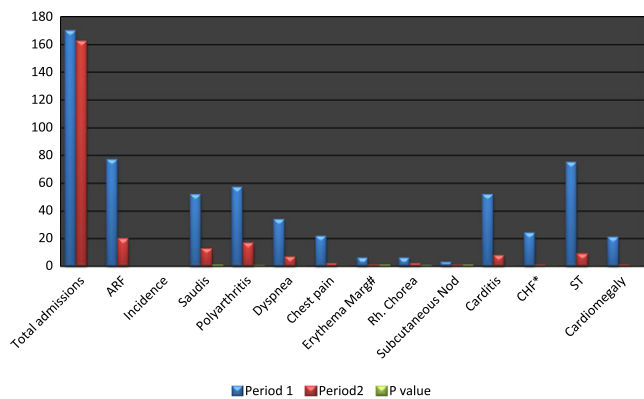
In the current study, 60% were males and 40% were females as compared to 56% and 44%, respectively, in the previous study with no significant statistical difference. In the current study, the age ranged between 5 and 12 years, with a

**Table 1** The differences between the frequency, demographic characteristics and clinical features of patients with acute rheumatic fever in the two study periods.

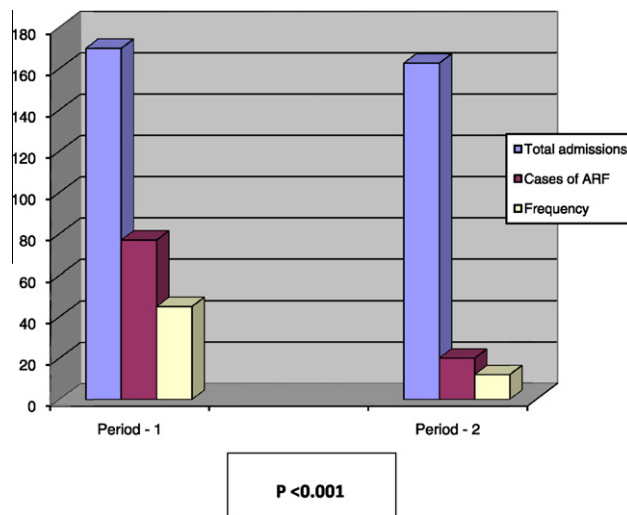
Clinical variable	ARF-Period 1	ARF-Period 2	P value
Total admissions	169.878	162.672	
ARF	77	20	
Incidence	45/100.000	12/100.000	< 0.001
Males	43	12	0.577
Females	34	8	0.804
Saudis	52	13	0.958
Fever	74	18	0.273
Polyarthritis	57	17	0.387
Polyarthralgia	67	18	1
Dyspnea	34	7	0.02
Chest pain	22	2	0.031
Palpitation	21	4	0.289
Erythema Marg <sup>a</sup>	6	1	1
Rh. Chorea	6	2	0.667
Subcutaneous Nod	3	1	1
> 50 mm	77	20	1
CRP	69	20	0.2
Mean temperature	38.18 ± 0.48	38.2 ± 0.52	0.982
Carditis	52	8	0.045
CHF <sup>b</sup>	24	1	0.036
ST	75	9	0.037
Cardiomegaly	21	1	0.037
MS	4	2	0.6
MR	41	12	0.372
AR	19	9	0.131

<sup>a</sup> Erythema marginatum.  
<sup>b</sup> Congestive heart failure.

mean of 9.1 ± 2.07 years in pediatric age group and 13–29 years, with a mean of 20.40 ± 6.10 years in adolescents and adults, compared with a mean of 8.7 ± 2.9 years in pediatric age group and 24.4 ± 9.5 years in adolescents and adults in our previous study, with no statistically significant difference, *P* = 0.869. Seventeen patients had polyarthritis (85%) and 18 had polyarthralgia (90%) in the current study compared with 75% and 87%, respectively, in the previous study with no significant statistical difference. Dyspnea occurred in only 35% of the cases of ARF in the current study as compared to 44% of the cases in the previous study, *P* = 0.02. Chest



**Figure 1** The main differences in the clinical variable of cases of acute rheumatic fever in the two study periods.



**Figure 2** A comparison between total hospitalizations in thousands and the frequencies of admissions of cases of ARF per 100,000 hospitalizations during the two study periods.

**Table 2** The main differences between the clinical features in patients with acute rheumatic fever in the two study periods.

Clinical features	Pediatric-period 1 (No = 36)	%	Pediatric-period 2 (No = 10)	%	P
Dyspnea	27	75	3	30	0.02
Chest pain	18	50	1	10	0.031
CHF <sup>a</sup>	19	52.7	1	10	0.028
ST <sup>b</sup>	36	100	5	50	< 0.001
Cardiomegaly <sup>c</sup>	18	50	0	0	0.004
LVE by ECHO <sup>d</sup>	13	36	2	20	0.042

<sup>a</sup> Congestive heart failure.  
<sup>b</sup> Sinus tachycardia.  
<sup>c</sup> Cardiomegaly by chest X-ray.  
<sup>d</sup> Left ventricular enlargement by echocardiogram.

pain was also a significantly less frequent complaint in the current study occurring in 10% of the cases as compared to 28.6% in the previous study, *P* = 0.031. There was no statistical significant difference concerning the frequency of other clinical and investigational parameters of the patients in the two study periods, such as palpitation, erythema marginatum, rheumatic chorea, subcutaneous nodules, highly elevated sedimentation rate (> 60 mm), positive c-reactive protein (CRP), mean ore temperature, sinus tachycardia, signs of heart failure or carditis, signs of mitral valve stenosis or regurgitation and signs of aortic regurgitation (Table 1).

The subgroup analysis of patient’s clinical parameters in pediatric age groups in the two studies revealed higher frequency of dyspnea in the previous study as compared to the current study, 75% and 30%, respectively, *P* = 0.02. There was also higher frequency of chest pain, sinus tachycardia, signs of congestive heart failure (CHF), radiological evidence of cardiomegaly and echocardiographic evidence of left ventricular dilatation in the pediatric patients of the previous study as compared to the current study and the differences

**Table 3** The main differences in the clinical features of acute rheumatic fever in adult age groups during the two study periods.

Clinical feature	Adults-period 1 (No = 43)	Adults-period 1 (No = 10)	<i>P</i>
Dyspnea	7	4	0.193
Chest pain	4	2	0.584
CHF <sup>a</sup>	6	4	0.09
ST <sup>b</sup>	39	4	< 0.001
LVE (Echocardiogram)	5	4	0.061
MR <sup>c</sup>	11	5	0.196
Average ESR <sup>d</sup>	101.5 ± 20.9	84.5 ± 23.4	0.029

<sup>a</sup> Congestive heart failure.

<sup>b</sup> Sinus tachycardia.

<sup>c</sup> Mitral regurgitation.

<sup>d</sup> Average erythrocyte sedimentation rate.

were statistically significant (Table 2). Whereas, dyspnea, chest pain, CHF, left ventricular dilatation and mitral regurgitation were more frequent in adult patients in the current study as compared to the previous study but the differences were not statistically significant (Table 3).

#### 4. Discussion

In the current study we have unequivocally demonstrated a significant decline in the frequency of admissions of new cases of ARF in a major university hospital, from 45 cases per 100,000 Hospitalizations per year to 12 cases per 100,000 hospitalizations per year during the pre-scheduled period of time, exactly similar to the period allocated to our previous study (11years and 8 months),  $P < 0.001$  (Abdul-Mohsen and Lardhi, 2000). The current frequency rate of cases of ARF in our study probably matches with the rate of 14.8 cases per 100,000 hospitalized children below the age of 21 years in the United States of America, which was reported by Miyake et al. (2007), as the majority of our patients (75%) were below the age of 21 years. This evident decline in the frequency of ARF is similar to the worldwide decline of the incidence of ARF that occurred during the second half of the last century (Carapetis et al., 2005; Carapetis et al., 2006; Mayosi, 2007 Robertson et al., 2006; Majeed et al., 1993). However, our findings may contrast to some extent with the findings of some of the United States investigators who reported a resurgence of ARF in the last 2 decades, and with the findings of Wang et al. who reported also a resurgence of adult onset ARF in the Southern Taiwan (Wald et al., 1987; Martin and Barbadora, 2006; Veasy et al., 1994; Wolfe, 2000; Wang et al., 2005). Furthermore, when we compare the finding of our 2 studies, there was no significant difference in the demographic parameters (Abdul-Mohsen and Lardhi, 2000). Polyarthritides and polyarthralgia were the most frequent clinical features in both studies with no statistically significant difference. These findings were in agreement with the clinical findings reported in a Hawaiian study in 1987 and in a Turkish study published in 2005 (Chun et al., 1987; Ozer et al., 2005). Dyspnea and chest pain as symptoms of acute rheumatic carditis (ARC) and CHF were more frequent in the previous study as compared to the current one ( $P = 0.02$  and  $0.031$ , respectively).

In the subgroup analysis, we have found also that the clinical parameters that probably indicate the presence of ARC, such as dyspnea, chest pain, sinus achycardia, radiological evidence of cardiomegaly, and echocardiographic evidences of left ventricular dilatation were significantly more frequent in the pediatric age group in the previous study compared to the present one. These findings may display a logic impression that this decline in the frequency of ARF in the kingdom is interestingly associated with another important decline in the frequency of ARC among cases of ARF. We strongly believe that this important decline is mainly due to the continuous efforts and vigilance in health promotion and primary prevention of ARF and its sequel RHD, through proper treatment of epidemics of streptococcal infection in school age children, emphasizing the importance of proper medical care access, patient education, and compliance in preventing ARF. However, we do not have a scientific explanation for the associated decline in the frequency of ARC as the current study was retrospective, and the sample volume was small. A multicenter prospective study, enrolling larger number of patients and involving extensive microbiological and immunological investigations is suggested. Such a study may be able to disclose any possible relation between the virulence and sero-typing of streptococcal infection and the occurrence of ARC.

#### 5. Conclusion

There is a significant decline in the frequency of Hospitalization of ARF in a large university hospital, Eastern Saudi Arabia in the 1st decade of the 21st century as compared to the last decade of the 20th century. This decline was associated with a noticeable decline in the frequency of ARC as progenitor of chronic RHD among cases of ARF in the current study.

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