RHEUMATIC FEVER: A MULTICENTER STUDY IN THE STATE OF SÃO PAULO

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SUMMARY: Rheumatic fever is still the most commonly seen rheumatic disease in Brazilian pediatric rheumatology clinics. It remains a significant health problem since subsequent cardiac sequelae represent one of the most important causes of chronic heart disease in children. We reviewed the clinical manifestations of rheumatic fever in 786 patients, followed at seven pediatric rheumatology clinics in the state of São Paulo, Brazil. All patients were diagnosed according to revised Jones' criteria. Regarding major criteria, 396 (50.4%) children exhibited carditis, 453 (57.6%) polyarthritis, 274 (34.8%) chorea, 13 (1.6%) erythema marginatum, and 12 (1.5%) subcutaneous nodules. Valvular lesions documented by echocardiography in the absence of accompanying auscultatory findings were found in 144 (18.3%) patients. Migratory polyarthritis was observed in 290 (64.0%) patients with articular involvement. Documented previous streptococcal infection assessed by serum antistreptolysin (ASO) titers occurred in 531 (67.5%) patients. Even though prophylaxis with benzathine penicillin was recommended to all patients, recurrent attacks were observed in 147 (18.7%). We emphasize the high frequency of chorea, silent carditis and recurrences in our series as well as the variable clinical presentation of arthritis in rheumatic fever. Multicenter studies should be encouraged to improve our understanding of the clinical features of rheumatic diseases in children and adolescents.

DESCRIPTORS: **Rheumatic fever. Epidemiology. Cardic disease. Department of Rheumatology. Pediatrics Society of São Paulo.**

Rheumatic fever (RF) and rheumatic heart disease represent an important health problem in several parts of the world. In developing countries, rheumatic heart disease is the most common cause of heart disease in persons younger than 40 years and, at more advanced ages, it is exceeded only by arterial hypertension and coronary disease[9,22,24]. The disease is associated with significant mortality and morbidity rates resulting in major individual, family, and social consequences. According to Brazilian Health Ministry data, over a period of 18 months including 1995 and the second semester of 1996, 18,500 cases of RF were treated, resulting in 1.8 million medical visits and 4500 cardiac surgeries, with a cost of R$19 million[18]. Thus, the socioeconomic cost of RF is high. Patients and their relatives suffer the physical and psychological consequences of this disease, and affected individuals are often unable to work during the most productive time of their lives. Furthermore, extensive financial resources are necessary for the medical and surgical treatment of these patients[20].

Few studies have dealt with the general epidemiological situation of RF in Brazil[1,4,7,10,11,16,19]. However, RF is known to be the most common connective tissue disease in the various pediatric rheumatology centers in Brazil[15]. Clinical-epidemiological differences between various geographic areas, even within the same country, fundamentally result from socioeconomic-cultural variations[6,7,22].

The objective of the present study was to investigate the clinical characteristics of patients with RF seen at seven pediatric rheumatology centers in the State of São Paulo.

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PATIENTS AND METHODS

We studied retrospectively the medical records of 786 children and

adolescents with a diagnosis of RF (modified Jones criteria[21], and exclusion of other diseases with a similar clinical course) seen at seven Pediatric Rheumatology centers in the State of São Paulo from January 1989 to December 1994. Five of the centers are located in the capital city, and two are located in nearby cities--one in Ribeirão Preto and the other in Botucatu (Table 1). Children with incomplete hospital records or with insufficient information for diagnostic confirmation were excluded. A single protocol was est0ablished for use by the participating centers for the study of the following demographic, clinical, and laboratory characteristics: age, sex, initial diagnosis prior to admission, frequency of major and minor Jones criteria, number of recurrences, evidence of previous streptococcal disease reflected by the presence of antistreptococcal antibodies (antistreptolysin O - ASLO - at titers higher than 300 U/Todd), or a positive throat culture for Group A beta-hemolytic streptococcus.

The diagnosis of carditis was based on the presence of at least one of the following manifestations: a heart murmur compatible with valvular disease, cardiomegaly, cardiac insufficiency, and pericarditis. The diagnosis of carditis was not made in the absence of clinical manifestations, even when echocardiography showed evidence of valvular disease.

RESULTS

A total of 786 patients fulfilled the proposed inclusion criteria: 404 boys (51.3%) and 382 girls (48.7%), with an average age of 9.4 years (range: 3 to 17 years).

Most of the patients (734, 93.3%) received an initial correct diagnosis of RF, whereas 52 patients (6.7%) first received other diagnoses such as reactive arthritis, juvenile rheumatoid arthritis, nonspecific muscle-skeletal pains, and septic arthritis.

Regarding the major criteria of Jones, arthritis was present in 453 patients (57.6%), carditis in 396 (50.4%) and chorea in 274 (34.8%). Erythema marginatum and subcutaneous nodules were observed in only 13 (1.6%) and 12 (1.5%) of the patients, respectively (Table 2).

Typically migratory polyarthritis occurred in 290 children (64.0%) with joint involvement.

One hundred and forty-four patients (18.3%) presented echocardiographic changes suggestive of valvular disease, with no correlated clinical manifestations.

Of the 396 children with cardiac involvement, according to Jones criteria, 119 presented cardiac failure (30.0%), and 39 (9.8%) presented pericarditis. Electrocardiographic and radiological changes were observed in 225 (56.8%) and 88 (22.2%) patients, respectively. Considering the 540 children with a diagnosis of rheumatic carditis (396 children) or with only echocardiographic changes (144 children), the type of valvular damage

Table 1 – Pediatric rheumatology services involved in the collaborative study.

	N (%)
Escola Paulista de Medicina – UNIFESP	231 (29.4)
Instituto da Criança da Faculdade de Medicina da USP	158 (20.1)
Faculdade de Medicina de Ribeirão Preto da USP	113 (14.4)
Faculdade de Ciências Médicas da Santa Casa de São Paulo	105 (13.4)
Faculdade de Medicina de Botucatu – UNESP	75 (9.5)
Hospital Municipal Infantil do Menino Jesus de São Paulo	52 (6.6)
Hospital dos Servidores Públicos de São Paulo	52 (6.6)
Total	786 (100)

Table 2 – Rheumatic fever patients exhibiting Jones[21] criteria symptoms (N_{total} = 786)

Characteristic	N	(%)
Major Criteria		
Carditis	396	50.4
Arthritis	453	57.6
Chorea	274	34.8
Erythema marginatum	13	1.6
Subcutaneous nodules	12	1.5
Minor Criteria		
Fever	456	58.0
Arthralgia	342	43.5
ESR elevation	497	63.2
ASLO elevation	499	63.5

most frequently observed was mitral insufficiency (409 patients, 75.7%), followed by aortic insufficiency (136 patients, 25.2%), tricuspid insufficiency (49 patients, 9%), and aortic stenosis (6 patients, 0.1%). Pulmonary insufficiency and tricuspid stenosis occurred in only three and one patients, respectively.

With respect to the minor Jones criteria, 456 patients (58.0%) presented fever, 342 (43.5%) arthralgia, and 497 (63.2%) an increased blood sedimentation rate (ESR) (Table 2).

Elevated levels of antistreptococcal antibodies detected with antistreptolysin-O were observed in 499 (63.5%) of the patients.

One hundred and forty-eight patients (18.8%) presented at least one recurrence of RF. Two recurrences were observed in 20 patients, three in 12, and four in two.

DISCUSSION

Despite the recrudescence of RF in developed countries, the United States in particular, starting from the second half of the 1980 decade, it is in underdeveloped countries that this disease is associated with high morbidity and mortality[22]. A low socioeconomic-cultural level, precarious living conditions, inadequate primary health care services, and the delayed and inadequate treatment of airway infections possibly represent the factors leading to this unfavorable picture[26].

In general, the clinical and laboratory characteristics observed in the pre ent study are similar to those reported in the literature[24], especially concerning Brazilian series (Table 3).

The present results indicate a worrisome epidemiological picture with respect to RF in the State of São Paulo. This series contains one of the largest number of children and adolescents with RF reported in the literature. Although the number of recurrences in this study was definitely underestimated, and the number of reported recurrences was very high (18.8%).

The World Health Organization recommends that both the initial outbreak and the recurrences of RF could be prevented through therapeutic strategies aimed at adequate treatment of streptococcal infections, i.e., through primary prophylaxis. Importantly, they recommend that these strategies should be easy to execute and of low cost[26].

The example of the program of RF prevention in Costa Rica is instructive. In that country, the indiscriminate treatment of all patients with tonsillitis with benzathine penicillin resulted in a reduction from 94 new RF cases in 1970 to 4 new RF cases in 1991[2].

Thus, it is urgently necessary to identify responsible local governmental strategies for offering the population an immediate and effective treatment of streptococcal infections of the throat, in concert with programs supporting secondary RF prophylaxis[3]. In addition, it should be determined whether faulty secondary prophylaxis results from the ineffectiveness of current approaches and/or from lack of treatment compliance[8].

In the present study, the initial RF diagnosis was correct for most cases. Other diagnostic hypotheses were raised for only 6.6% of cases. These data confirm that the diagnosis of RF usually does not present major difficul-

Table 3 – Frequency of the major and minor Jones' criteria in different locations.

	Total	Arthritis	Carditis	Chorea	Erythema marginatum	Subcutaneous nodules
	n	%	%	%	%	%
Salt Lake City (EUA)[25]	74	62	72	30	4	8
Italy[5]	85	43	42	5	6	1
India[12]	70	67	38	11	1	4
Florianópolis[4]	53	60	94	7.5	1.8	1.8
Goiânia[7]	52	82	80	30	7	9
Porto Alegre[11]	51	84.3	56	11.8	11.8	7.8
Ribeirão Preto[19]	120	77	79	32	1.7	2.5
Uberlândia[10]	148	53	70	41	3	3
São Paulo*	786	57.6	50.4	34.8	1.6	1.5

* present study

ties, especially when Jones criteria are used in a correct manner, although other diseases such as juvenile rheumatoid arthritis, systemic lupus erythematosus, and acute lymphoblastic leukemia may satisfy the same criteria.

Despite the importance of the Jones criteria for the diagnosis of RF, especially in the initial outbreaks, their interpretation is limited in medical practice in some specific clinical situations. For example, what is the meaning of the mitral regurgitation identified only by echocardiogram without the detection of a heart murmur upon auscultation during an acute RF episode? The frequency of carditis in the present study was similar to that reported by others (Table 3). However, if we consider isolated echocardiographic changes to be also carditis, especially mitral reflux without a corresponding heart murmur upon auscultation (silent mitral regurgitation), the frequency of cardiac involvement increases from 50.4% to 68.7%.

The American Cardiology Association supports the use of the criteria of carditis established by Jones about 50 years ago, considering the echocardiogram as a complementary method for the clinical diagnosis[21]. It does not seem to make sense to reject the findings of a sensitive and objective technique for the characterization of valvular lesion. Indeed, some cardiologists that specialize in echocardiography state that echocardiography can differentiate between physiological and pathological mitral reflux[17].

Chorea occurred in 34.8% of the cases studied. This frequency is relatively elevated compared to that observed in developed countries in the 1950's and 1960's, but seems similar to increased frequency of chorea observed in epidemics in the United States and especially observed recently in countries like Australia[22]. Chorea can be easily recognized, and a neurologist or rheumatologist is immediately contacted for medical care, since the embarrassing involuntary movements, the emotional lability, and the obsessive-compulsive disorders associated with the condition cause a profound discomfort to the child and his relatives[23]. However, it is probable that variations in the frequency of chorea between regions of the same country or between different countries result from differences between streptococcal strains with a greater potential for involvement of the base nuclei.

Approximately one third of the patients with joint involvement reported here presented polyarthritis without the classical migratory characteristics, but with the presence of additive, symmetrical polyarthritis involving small joints and the spine, a poor response to non-hormonal anti-inflammatory agents, and persistence of articular manifestations for more than six weeks. These "atypical" articular manifestations have been frequently described and have been considered by some as a specific clinical entity, i.e., post-streptococcal reactive arthritis13. However, it seems reasonable to include these manifestations in the possible spectrum of articular involvement of RF14. The Pediatric Rheumatology Committee of the Pediatric Society of São Paulo does not consider

post-streptococcal reactive arthritis to differ from RF and recommends the use of secondary prophylaxis in this situation.

The confirmation of previous streptococcal infection on the basis of the elevation of antistreptococcal antibodies (ASLO) was possible in 63.5% of the patients studied. It is known that levels of these antibodies increase during the early phase of the RF outbreak[24]. Thus, ASLO elevation is expected in polyarthritis and carditis. However, ASLO is not usually elevated in isolated chorea, since this is a late manifestation of the disease. This fact may explain in part the relatively low frequency of ASLO elevation in the present study, since 34.8% of the patients studied presented chorea.

Few patients presented erythema marginatum (1.6%) and subcutaneous nodules (1.5%). The low frequency and lack of specificity of these manifestations confirmed with several studies[24] suggest that, with respect to these signs, the major criteria for the diagnosis of RF (Jones criteria) should be revised.

CONCLUSION

In conclusion, the large number of outbreaks and recurrences of RF observed in the present study indicates an unfavorable situation for this disease in the State of São Paulo. Educational public health policies and effective programs aiming at primary and secondary prophylaxis of RF involving pediatricians, cardiologists, rheumatologists, and other health workers should be implemented within a short period of time.

RESUMO

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SILVA, C. H. M. da e col. - Febre reumática: Um estudo multicêntrico no estado de São Paulo. **Rev. Hosp. Clin. Fac. Med. S. Paulo 54** (3): 85 - 90,1999.

A febre reumática é a doença do tecido conectivo mais comum no nosso meio e caracteriza-se, sobretudo, pelo elevado custo social e econômico decorrente da cardiopatia reumática. Com o objetivo de analisar as características clínicas desta doença, foram estudados, retrospectivamente, os prontuários de 786 crianças diagnosticadas de acordo com os critérios de Jones e cadastradas em sete serviços de Reumatologia Pediátrica do Estado de São Paulo. Com relação aos critérios maiores, 396 (50,4%) apresentaram cardite; 453 (57,6%), artrite; 274 (34,8%), coréia; 13 (1,6%), eritema marginado e 12 (1,5%), nódulos subcutâneos. Poliartrite migratória clássica ocorreu em 290 crianças (64,0%) com comprometimento articular. Cento e quarenta e quatro (18,3%) dos pacientes apresentaram alterações ecocardiográficas sugestivas de valvopatia, sem manifestações clínicas associadas. A elevação dos títulos de antiestreptolisina-O foi evidenciada em 531 pacientes (67,5%). Apesar da profilaxia secundária recomendada, 147 (18,6%) crianças apresentaram ao menos uma recorrência. As elevadas freqüências da coréia, de alterações cardíacas subclínicas detectadas pelo ecocardiograma e ainda de recorrências, bem como a grande variabilidade da apresentação clínica da artrite da febre reumática, merecem ser destacadas e ressaltam a importância dos estudos multicêntricos para determinar o comportamento das patologias de modo geral e, em particular da patologias reumáticas na infância.

DESCRITORES: **Febre reumática. Epidemiologia. Cardite reumática.**

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APPENDIX: STUDY GROUP

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