

CORRELATION BETWEEN THE SEVERITY OF CARDITIS AND THE LEVEL OF ACUTE PHASE REACTANTS AND ANTI-STREPTOLYSIN O TITER IN ACUTE RHEUMATIC FEVER: A RETROSPECTIVE STUDY IN SHIRAZ

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ABSTRACT

In order to find the correlation between the severity of carditis in acute rheumatic fever (ARF) and the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and anti-streptolysin O (ASO) titers, we performed a retrospective study in Shiraz on one-hundred and four patients. The mean age of the patients was 11 years. Fever was seen in 85.5%, arthralgia in 95.2%, arthritis in 81.7%, carditis in 82.5%, chorea in 3.8%, and subcutaneous nodules in 0.9% of patients. Mitral regurgitation was the most frequent valvar involvement (79.6%). Sixteen patients (15.4%) had severe carditis. The ESR level was ≥ 20 Wintrobe units in 98.0%, the CRP was elevated in 83.0%, and the ASO titer was ≥ 400 Todd units in 91.0% of patients. There was no significant statistical difference between those patients with mild and severe carditis concerning the level of ESR, CRP, and ASO titers. There was also no significant statistical difference between the level of these parameters and the presence or absence of carditis, and the patient's age (≤ 8 years or > 8 years old).

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INTRODUCTION

Rheumatic heart disease (RHD) is one of the most common acquired heart diseases in underdeveloped and developing countries, with a prevalence rate of 0.7-4.7/1000 people.¹ Its long term sequelae can be disabling for the patient, especially with added complications such as congestive heart failure, infective endocarditis, thromboembolism, etc. Modified Jones' criteria are still the best and most commonly used criteria for the diagnosis of acute rheumatic fever (ARF).^{2,3} Some patients have severe involvement of the heart while others have a more benign course.^{4,5} It is well documented that the immune system and individual susceptibility play a major role in the

pathogenesis of ARF.^{6,9} The inflammatory and immune responses to group A beta-hemolytic streptococcal pharyngitis and ARF include increased erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels and anti-streptolysin O (ASO) titers. There are some reports that have shown the cardiotoxicity of streptolysin O for the mammalian heart.^{10,11} We found only one report that showed a correlation between the occurrence of carditis in ARF and the anti-streptolysin O (ASO) titer.¹² We did not find any study that showed a correlation between the severity of carditis in ARF and the level of acute phase reactants (ESR, CRP) or the ASO titer. We therefore performed a retrospective study in order to determine the presence of any correlation between these parameters.

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Table I. Observed symptoms and signs in the study group (104 patients).

Symptom/Sign	Frequency(%)	Symptom/Sign	Frequency(%)
Arthralgia	95.2%	Signs of CHF	6.7%
Fever	85.5%	Chorea	3.8%
Arthritis	81.7%	Erythema Marginatum	0%
Heart Murmur	76.0%	Subcutaneous Nodule	0.9%

Table II. Echocardiographic findings in the study patients (104 patients).

Finding	Frequency(%)	Finding	Frequency(%)
Isolated MR	40.3%	MR, AR, TR, PR	1.9%
MR, AR	26.9%	MR, AR, PR	1.9%
MR, AR, TR	5.7%	Pericardial effusion	3.8%
Isolated AR	2.9%	Normal	17.5%
MR, TR	2.9%	—	—

MR= Mitral Regurgitation

TR= Tricuspid Regurgitation

AR= Aortic Regurgitation

PR= Pulmonary Regurgitation

PATIENTS AND METHODS

Study patients were selected from patients who were admitted with a diagnosis of ARF to the hospitals affiliated to Shiraz University of Medical Sciences, Shiraz, Iran, during 1992-1997. Study criteria required that patients had (1) a diagnosis of ARF according to modified Jones' criteria, (2) an available echocardiography report, (3) available ESR, CRP, and ASO titer results and (4) age less than or equal to 15 years.

One hundred and four patients met our inclusion criteria. Our criteria for the severity of cardiac involvement were one or more of the following findings: (1) severe isolated valvular regurgitation documented in the echocardiography, (2) moderate regurgitation of 2 or more valves in echocardiography, (3) moderate cardiomegaly in the chest X-ray (a cardiothoracic ratio of more than 0.65), (4) congestive heart failure, and (5) pericarditis.

Statistical analysis of data was done by paired t test and analysis of variance and a *p* value less than or equal to 0.05 was considered to be significant.

RESULTS

One hundred and four patients were included in the

study. The male to female ratio was 1.9/1. The mean age was 11 years (range 3-15 years), and 60.6% of cases were older than 10 years. The youngest patient was a 3 year old boy who presented with arthritis, congestive heart failure, and moderate to severe mitral regurgitation in echocardiography. His ASO titer was 800 Todd units. Signs of pharyngitis were seen in 22.3% of patients. Table I shows the frequency of other symptoms and signs in the study group.

Mild cardiomegaly and/or pulmonary congestion was seen in 4.8% of patients. Prolonged PR interval in the electrocardiogram was seen in 7.6% of cases. Throat cultures were positive for group A beta-hemolytic streptococci in 7.6% of patients.

Echocardiographic findings are shown in Table II. Mild and/or moderate mitral regurgitation (MR) was seen in 71.0% and severe MR in 8.6% of cases. Regurgitation of the other valves was mild. Echocardiography showed valvar regurgitation in 7 (6.7%) patients despite a normal cardiac exam (MR in 3, aortic regurgitation (AR) in 1, MR and AR in 2, and MR, AR and pulmonary regurgitation (PR) in one patient). Sixteen patients (15.4%) met our criteria for severe cardiac involvement. 62.5% of these patients were male and 37.5% female; 6.3% were <5 years old, 18.7% were 5-10 years old, and 75.0% were 10-15 years old.

The ESR level was ≥ 20 Wintrobe unit in 98.0% of patients (≥ 60 Wintrobe units in 31.0%) who presented in the acute phase excluding those patients who presented with chorea). The mean \pm standard deviation (SD) of the ESR level as a whole was 51.7 ± 18.5 Wintrobe units. In the mild group it was 52.9 ± 17.2 and in the severe group it was 55.7 ± 16.4 Wintrobe units, and the p value was not significant.

CRP was positive in 83.0% of patients. Thirty-one patients (32.9%) had a quantitative CRP measurement and data from these patients was used for comparison of the severe and mild group. The mean \pm SD of the CRP level was $1/125.1 \pm 1/87.8$ units in the mild group, and $1/160.0 \pm 1/123.9$ units in the severe group ($p > 0.05$). The ASO titer was ≥ 400 Todd units in 91.0% of patients (20.2% had an ASO titer level ≥ 1200 Todd units). The mean \pm SD of ASO titer in mild and severe groups was 798.8 ± 388.8 Todd units and 910.0 ± 522.4 Todd units, respectively. Even though the mean value was higher in the severe group, the p value was not significant. We also compared the ESR and ASO titer level in those patients with and without carditis, regardless of its severity. The mean \pm SD of ESR in patients without carditis and with carditis was 53.2 ± 13.6 and 51.1 ± 20.3 Wintrobe units, respectively ($p > 0.05$). The mean \pm SD of ASO titers in patients without carditis and with carditis was 813.3 ± 345.1 and 802.0 ± 429.3 Todd units, respectively ($p < 0.05$). The ESR and ASO titer levels were not significantly different in those patients with and without carditis (and also for mild and severe carditis), who were ≤ 8 years old and > 8 years old.

The patients were treated with acetylsalicylic acid (72.7%), corticosteroids (5.8%), or both drugs (15.7%). Some patients did not receive any medication (5.8%).

DISCUSSION

Acute rheumatic fever and RHD are still common in underdeveloped and developing countries and there are a few reports that show a new outbreak in developed countries (e.g., the USA).^{13,14} We had 104 patients during a 5 year period. The clinical findings in these patients were comparable to those reported in the literature.^{4,5,13-15} The incidence of carditis is high in our study compared to other reports. We think this is partly due to our echocardiographic diagnosis of carditis in those patients with negative auscultatory findings.¹³ The upper normal limit of ASO titer is variable in different countries and depends on the endemicity of streptococcal infections.^{4,16} Because streptococcal infections are common in our country, we chose 400 Todd units as the upper normal limit of the ASO titer. We defined the severity of ARF by our criteria and compared the level of acute phase reactants (ESR and CRP) and the ASO titer with the severity of carditis in ARF. It was shown previously that persistent rheumatic heart disease is

more common in those patients with an initial severe carditis, even with regular secondary benzathine penicillin prophylaxis.¹⁷ Majeed et al. found a significant correlation between ASO titer and carditis in children who were ≤ 8 years old.¹² We did not find any significant correlation between ESR, CRP, and ASO titer in our mild and severe subgroups. We also compared the ESR and ASO titer levels between patients with and without carditis, and the p value was not significant. We also compared the ESR and ASO titer level between patients ≤ 8 years old and those > 8 years old, with and without carditis, and the p value was not significant.

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