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ORIGINAL ARTICLE

Acute Rheumatic Fever In Egyptian Children: A 30- Year Experience in a Tertiary Hospital

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Abstract:

Acute rheumatic fever (ARF) is a leading cause of pediatric acquired heart disease amongst indigenous populations in Egypt, mainly presenting in children aged 5–15 years. This retrospective study was carried out in Tanta University Hospital, Tanta, Egypt to determine the hospital average new cases of acute rheumatic fever (ARF), and its characteristics in the past 30 years. We reviewed and retrospectively analyzed the medical records of all children hospitalized and diagnosed with ARF based on Jones criteria in Pediatric Department of Tanta University Hospitals in the period between January 1982 and December 2011. 2946 children with ARF were admitted in this period. 40.9%were admitted between 1982 and 1991, 38.86% between 1991 and 2001, and only 20.3% between 2001 and 2011. Male/female ratio was 1:1.2.The mean age at diagnosis was 9 ± 3.0 years (range 3-16). Carditis was detected in 48.9%, arthritis in 37.5 %, chorea in 4.9%, and combined lesions in 8.7%. Mitral regurgitation was the most common echocardiographic finding in patients with carditis (43.3%), isolated aortic regurgitation in (11.1%); double mitral lesion in (1.4%), mitral stenosis in (0.76 %) and aortic stenosis in only (0.34%). Over the 30-year study period, there was average of annual new cases of 98 patients/year with peaks at 1982,1986,1987 and 1991. Although the incidence of ARF has decreased in the last decade, it still continues to be an important public health problem in Egypt, despite the progress made in the socio-economic development of the country, and is often associated with cardiac involvement.

Keywords: *Acute Rheumatic Fever, Children*

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Introduction

Acute rheumatic fever (ARF) is an inflammatory disease that occurs after insufficiently treated pharyngeal infection with group A beta hemolytic streptococci [1].

ARF is still considered an endemic disease in developing countries and one of the major form of chronic cardiac disease in child aged group. It accounts for 25-45 % of chronic cardiac disease in developing countries [2].

The incidence of ARF is still high in developing countries (about 100-200) times greater than happened in developed countries. Predisposing factors are related to inadequate health care, overcrowding and poor education. The most common age affected in children is between 5-15 years [3].

Over the last decades, ARF has significantly decreased in incidence in most developed countries due to improvement of socioeconomic condition and early initiation of penicillin in treatment of upper respiratory tract infection.4

Diagnosis of ARF is based on Jones criteria that was put in 1950 and modified twice in 1965 and 1992 by the American Heart Association which include major signs (i.e. carditis, polyarthritis, Sydenham chorea, erythema marginatum and subcutaneous nodule) and minor criteria (i.e. arthralgia, fever above 39 C, elevated acute phase reactant and prolonged PR interval on electrocardiography) [5-7].

To diagnose a case to have ARF, the patient must have two major signs or one major sign and two minor signs plus laboratory evidence of recentinfection [8,9].

Arthritis and carditis are the most common presenting symptoms in ARF, however carditis is responsible for morbidity and mortality of the disease while all other major symptoms resolve completely without any sequale [10,11].

Material and Methods

In this study, we performed a retrospective study for the medical records of children diagnosed with ARF according to Jones and modified Jones criteria that were admitted to pediatric department, Tanta University Hospital, Egypt between January 1982 and December 2011. The patients were referred from primary health clinics, private clinics, or through the emergency department of the hospital.

The data recorded for every patient include: name, age, sex, address, socioeconomic state, presenting symptoms, cardiac involvement, investigations done, treatment given and family history of ARF.

The diagnosis of ARF was based on clinical features and evidence of recent streptococcal infection. All the patients had cultures of the throat, anti-streptolysin O titre, erythrocyte sedimentation rates performed by standard methods.

Standard ECG, two dimensional (2D) and Doppler echocardiography were done for all patients. The valvular disease in ARF was suggested clinically by the presence of an audible murmur and confirmed by echocardiography. We used an old fashioned echocardiography machine (Aloka) in our pediatric cardiology unit since 1980s till 2007 where we depend mainly on M mode, 2D, Doppler study for diagnosis of cardiac affection then we replaced it by Vivid 7 (General Electric) version of echocardiography machine where better resolution and new modes were added e.g. tissue Doppler, 3 and 4 Dimensional echocardiography that helped much in diagnosis of cardiac affection of rheumatic cases.

Arthritis was diagnosed by present of swelling, hotness of joints, and limitation in joint movement. Sydenham chorea diagnosis was based on the exclusion of other causes and forms of chorea and existence of arthritis and/or carditis together. Erythema marginatum, an uncommon manifestation, was found as a macular rash, coalescent with a serpiginous form and almost coppery pink at the border and light colored center, and it was mainly located on the trunk and inner surface of the proximal limbs.

The patients were divided into 3 groups: The first group included patients from 1982-1991; The second group included patients from 1992-2001; The third group included patients from 2002-2011.

Results

During the 30 years study period, 2946 charts were found to fulfill Jones criteria of ARF and were included in the study analysis. The annual average number of new cases was 98 patients/year with outbreaks at 1982, 1986, 1987, and 1991. The number of cases decreased significantly in the last 5 years reaching 8 cases/year at 2011(Figure 1).

Median age was 9 ± 3 years (range 3 to 16), There was a female predominance (F/M ratio was 1.2:1) as 1640 (55.6 %) were female., 79.67 % of patients presented in the first 20 years while only 20.33% of patients presented in the last 10 years .

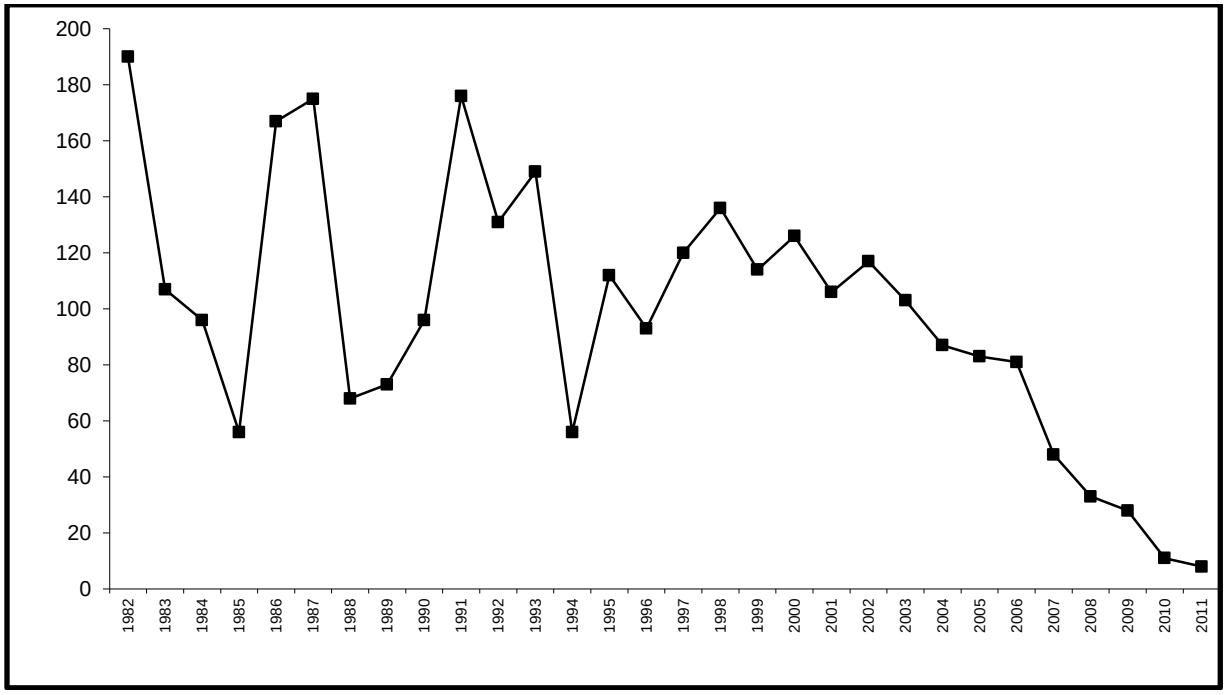

Figure 1. Distribution of new cases with ARF through 30 years of study

Age at presentation varied from (3-16 years) with median of 9±3 years. Most cases presented between (5 and10 years) and this accounts for 50.4% of patients, 45.5% of patients presented at the age of 11 to 15 years, 3.8% of patients presented in age less than 5 years while only 0.2% of patients presented at age more than 15 years (Table 1) (Figure 2).

Table 1. Age distribution among children with ARF in the study

	Group 1 (1982-1991)	Group 2 (1992-2001)	Group 3 (2002-2011)	Total (n)	%
Number of patients	1204 (40.9%)	1143 (38.8%)	599 (20.3%)	2946	100
Less than 5 years	26	43	42	111	3.8
5-10 years	682	548	255	1485	50.4
11-15 years	496	552	297	1345	45.6
More than 15 years	------	-------	5	5	0.2
				ANOVA test	
Mean ± SD	9.47 ± 2.59	9.76 ± 2.74	9.770 ± 2.99	F=7.713	<0.001
Median (IQR)	9.427 (3.46)	9.71 (3.56)	9.99 (3.9)		

Clinical presentation

Carditis was the most frequent clinical manifestation of ARF in our study as it was seen in 1441 cases (48.9%) followed by arthritis; 1104 cases (37.5 %), Sydenham chorea; 145 cases (4.9%), combined arthritis and carditis; 193 cases (6.6%), combined carditis and chorea 62 cases (2.1%), while the least presentation was carditis and erythema marginatum and was only detected in one case (0.03%) (Table 2)

Among 1441 patients with carditis diagnosed clinically or by echocardiography, 796 were

Figure 2. Comparison between mean and SD of age regarding the three groups

female (55.2%), 645 were male (44.8%). 35patients (2.4 %) had congestive heart failure and 621 children had involvement of more than one valve (43.1%). Isolated mitral valve regurgitation were detected in 624 patients (43.3%), isolated aortic valve regurgitation were detected in 160 patients (11.1%); double mitral lesion in 20 patients (1.4%), mitral stenosis in 0.76 % (n = 11) and aortic stenosis in 0.34% (n = 5) (Table 3).

Table 2. Major manifestation of ARF over 30 years of the study

	Group 1 (1982-1991)		Group 2 (1992-2001)		Group 3 (2002-2011)		Total (n)	%
Number of cases	1204 (40.9%)		1143 (38.8%)		599 (20.3%)			
Sex	Female	Male	Female	Male	Female	Male		
Number	690	514	633	510	317	282	2946	100
Presenting symptoms:								
Carditis	318	253	317	253	161	139	1441	48.9
Arthritis	246	197	235	188	123	115	1104	37.5
Chorea	70	31	22	12	5	5	145	4.9
Carditis and arthritis	41	28	38	45	18	23	193	6.6
Carditis and chorea	14	5	21	12	10	-----	62	2.1
Carditis and skin	1	-----	------	------	-------	-----	1	0.03

Isolated polyarthritis, as the only major criteria was observed in 37.5 % patients (n = 1104). Combined arthritis and carditis were presented in 193 cases (6.6%).

Arthritis involved large joints e.g. the knees, elbows, wrists, hips and ankles. The arthritis was migratory in all cases.

145 children (4.9 %) presented with the manifestation of isolated chorea. It was seen significantly more frequently in females (97/145 = 66.9 %) than in male. Combined chorea and carditis were presented in 62 patients (2.1%). Erythema marginatum was found in only one case (0.03%).

Table 3. Pattern of valvular disease in 1441 patient with carditis.

Valvular lesion	Number	%
Mitral valve regurgitation	624	43.3
Aortic valve regurgitation	160	11.1
Double mitral lesion	20	1.4
Mitral stenosis	11	0.76
Aortic stenosis	5	0.34
Combined valve lesion	621	43.1
1. **Mitral and aortic regurgitation**	567	
2. **Mitral regurgitation with double aortic lesion**	34	
3. **Mitral, aortic and tricuspid regurgitation**	11	
4. **Mitral and tricuspid regurgitation**	6	
5. **Mitral, aortic, and pulmonary regurgitation**	2	
6. **Mitral, tricuspid, and pulmonary regurgitation**	1	
Total	1441	100

Discussion

Despite a low prevalence of ARF in the industrialized countries, ARF is still a real problem in the third world like Egypt [12]. The decreased incidence of ARF in the world has been attributed to improved living conditions and medical care, the introduction of antibiotics and the changes in prevalence of rheumatogenic group A Streptococcus [13]. Although, we believe that poor social and economic factors and in particular bad housing conditions are the major reasons for that high rates found in the developing countries like Egypt, but also genetic predisposition, overcrowding and diminished access to primary health care should be kept in mind as other predisposing factors.

During the study period, we have seen an average of 98 new cases of ARF/year with significant outbreaks at 1982, 1986, 1987, and 1991.We reported an average rate of 120.4 new cases/year in the period 1982-1991, 114.3 cases/year in 1992-2001 and 59.9 cases/year in 2001-2011. So the present study indicates that the average new cases of ARF was high at the beginning of the 1980s decade and had dropped markedly by the end of 2011. This apparent reduction in the number of new cases of ARF admitted to our hospital in the last few years probably reflects improving socioeconomic state, housing conditions, health care services, primary prevention of ARF by early detection, diagnosis and appropriate treatment of pharyngitis with antibiotics, and better health education of people about the association between sore throat and RF and the importance to complete antibiotic course to prevent rheumatic fever.

Rheumatic fever is more frequent in the age between 5 and 15 years. It is uncommon under the age of 5 years and beyond the age of 15 years.13 In our study, 96% of patients were aged between 5 and 15 years, and only 3.8% of patients were under the age of 5 years. This agreed with the results of Örün et al., [4]. Age between 5-15 years is still carrying the highest risk for ARF in Egypt because at these ages children are in schools which are badly ventilated and overcrowded and these favor the spread of streptococcal infection. In general, female gender was predominant in all RF presentations with a female to male ratio of 1.3:1 that was similar to many other studies in which girls predominate [14].

Carditis was the most common isolated major manifestation of ARF in our study and was seen in 48.9% of our patients; that was similar to the results observed by Bitar et al., [15] who reported very high incidence of carditis in their study. A less incidence was found in the study done by Al Qurashi, [16] who reported carditis in only 36% of patients with ARF. Among 1441 patients with carditis diagnosed clinically or by echocardiography, thirty-five patients (2.4%) had congestive heart failure reflecting severe carditis. The most common valvular lesion was isolated mitral valve regurgitation that was detected in

624 patients (43.3 %), 621 children had involvement of more than one valve (43.1%), isolated aortic regurgitation were detected in 160 patients (11.1%); This pattern of valvular involvement in our study was similar to the results of other works [16-18].

The frequency of isolated polyarthritis in our study was 37.5 % of patients. Arthritis was associated with carditis in only 6.6% of patients. So, the total percent of children who had arthritis was 44.1%. The arthritis involved a few large joints e.g. the knees, elbows, wrists, hips, and ankles. The arthritis was migratory in all children with multiple joint involvements. Our result was similar to that reported by other workers [15,16,19].

Isolated chorea was present in 4.9% of children with ARF and the ratio can rise to 7% if we added the cases that presented with combined chorea with carditis. That was similar to the results of Breda et al., who reported chorea in only 5.7% of patients presented with ARF. Diagnosis of isolated chorea was based on exclusion of other causes or chorea [17]. Most cases were treated with haloperidol in the first 20 years of study then valproic acid proved to have a high success rate in reduction of symptoms of chorea in the last decade. All our patients who had initial attack of ARF with isolated chorea seem not to develop valvular lesion later on.

Although our study involves a large number of ARF in children admitted to Tanta University Hospital, its retrospective nature and the evaluation of only hospitalized cases constitute limitation factors. It is even possible that the real annual number of new cases of ARF in our environment might be higher than the rate observed because we have only included hospitalized patients with ARF; so the number of new cases of ARF may have been underestimated if patients were managed without hospitalization or hospitalized in other secondary care centers surrounding Tanta University Hospital. Also, the results of the present study reflect the clinical picture of ARF in only one city from the third world.

Conclusion

Although, ARF has become a rare disease in industrialized countries, it continues to occur in the developing countries like Egypt, and is often associated with cardiac affection. The percentage of new cases of ARF is decreasing in Egypt due to improved socioeconomic state, better health services, early diagnosis and adequate treatment of pharyngitis; however, we need more efforts to eradicate the disease. Further studies are needed to identify the virulent factors and epitopes of rheumatogenic streptococcal strains as well as the genetic markers of predisposition to explain the differences in this clinical presentation.

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