

Demographic, clinical, laboratorial, and radiological characteristics of rheumatic fever in Brazil: systematic review

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ABSTRACT

Rheumatic fever (RF) is characterized by a non-suppurative inflammatory process that begins after a group A beta-hemolytic streptococci infection. Its prevalence is higher in developing countries, such as Brazil. However, in our country, systematic epidemiologic data on the disease are scarce and incomplete. Rheumatic fever has an estimated incidence of 3% among Brazilian children and adolescents. We undertook a systematic review of the main Brazilian studies using the LILACS, Scielo, and Medline databases searching for expressions like *Febre Reumática* and Rheumatic Fever. Ten epidemiological studies were selected and comparative analysis did not show a predominance of gender, clinical presentation, and laboratorial and radiological parameters in the different regions of the country.

Keywords: rheumatic fever, Brazil, epidemiology.

RHEUMATIC FEVER

Rheumatic fever (RF) is a late, non-suppurative complication of and oropharyngeal infection with group A beta-hemolytic streptococci. It is estimated that approximately 0.3 to 3.0% of individuals infected with known rheumatogenic strains of *Streptococci* will develop RF,^{1,2} and approximately one to two thirds of them will develop rheumatic heart disease.

The disease is rare in many developed countries, but in developing countries RF continues to be a huge economical and social burden. In Brazil, chronic rheumatic cardiopathy still is the major cause of cardiac disease among children and young adults.

It is estimated a yearly incidence of 500,000 new cases of RF worldwide, leading to a prevalence of more than 15 million cases of rheumatic carditis. Approximately 233,000 people die every year as a consequence of this disorder.³ Latin America

has an incidence of 21,000 cases of acute RF every year. Data in Brazil are scarce. In 2002, 5,000 new cases were reported (Brazilian Geographical and Statistical Institute - IBGE, from the Portuguese). Data from the Federal Health Department estimate an incidence of RF of approximately 3% among children and adolescents, being responsible for 40% of the cardiac surgeries in the country.⁴

The objective of the present study was to analyze the demographic, clinical, laboratorial, and radiological characteristics of RF in Brazil by reviewing studies in the LILACS, Scielo, and Medline databases.

METHODOLOGY

The LILACS, Scielo, and Medline databases were searched using the following sites: www.bireme.br, www.scielo.org, and www.ncbi.nlm.nih.gov/pubmed, and the key words: *Febre*

Received on 07/15/2009. Approved on 08/07/2009. We declare no conflict of interest. Hospital das Clínicas of the Medical School of Universidade de São Paulo – FMUSP

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Reumática and Rheumatic Fever. The search yielded 5,508 studies, and all studies in the Scielo database were also in the LILACS database. Studies in Portuguese were then selected, resulting in 334 studies. Of those, only epidemiologic studies that analyzed the demographic, clinical, laboratorial, and radiological characteristics of Brazilian populations with RF, according to Jones' criteria, were considered eligible. Only 11 studies fulfilled all requirements.⁵⁻¹⁵ One of those studies⁵ was excluded because the population was described in more details on a later article,⁶ in 1993, resulting in a total of 10 studies.

RESULTS

Of the ten studies analyzed, four studied populations in the state of São Paulo (Ribeirão Preto, São Paulo, and Botucatu),⁷⁻¹⁰ one in Santa Catarina (Florianópolis),⁶ one in Goiás (Goiânia),¹¹ one in Rio Grande do Sul (Porto Alegre),¹² two in Paraná (Curitiba),^{13,14} and one in Acre (Rio Branco)¹⁵ (Table 1).

The study period ranged from 1972 to 2005, with a predominance of the decades of 1980 and 1990. All studies were retrospective, five of them included only one center,^{9,10,11,13,15} four were multicenter,^{6,7,8,12} one focused on data from the County Health Department,¹⁴ and three studies focused on hospitalized patients.^{6,7,12} A total of 2,355 patients were analyzed in the ten studies selected, with ages ranging from 3 to 38 years, but only one study evaluated patients older than 17 years¹¹ (Table 1).

Table 2 shows the clinical characteristics based on Jones' major criteria. 'Arthritis' predominated in most populations described, ranging from 21.4 to 84.3% (mean 63.3%). Carditis had a prevalence between 43.4 and 94.3% (mean 52.0%). The two studies in which the frequency of carditis was higher than that of arthritis included one from a Cardiology department (69.7%)¹⁵ and one that included hospitalized patients (94.3%).⁶ The incidence of chorea ranged from 49.4%, in a general pediatrics rheumatology hospital, to 6.1% (mean 27.7%).^{13,15}

A higher frequency of mitral valve involvement, ranging from 42 to 96.9% (mean 79.5%) was observed in all populations studied; the aortic valve was the second most affected (3.1 to 26.2%, mean 21.1%).^{6,8-15} The concomitant involvement of the mitral and aortic valves ranged from 3.1 to 26.2% (mean 20.7%). Only one study reported the involvement of the tricuspid and pulmonary valves with an incidence of 9.2% and 0.55%, respectively.⁸

Minor criteria (Table 3) were observed in 60.2% of the patients of three studies.^{6,8,12} Arthralgia had a mean incidence of 42.2%, being described in two studies.^{6,8} An increase in the PR interval was reported in two studies, with a mean incidence

of 10.4%.^{6,15} All studies focused on clinical and laboratorial data^{6-9,11-15} and determined the levels of anti-streptolysin O (ASLO) for evidence of a streptococcal infection, with an incidence ranging from 48.7 to 68.1% (mean 68%). Only Gus *et al.* described oropharyngeal cultures in seven of their patients, which was positive in only one of them.¹² A mean of 65.9% of the patients had elevated inflammatory activity assays. The erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), mucoproteins, 2-globulins, 1-acid glycoprotein, and gamma globulin levels were evaluated (Table 4).

The incidence of echocardiographic changes without clinical carditis in three populations analyzed ranged from 6.7 to 18.3%.^{8,9,10} The chest X-ray showed an increase in the cardiothoracic index in 20.2% of the patients described by Borges *et al.* in 2005¹⁵. Electrocardiographic changes were reported in 55.1% of the patients and the included, besides the increase in the PR interval, sinus tachycardia, sinus bradycardia, sinus arrhythmia, premature ventricular contraction (PVC), overload, atrioventricular blocks, and changes in ventricular repolarization (Table 5).

Studying the incidence of breakouts of RF according to the seasons, three studies demonstrated a predominance during the winter months^{11,12,13} and two others during the summer months.^{6,9} Comparative analysis of those studies showed that 22.3 to 52.9% of the cases were seen during the winter months, with a mean of 33.0%, and 7.8 to 30.9% of the cases during the summer months, with a mean of 26.5%. Five studies evaluated the incidence of relapses, which ranged from 15 to 34% with a mean of 21.5%.^{8,9,11,14,15}

DISCUSSION

Analyzing the worldwide epidemiology of RF, a wide reduction in the incidence of acute RF after II World War, explained by greater access to antibiotics, especially in Europe, United States, and Japan, can be observed. This is comparable to what was seen in developing countries like Brazil, but in a smaller scale than that observed in developed nations.¹⁶

This systematic review demonstrated the presence of Brazilian literature on the demographic, clinical, laboratorial, and radiologic aspects of RF in different regions of the country: North, Midwest, South, and Southeast. We found studies published from the decade of 1980 to 2009.

Demographic, clinical, laboratorial, and radiological characteristics were comparable among the different Brazilian studies.

A significant predominance of carditis over arthritis was observed in two studies, possibly due to the characteristics

of the Service (cardiology and hospitalized patients) and not of the region or the decade in which they were undertaken. A predominance of mitral valve involvement followed by the aortic valve, isolated or associated with mitral valve involvement, was demonstrated in all studies. The presence of echocardiographic changes suggestive of rheumatic carditis in patients without cardiac symptoms, with an incidence of 20%, was described in two studies.

The studies do not agree on the predominance of RF according to the season, winter and summer, but it was slightly higher in the winter months when all studies are analyzed. A 20% relapse of RF was observed.

Comparative analysis of the region of the country and the time of the study did not show a predominance of gender, clinical presentation, and laboratorial and radiological characteristics in the study patients.

Table 1

Place, period, type of study, and demographic characteristics of the patients in the studies on rheumatic fever in Brazil

Author	City	Date	Type of study	Type of patients	N	Fem. (%)	Age, years
Laus E, 1980	Ribeirão Preto	1972 -1976	Retrospective, multicenter – general hospital	Hospitalized	338	52.0	10-15
Baião TL <i>et al</i> , 1993	Florianópolis	Jan 1988 - Dec 1991	Retrospective, two services - pediatrics and general	Hospitalized	53	41.5	10-15 (60.4%)
Carmo HF <i>et al</i> , 1994	Goiânia	Feb 1987- Jul 1993	Retrospective, single service, general	General	52	50.0	7-38
Gus I <i>et al</i> , 1995	Porto Alegre	Jun 1992 - Sept 1993	Retrospective, multicenter – general pediatrics and cardiology	Hospitalized 1 st bout	51	33.3	5-13 (90.2%)
Silva CH <i>et al</i> , 1999	São Paulo, Ribeirão Preto, Botucatu	Jan 1989 - Dec 1994	Retrospective, multicenter - rheumatology	General	786	48.7	9.4 (3-17 years)
Spelling PF <i>et al</i> , 2000	Curitiba	April 1986 - April 1997	Retrospective, Single service – pediatric rheumatology	General	81	50.0	9-11 (53.1%)
Torres RPA <i>et al</i> , 2000	Curitiba	Oct 1986 - Jul 1994	Retrospective, records of the County Health Department	General	500	51.6	11.5 ± 4.5
Borges F <i>et al</i> , 2005	Rio Branco	Jul 2003 - Feb 2004	Retrospective, Single service - cardiology	General	99	59.6	9.1
Terrerri MT <i>et al</i> , 2006	São Paulo	1995 -2005	Retrospective, single service - Rheumatology	General	193	57.5	9.9 (3-15 years)
Paulo LTSP <i>et al</i> , 2009	São Paulo	N/R	Retrospective, Single service - Rheumatology	General	202	56.0	10.5 (2-16 years)
Total	Seven different cities	1972 -2005	All retrospective	Three hospitalized Seven general	2,355	51.2	5 - 38

N/R – not reported

Table 2
Incidence of major rheumatic fever criteria in the studies

Author	Major criteria				
	Arthritis (%)	Carditis (%)	Chorea (%)	<i>Erythema marginatum</i> (%)	SC nodules (%)
Laus E, 1980	N/R	N/R	N/R	N/R	N/R
Baião TL et al, 1993	60.4	94.3	7.55	1.89	1.89
Carmo HF et al, 1994	82.0	80.0	30.0	7.0	9.0
Gus I et al, 1995	84.3 Migr 93	56.0	11.8	11.8	7.8
Silva CH et al, 1999	57.6 Migr 64.0	50.4	34.8	1.6	1.5
Spelling PF et al, 2000	59.3	66.7	49.4	1.2	0
Torres RPA et al, 2000	74.6	43.4	14.8	0.8	0.6
Borges F et al, 2005	21.4 Migr 52.4	69.7	6.1	N/R	N/R
Terreri MT et al, 2006	70.5 Migr 72.8	50.8	35.2	2.6	2.1
Paulo LTSP et al, 2009	70.0 Migr 72.0	46.5	35.0	3.0	2.0
Total	63.6	52.0	27.7	2.0	1.8

N/R – not reported. Migr – classical migratory arthritis

Table 3
Incidence of minor criteria for rheumatic fever and streptococcal evidence in the studies analyzed

Author	Minor criteria				Streptococcal evidence
	Fever (%)	Arthralgia (%)	Increased PR interval (%)	Elevated inflammatory activity assays (%)	ASLO (%)
Laus E, 1980	N/R	N/R	N/R	N/R	N/R
Baião TL et al, 1993	73.6	22.6	7.5	75.5	62.3
Carmo HF et al, 1994	N/R	N/R	N/R	77.0	56.0
Gus I et al, 1995	80.4	N/R	N/R	70.5	62.7
Silva CH et al, 1999	58	43.5	N/R	63.2	63.5
Spelling PF et al, 2000	N/R	N/R	N/R	71.8	48.7
Torres RPA et al, 2000	N/R	N/R	N/R	N/R	84.5
Borges F et al, 2005	N/R	N/R	12.0	61.6	58.6
Terreri MT et al, 2006	N/R	N/R	N/R	70.1	68.1
Paulo LTSP et al, 2009	N/R	N/R	N/R	N/R	N/R
Total	60.2	42.2	10.4	65.9	68.0

N/R – not reported

Table 4

Incidence of increased inflammatory activity assays among patients with rheumatic fever in the studies analyzed

Author	Elevated ESR (%)	Elevated CRP (%)	Elevated mucoproteins (%)	Elevated alpha-2 globulin (%)	Elevated alpha-1 acid glycoprotein (%)	Elevated gamma globulin (%)
Laus E, 1980	N/R	N/R	N/R	N/R	N/R	N/R
Baião TL <i>et al</i> , 1993	75.47	64.15	71.07	73.53	N/R	N/R
Carmo HF <i>et al</i> , 1994	77.0	N/R	70.0	58.0	N/R	N/R
Gus I <i>et al</i> , 1995	N/R	70.5	82.3	N/R	N/R	N/R
Silva CH <i>et al</i> , 1999	63.2	N/R	N/R	N/R	N/R	N/R
Spelling PF <i>et al</i> , 2000	71.8	N/R	57.5	55.5	N/R	N/R
Torres RPA <i>et al</i> , 2000	N/R	N/R	N/R	N/R	N/R	N/R
Borges F <i>et al</i> , 2005	N/R	24.2	61.6	N/R	N/R	N/R
Terreri MT <i>et al</i> , 2006	70.1	26.2	N/R	N/R	45.8	65.2
Paulo LTSP <i>et al</i> , 2009	N/R	N/R	N/R	N/R	N/R	N/R
Total	66.1	36.5	66.5	61.3	45.8	65.2

N/R – not reported.

Table 5

Incidence of electrocardiographic, echocardiographic, and radiological changes among patients with rheumatic fever

Author	Abnormal ECG (%)	Abnormal Echo (%)	Abnormal chest X-ray (%)
Laus E, 1980	N/R	N/R	N/R
Baião TL <i>et al</i> , 1993	75.5	N/R	N/R
Carmo HF <i>et al</i> , 1994	N/R	N/R	N/R
Gus I <i>et al</i> , 1995	N/R	N/R	N/R
Silva CH <i>et al</i> , 1999	56.8	18.3% without clinical carditis	22.2
Spelling PF <i>et al</i> , 2000	N/R	N/R	N/R
Torres RP <i>et al</i> , 2000	N/R	N/R	N/R
Borges F <i>et al</i> , 2005	30.3	N/R	20.2
Terreri MT <i>et al</i> , 2006	N/R	6.7% without clinical carditis	N/R
Paulo LTSP <i>et al</i> , 2009	58.0	13.0% without clinical carditis	42.0
Total	55.6	15.5	25.7

N/R – not reported.

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