Rheumatic fever recurrence: Risk factors and clinical characteristics

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ABSTRACT

Background: Rheumatic fever recurrence (RFrec) contributes to the worsening of rheumatic valve disease. There are few studies describing the factors associated with recurrence.
Objectives: To analyze the potential risk factors for RFrec in an outpatient cohort.
Methods: We evaluated 148 patients from a cohort of 218 patients treated at rheumatic fever (RF) clinics of the University Hospital Prof. Edgard Santos (Salvador-BA), with at least two years of follow-up.
Results: The mean age was 29.7 ± 12.7 years, with 64% female. RFrec occurred in 14.2% of patients. Patients with and without recurrence differed in age ($23.4 \pm 9.9 \times 30.8 \pm 12.7$ years, $p = 0.024$), age ≤ 23 years (82.3% vs 39.6%, $p = 0.001$), non-adherence to prophylaxis (36.8% vs 15.5%, $p = 0.027$), prior heart failure (HF) (38% vs. 17%, $p = 0.03$), presence of aortic regurgitation on echocardiography (71% vs. 44%, $p = 0.05$) and diastolic dimension of the left ventricle ($58.0 \pm 16.2 \times 51.6 \pm 8.6$ mm, $p = 0.025$). Estimated relative risk of RFrec were: age ≤ 23 years RR 5.6 (95% CI 1.7 to 18.5) − $p = 0.001$; non-adherence to prophylaxis RR 2.6 (95% CI 1.1 to 5.9) − $p = 0.027$; prior HF RR 2.4 (95% CI 1.1 to 5.2) − $p = 0.03$. In multivariate analysis, these three parameters showed significant independent association with RFrec.
Conclusions: RFrec occurred in 14.2% of patients. Age ≤ 23 years, lack of adherence to secondary prophylaxis and prior HF were independent predictors of recurrence.

1. Introduction

Rheumatic fever (RF) still occurs with high prevalence in some countries. It is estimated that there are at present about 15 million cases of rheumatic heart disease (RHD), causing 233,000 deaths annually. The incidence of RF is estimated at 500,000/year [1]. In Brazil, the RF is still a very common disease among young people, and cardiac sequel is the main cause of chronic heart disease (HD) in children and adolescents [1].

Repeated episodes of RF become an important mechanism for worsening of RHD. Recurrent outbreaks are associated with increased frequency of carditis and the most severe cases of cardiac involvement [2–4]. The incidence of rheumatic fever recurrence (RFrec) has been reported between 15 and 34% [5–7].

Prior carditis and younger age have also been associated with higher rates of RFrec [8–11]. The identification of risk factors for recurrence of RF and the implementation of preventive measures on the factors that can be modified are of paramount importance in control the severity of the cardiac sequelae.

This study aimed to evaluate the frequency of RFrec, the demographic characteristics of the sample, the clinical patterns and the potential risk factors for recurrence in patients followed up in a reference service.

2. Methods

We evaluated the records of all patients seen at the clinic of RF/RHD of the University Hospital Professor Edgard Santos (HUPES), Federal University of Bahia, since its admission until October 2011. The outpatient RF/RHD clinic is reference in Bahia, weekly works and treat patients with rheumatic disease of different ages. Were excluded patients with incomplete data, with doubtful diagnosis of RFrec and, for those without evidence of RFrec, a follow-up time less than two years. None of the patients included had presented recent episode (<90 days) of RFrec.

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To collect the data, a structured form was elaborated and completed by trained researchers. Information was collected from medical records and by direct contact with the patient, as well as with family members whenever necessary. The collected variables included sociodemographic characteristics, living conditions, clinical data on admission, detailed cardiac auscultation, results of laboratory tests, electrocardiogram and imaging. Race/ethnicity was self-reported. It was considered the first echocardiogram from admission as the baseline echocardiogram to data collection: dimensions of cardiac chambers and great vessels, ventricular diastolic and systolic function, anatomy and function of the valves. For the diagnosis of RFrec, it was considered the modified Jones' criteria [1,12].

2.1. Statistical analysis

Statistical analysis was performed using SPSS Statistics 17.0. Categorical variables were reported as proportions and continuous variables as means ± standard deviation (SD) or median. Continuous variables were compared by the Student t-test or Mann Whitney. Categorical variables were compared using the chi-square test. The sample was divided in two groups of patients, with and without RFrec. Bivariate comparisons were made between those groups and the prognostic features. Association measures used were the odds ratio (OR) and the relative risk (RR), with their respective 95% confidence intervals. Models of multivariate binary logistic regression analysis, using enter strategy, were created in order to get the adjusted ORs of the predictors of the study outcome variable (FRrec). ROC curve was performed to get the best cut-off point for age to predict FRrec. So, for analytical purposes, the current age of the patient was categorized as ≤ or >23 years, according to the ROC curve. Was considered statistically significant a two-tailed $p < 0.05$.

The project of this study was submitted to and approved by the Ethics Committee of HUPES Complex.

3. Results

From a total of 218 patients, we included 148 in the study: 36 were discharged of the ambulatory with a follow-up time less than two years or because the diagnosis of rheumatic disease was uncertain, 12 had doubtful diagnosis of recurrence, 20 had incomplete data, and two patients were admitted after October 2011. Ninety-five patients (64.2%) were female and 90.5% of those who reported their race/ethnicity declared themselves black or mixed-race (mulatto). The mean age was 29.7 ± 12.7 years, median 25 years, minimum 4 y.o., maximum 61 y.o. The mean age at the time of RF diagnosis was 15.3 ± 10.3 years. The mean number of rooms in the house was 5.2 ± 2.0, with about 1.11 ± 0.9 people/room. There were only 2 (2.2%) patients classified as illiterate and 64% reported schooling to complete primary level. Family income was homogeneous, with almost 99% of the sample referring incomes of up to 4 Brazilian minimum wage (Table 1).

Only 2 (1.4%) patients showed allergy to penicillin G benzathine (PGB). No cases of anaphylaxis. Around two thirds of the patients referred adherence above 90% to secondary prophylaxis with PGB. Almost 85% of patients already exhibited some sign(s) of RHD.

3.1. Patients with versus without RF recurrence (Table 2)

Of the 148 patients, 21 (14.2%) presented RFrec during the study period. Patients with and without recurrence differed in age (23.4 ± 9.9 × 30.8 ± 12.7 years, p = 0.024), age ≤ 23 years (82.3% vs 39.6%, p = 0.001), non-adherence to prophylaxis (36.8% vs 15.5%, p = 0.027), prior heart failure (HF) (38% vs. 17%, p = 0.03), presence of aortic regurgitation (AR) on echocardiography (71% vs. 44%, p = 0.05) and LV end-diastolic dimension − LVEDD − (58.0 ± 16.2 × 51.6 ± 8.6 mm p = 0.025). LV end-systolic dimension (LVESD), left atrial dimension and LV ejection fraction did not show significant difference between groups. There was also no significant difference between groups

Table 1
Baseline characteristics of the sample.

	Measurements
Age in years	
Mean ± SD	29.7 ± 12.7
Median	25
Minimum–maximum y.o.	4–61
Age at diagnosis of RF (years)	15.3 ± 10.3
Gender female % (n)	64.2 (95)
Race/ethnicity % (n)	
Black	23.7 (35)
Mixed-race	27.7 (41)
White	5.4 (8)
Not defined	43.2 (64)
Education % (n = 91)	
Illiterate	2.2 (2)
Incomplete primary education	34.1 (31)
Complete primary education	29.7 (27)
Incomplete high school	16.5 (15)
Completed high school	16 (15)
College education	1.1 (1)
Family income in MinW % (n = 80)	
<1	37.5 (30)
1–4	61.3 (49)
5 ou mais	1.2 (1)
Adherence to the PGB % ≥90%	69 (96)
Rheumatic heart disease % (n)	84.4 (124)
Previous valve surgery % (n)	17.6 (27)

SD: standard deviation. RF: rheumatic fever. MinW: minimum wage in Brazil, equivalent to R$ 545.00 in 2011. PGB: penicillin G benzathine.

regarding gender, education level, number of people in the house, proportion people/rooms. Very low family income and race/ethnicity black predominated in the group with recurrence, but without statistical significance.

Arthritis (42.9%), symptomatic heart failure (57%) and 'new' heart murmur (33.3%) were commonly seen during the acute episode.

Table 2
Comparison of the characteristics of individuals with and without recurrence of rheumatic fever.

	Recurrence n = 21	No recurrence n = 127	p
Age in years (mean ± SD)	23.4 ± 9.9	30.8 ± 12.7	0.024
Age ≤ 23 years	82.3	39.6	0.001
Females%	57.1	65.4	0.47
Race/ethnicity%			
Black	56.3	38.2	0.29
Mixed-race	31.2	52.9	
White	12.5	8.8	
Adherence to secondary prophylaxis >90% of doses (%)	57.9	70.7	0.26
No adherence to prophylaxis	36.8	15.5	0.027
Family income <1 MW (%)	50	36.2	0.49
People/home (mean ± SD)	4.93 ± 2.27	4.59 ± 1.93	0.56
People/room (mean ± SD)	0.87 ± 0.43	1.1 ± 0.97	0.43
Education ≤9 years (%)	30	44	0.50
Prior heart disease (%)	76	85	0.30
Prior valve surgery (%)	24	23	0.93
Prior heart failure (%)	38	17	0.03
Valvular lesions by echo (%)			
Mitral regurgitation	86	81	0.66
Aortic regurgitation	71	44	0.05
Tricuspid regurgitation	57	57	0.98
Double mitral lesion	14	24.5	0.51
Double aortic lesion	0	5	0.38
Pulmonary hypertension by echo %	21	22	0.93
LAD in mm (mean ± SD)	43.9 ± 14.9	41.9 ± 10.3	0.53
LVDD in mm (mean ± SD)	58.0 ± 16.2	51.6 ± 8.6	0.025
LVSD in mm (mean ± SD)	34.2 ± 11.2	31.8 ± 7.5	0.47
LVEF in % (mean ± SD)	65.4 ± 12.2	68.5 ± 8.2	0.41

RF: rheumatic fever; SD: standard deviation; MW: minimum wage in Brazil, equivalent to R$ 545.00 in 2011. ECHO: echocardiography. PH: pulmonary hypertension.