

Clinical and Demographic Characteristics of 99 Episodes of Rheumatic Fever in Acre, the Brazilian Amazon

Fátima Borges, Maria Luiza A. Barbosa, Renata Beyruth Borges, Olívia C. Pinheiro, Carlos Cardoso, Claudilson Bastos, Roque Aras
Rio Branco, AC / Salvador, BA - Brazil

Objective

To report clinical manifestations and demographic characteristics of patients with rheumatic fever treated in a public hospital in the state of Acre.

Methods

A cross-sectional study was conducted of patients consecutively seen in the Cardiology Ward at FUNDHACRE. Demographic, clinical and laboratory data were assessed through a questionnaire. The diagnosis of rheumatic fever was made based on Jones' criteria, associated with laboratory data, electrocardiography, chest X-ray, and bi-dimensional echocardiography. Patients with other heart diseases, diabetes, obesity, inflammatory disease, and infections were excluded. Those who smoked, were pregnant, or used anti-inflammatory medication or hormone therapy were also excluded.

Results

From July 2003 to February 2004, 99 patients with rheumatic fever were assessed (mean age, 11 years, $SD = \pm 10.18$) with a predominance of females (59.6%), and a racial phenotype of a mixture of Caucasian and Indian (60.6%). Three individuals were excluded because they did not meet the diagnostic criteria. Mean age was 9.1 years old, and in 30.4% of the patients, the disease was diagnosed at the first episode of rheumatic fever. The most frequent clinical manifestations were carditis (69.7%), arthritis (21.4%), and chorea (6.1%). Mitral regurgitation was the most common lesion (36.4%) followed by the association of mitral regurgitation and aortic regurgitation (9.1%).

Conclusion

Rheumatic carditis was the most common manifestation of rheumatic fever, predominant in the group with a racial mixture of Caucasian and Indian (60.6%). Low compliance with antibiotic therapy contributed to the recurrence of the disease and to cardiac sequelae.

Key words

rheumatic fever, carditis, chorea

Rheumatic fever is a delayed inflammatory complication, non-suppurative, with recurrent immunologic bases, frequently occurring in individuals from 5 to 15 years old, from both sexes after recurrent infections of group A streptococcal pharyngitis¹. It is the main cause of heart disease in infancy and adolescence². It is characterized by heart, joint, central nervous system, skin, and subcutaneous cellular tissue involvement³.

Rheumatic fever remains a serious public health problem. About 30 million people suffer from the disease around the world⁴. In developed countries, the prevalence of the disease has decreased due to improvement in social, economic, and cultural conditions, together with the use of antibiotics for respiratory infections⁵. In Brazil, the prevalence of rheumatic fever is 3 to 5% in children and adolescents⁶.

This study aimed at describing the clinical manifestation of rheumatic fever, the frequency of valvular lesion, and the demographic characteristics of a hospital population in the State of Acre.

Methods

All patients with a clinical suspicion of rheumatic fever in the city of Rio Branco, Acre referred to the Cardiology and Rheumatology Ward at FUNDHACRE were consecutively assessed. The hospital is part of the federal Unique Health System (SUS/Sistema Único de Saúde) and is connected to the Medical School in Acre, which takes care of the general population of the cities and rural areas of the state.

After patients were informed about the study and gave their written consent, those from both sexes with symptoms who completed the clinical chart were included. The questionnaire contained data from the clinical history, physical examination, laboratory examinations (erythrocyte sedimentation rate, C-reactive protein, throat swab culture, mucoprotein, antistreptolysin O, blood count). Electrocardiograms, chest X-ray in posterior-anterior projections, and echocardiograms were performed, together with collection of information concerning marital status, sex, religion, occupation, family income, educational background, date of birth, weight, height, and number of people in the family. The patients who met the modified Jones' criteria were considered to have a diagnosis of rheumatic fever⁷.

Patients with chronic inflammatory processes (osteoarthritis, collagen disease), infections, or acute inflammatory processes in the preceding 3 weeks (unrelated to rheumatic fever), use of anti-inflammatory drugs in the preceding 3 weeks, on hormone

replacement therapy, diabetes mellitus, and obesity (BMI > 30) were excluded. Those who were smokers and pregnant women were also excluded.

Initially, patients were assessed by a medical team comprising a cardiologist and a rheumatologist, and the diagnosis of the disease was made based on modified Jones' criteria⁷. Fifteen milliliters of blood from the brachial artery were collected and maintained in tubes (Vacutainer) with EDTA anticoagulant for blood count and erythrocyte sedimentation rate and in tubes without anticoagulant to dose high-sensitivity C-reactive protein, mucoproteins, conventional C-reactive protein, and antistreptolysin O (AEO). The values used in the criteria adopted by the modified Jones were considered abnormal laboratory values. These were PCR up to 6mg/L; erythrocyte sedimentation rate up to 20 mm in the first hour; PCR-AS up to 0.30 mg/L; mucoproteins < 4.0 mg%, and antistreptolysin O up to 200 UI/L.

Aiming at assessing the compliance with treatment and the use of antibiotic medication as secondary prophylaxis, the following variables were added to the questionnaire: regular use of benzathine penicillin, hormonal and nonhormonal anti-inflammatory drugs, digitalis, diuretics, ACE inhibitors, calcium channel blockers, platelet inhibitors, and beta-blockers.

The Ethics and Research Committee approved the study, and it was only conducted after written informed consent was given.

Descriptive statistical analysis was used, indicating the values of means and medians. The chi-square test and Fisher's exact test were used to compare proportions, with a 95% significance level ($P < 0.05$).

Results

From July 2003 to February 2004, 99 patients with a diagnosis of acute rheumatic fever were assessed (mean age, 11 years $SD = \pm 10.18$). Female sex was predominant, accounting for 59.6% of the population sample, and in the distribution according to racial group, we verified that the mixture of Caucasian and Indian was the most prevalent race (60.6%). Three patients were excluded because they did not fulfill the diagnostic criteria. Mean age at the onset of the disease was 9.1 years, and in 30.4% of the cases, the disease was diagnosed at the first episode of rheumatic activity, while 65.7% experienced 2 episodes or more. Age and sex were not associated with valvular involvement.

The most frequent clinical manifestations were carditis in 69 patients (69.7%), arthritis in 21 patients (21.4%), and chorea in 6 patients (6.1%). Of the 69 patients with active carditis, 21 patients developed heart failure, distributed according to NYHA (*New York Heart Association*) as follows: 9 patients were in Functional Class I, 5 patients were in Functional Class II, 4 patients were in Functional Class III, and 3 patients were in Functional Class IV. Severe secondary pulmonary hypertension was found in 1 and mild secondary hypertension was found in 3 patients. Isolated mitral regurgitation was the most common lesion (36.4%), followed by the association of mitral regurgitation and aortic regurgitation (9.1%). The presence of carditis was observed in 39 mestizo patients (Caucasian and Indian), 17 in Caucasian patients, and 13 in non-Caucasian patients.

Joint involvement was manifest by arthritis occurring in 21 patients; however, it was more prevalent in mestizo (Caucasian and Indian) (13), followed by Caucasians (6), and non-Caucasians

(2). Clinical and evolution characteristics typical of the joint picture of rheumatic fever occurred in our population, represented by 11.1% as migrating arthritis, 6.1% with additional features, and 4% monoarthritis.

Of the 99 patients studied, 70 (70.7%) had valvular lesions with a predominance of mitral failure in 36 patients (36.4%); 9 patients (9.1%) had mitral failure associated with aortic failure; 4 patients (4.0%) had a mitral prosthesis associated with aortic failure; 3 patients (3.0%) had mitral failure associated with tricuspid failure; 2 patients (2%) had mitral stenosis, tricuspid failure, mitral failure associated with aortic double lesion, mitral prostheses and mitral valvuloplasty, and 1 patient (1%) had other valvular lesions. Acute rheumatic fever was found in 30 patients (30.3%) at the first episode of the disease and in 66 patients (66.7%) with a recurrence of 2 or more episodes.

Demographic and clinical characteristics of patients are found in table I. Frequency of recurrent tonsillitis was 80.8%. Five patients (5%) underwent cardiac surgery: 2 patients (2%) received aortic bioprostheses, one patient received an aortic bioprosthesis with mitral commissurotomy, one received a mitral aortic bioprosthesis, and another patient received a mitral bioprosthesis. Sixty-one patients (61.6%) did not comply with the antibiotic prophylaxis. In our study, of 38 patients (38.4%) who used penicillin benzathine regularly, 27 (27%) had a new episode of rheumatic fever.

Serum levels of mucoproteins were increased in 61 patients (61.6%) and those of C-reactive protein in 24 patients (24.2%). Regarding antistreptolysin, we also observed an increase in 58 patients (58.8%) with rheumatic fever. VHS levels were higher in the group with arthritis with statistical significance ($P < 0.026$), when compared with that in the carditis group.

Table I - Clinical and demographic characteristics in 99 patients with rheumatic fever

Clinical and Demographic Characteristic	(n)
Sex Female	59 (59.6%)
Mean age (years)	11 \pm 10.18
Race	
Mestizo (Caucasian and Indian)	60 (60.6%)
Caucasian	23 (23.20%)
Black	0.0%
Non-Caucasian	16 (16.20%)
Age at the onset of the disease (mean)	9.1 anos
Recurrent tonsillitis	80.8%
Number of outbreaks of the disease	
First	30 (30.3%)
Recurrence	69 (66.7%)
Clinical manifestations	
Carditis	69 (69.7%)
Arthritis	21 (21.4%)
Chorea	6 (6.1%)
Erythema Marginatum	3 (3%)
Most frequent valvular heart diseases	
MF	36 (36.4%)
MF/AoF	8 (8.1%)
HF	
FCI	9 (9.1%)
FCII	5 (5.1%)
FCIII	6 (6.1%)
FC IV	4 (4%)
Secondary prophylaxis	
Penicillin benzathine	38 (38.4%)
Fail in the prophylaxis	61 (61.6%)
Heart surgery	6 (96.1%)

MF - mitral failure; MF/AoF - mitral/aortic failure; HF - heart failure; FC - functional class according to NYHA.



In the group of patients with arthritis, 16 patients (16%) had high antistreptolysin (ASLO) levels, whereas 4 patients (4%) had normal levels. Mucoproteins values were above normal in 15 patients (15%), and 4 patients had normal levels without statistical significance. C-reactive protein was normal in 11 patients (11%) and altered in 10 patients (10%) with statistically significant levels ($P < 0.02$).

In the group of patients with carditis, the erythrocyte sedimentation rate was elevated in 37 patients (56%), which is half of the patients, but with no significant difference when compared with patients that did not have changes in the erythrocyte sedimentation rate. AEO values were increased in 41 patients (41.4%), mucoproteins in 40 patients (40.4%), and C-reactive protein in 18 patients (18.2%), with no statistically significant difference in this group.

Conduction disturbances were recorded on electrocardiograms in 30 patients (30.3%), and an increase in the P-R space was observed in 7 children (7%) with ages up to 13 years old, and in 5 children (5%) over 13 years old. Among the arrhythmias, sinus tachycardia was present in 12 patients (12.1%), followed by sinus bradycardia in 7 patients (7.1%), atrial fibrillation in 4 patients (4%), supraventricular extrasystole in 1 patient (1.0%), and total atrial ventricular block in one patient.

In the group of patients with carditis, arrhythmias occurred in 25 patients (50.5%), and in the group with arthritis, they occurred in only 6 patients. Conduction disturbances were identified in 20 patients (20.2%) with active carditis. In 17 patients, first-degree right bundle-branch block occurred, and in 2 patients second-degree right bundle-branch block occurred.

Chest X-rays demonstrated normal pulmonary transparency in 79 patients (79.8%), and among the patients with active carditis, 25 of them (36%) had an increase in the cardiac and thoracic index, with a significance level when compared with those individuals without carditis ($P < 0.031$).

Discussion

Rheumatic fever is still a severe health problem in Brazil⁸⁻¹⁰. In our series of patients, we have observed an increased frequency of valvular lesions and carditis (69.7%), demonstrating the severity of initial attacks or of recurrences of the inflammatory activity, with heart lesion that will certainly contribute to the increase in the prevalence of heart disease in our country.

Regarding race, we observed the predominance of mestizos (Caucasian and Indian) (60.6%), a characteristic of the north region of Brazil. This population group that has not been reported on in other national publications may have some genetic predisposition to infection by streptococcus, as described in other groups of Caucasians and non-Caucasians associated with HLA Class II in different countries and ethnic groups. On the other hand, the high frequency of cardiac lesions in 42 patients (70%) of this group may be explained by the greater proportional number of the sample studied. However, when we assess the Caucasian (23.2%) and non-Caucasian (16.2%) population, we find the same severity of valvular lesions in 15 patients (65%) and 13 patients (81%), respectively. These data suggest that other factors are probably involved in addition to a genetic predisposition, such as low educational, social, and economical level; the environment in the Amazon, with a hot and humid weather, and a rainy season, which favor the infectious agent¹¹⁻¹³.

Despite the low diagnostic output in carditis identification, the alterations found in the electrocardiographic records analysis are in agreement with reports in other publications¹⁴⁻¹⁶, both in the frequency of arrhythmias and in the presence of abnormalities involving the P-R interval prolonging.

Despite the increase in the number of children with pure chorea or chorea associated with carditis in recent years, this symptomatology has not been reported much in developing countries, which is different from our study where Sydenham's chorea occurred in 6.1% of patients¹⁷.

Overall, the evidence of inflammatory activity has changed, with greater frequency in patients with arthritis. These data, which are controversial because they predict that the intensity of arthritis is related more to the inflammatory process involving the heart, were also found in our patients. C-reactive protein did not demonstrate an increase consistent with inflammatory activity, probably because of the fugacity of its elevation, which may be associated with the course of the disease and the duration of the involvement from the collection of blood samples. When we compared values of erythrocyte sedimentation rate and C-reactive protein between the patients with arthritis and carditis, we found that the inflammation was (VHS and PCR) more elevated in the group with arthritis with statistical significance ($P = 0.026$).

Echocardiography has become an essential diagnostic method for the assessment of patients with rheumatic fever, because it enables a detailed analysis of the cardiac lesions and because it is more specific than clinical evaluation¹⁸. Of the 67 patients with cardiac involvement, 36 had mitral regurgitation, without an organic murmur at clinical examination. Six patients were diagnosed with mild mitral regurgitation, demonstrated by echocardiography, and 2 had physiologic mitral regurgitation. These data are in accordance with that of other authors who identified valvular abnormalities in patients with rheumatic fever without clinical presentation of carditis, suggesting that some patients may have a subclinical course of carditis with valvular lesions¹⁹.

In our study, a high rate of failure to comply with antibiotic prophylaxis with penicillin benzathine occurred, leading to a greater risk of recurrence and of cardiac complications, which may be explained by the lack of campaigns to educate the population, low social and economical level, and poor education of the family in the population studied.

Special attention must be paid to the primary prophylaxis of acute rheumatic fever. The upper airway infections caused by group A streptococcus β -hemolytic must be diagnosed and treated early. The population must be informed through mass media communication, giving priority to care for patients in health care units and public hospitals, enabling the needy population to have access to public health policies, thus improving compliance with the treatment. Secondary antibiotic prophylaxis is extremely necessary in this population, because of the severity of recurrence of rheumatic fever reducing lesions and valvular sequelae²⁰.

In conclusion, we have observed that although rheumatic fever occurred more often in the racial group of mestizos (Caucasians and Indians), severe heart involvement was a factor regardless of ethnic group. A public health campaign in the region must be introduced to stop the cycle of streptococcus infection and the occurrence of rheumatic fever, in addition to the systematic use of secondary antibiotic prophylaxis.

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