

ACUTE RHEUMATIC FEVER IN THE SOUTHEASTERN METROPOLITAN AREA OF SANTIAGO, CHILE, 1976-1981¹

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A study of 230 acute rheumatic fever cases was conducted at Santiago's Sótero del Río Hospital in order to help enlarge the fund of information available on rheumatic fever in Chile. This article reports the results of that study.

Introduction

By the beginning of the 1970s, a number of Chilean authors (1,2,3) had provided information about rheumatic fever in its various forms. The general picture provided by that information was as follows:

The disease prompted a total of 40,000 medical consultations per year (4.4 per 1,000 inhabitants), generated 5,000 hospital admissions per year (54.5 per 100,000 inhabitants), and gave rise to 160 disability pensions per year (10.9 per 100,000 eligible persons). It also caused 790 deaths, giving Chile a mortality of 8.4 deaths per 100,000 inhabitants—the highest recorded mortality from this cause in Latin America.

The disease affected mainly younger age groups; 54% of the hospitalized patients were under 25 years of age, and the average age of those dying from this cause was 43 years.

Some 40% of the hospitalized fatal cases occurred in Santiago. In all, the risk of hospitalization and death from this cause was 29% higher among women than among men. A definite as-

sociation was found between occurrence of the disease and the seasons of the year, but no clear link between disease incidence and geographic areas was detected.

As of the beginning of the 1970s overall mortality was considerably lower than it had been in the 1930s and 1940s, when the average recorded mortality was 12.3 deaths per 100,000 inhabitants. However, rates of hospital admission for this cause were about the same in the two periods.

Regarding the streptococcal infection presumed to give rise to the disease, it was established (2) that the rate of pharyngeal carriers was 19% among children two to 15 years old, and that the monthly incidence of clinical infection was 3%. However, when this infection was investigated by determining serum antibody titers in a second control visit,⁴ an incidence of recent infection on the order of 15% was detected (2). Within this context, it should be mentioned that four-fifths of those manifesting symptoms had not consulted a physician, and of those who did so only half had received proper treatment.



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The study reported here was undertaken for the purpose of learning more about the prevailing rheumatic fever situation in Chile. It was designed as an exploratory study directed at defining the

⁴An anti-streptolysin O titer of 200 or more was considered positive.

epidemiologic characteristics of the disease within Santiago's Southeastern Metropolitan Health Service Area during the period 1976-1981.

Materials and Methods

The study population included all patients hospitalized during the years 1976-1981 in the medical and pediatric departments of the Sótero del Río Hospital who had been clinically diagnosed, using Jones' modified criteria (4) for guidance, as having acute rheumatic fever. This group consisted of 217 patients who had suffered 230 episodes of acute rheumatic fever during the study period. (The data to be presented refer to these specific episodes rather than to individual patients.)

All of the patients underwent a standardized examination procedure consisting of (a) procurement of a detailed medical history by a physician; (b) study of the patient's socioeconomic status and of home contacts by a field nurse; (c) general laboratory tests including a hemogram, sedimentation (ESR), and specific tests such as an electrocardiogram (ECG), a chest X-ray, a pharyngeal smear culture, and tests for determining levels of anti-streptolysin O (ASO), anti-DNase-B (ADB), and anti-streptozyme (ASTZ); (d) development of an ad hoc treatment plan; and (e) collection of data on the clinical and laboratory evolution of the episode.

The criteria used to identify major and minor

Jones manifestations were in accord with the recommendations of the American Heart Association (4), the World Health Organization (5), and Markowitz (6).

Isolation and identification of beta-hemolytic streptococcus (BHS) was accomplished by means of the technique recommended by Facklam (7). Streptococcal antibody titers were determined using the Rantz and Randall technique for ASO (8), the technique recommended by Wampole Laboratories, USA, for ADB (9), and the technique recommended by Bisno and Ofek for STZ (10). An ASO titer of 333 or more Todd units, an ADB titer of 480 or more ADB units, an ASTZ titer of 200 or more STZ units, and any positive response involving a change of more than two tube-dilutions in consecutive samples were all regarded as significant.

Results

General Characteristics of the Study Population

Tables 1 through 5 show basic data (patient age, sex, residence area, and socioeconomic status; and year and season of occurrence) about the 230 acute rheumatic fever episodes involving hospitalization during the study period. The socioeconomic classification of the patients (see Table 5) was based on the observable situation, the percentage of family-group members under

Table 1. The distribution of the 230 acute rheumatic fever cases studied according to the patient's age group and sex.

Age of patient (in years)	Sex of patient					
	Male		Female		All cases	
	No. of cases	%	No. of cases	%	No. of cases	%
≤ 4	2	0.9	1	0.4	3	1.3
5-9	19	8.3	11	4.8	30	13.0
10-14	49	21.3	59	25.7	108	47.0
15-19	15	6.5	28	12.2	43	18.7
20-24	8	3.5	18	7.8	26	11.3
25-29	3	1.3	7	3.0	10	4.3
≥ 30	4	1.7	6	2.6	10	4.3
Total	100	43.5	130	56.5	230	100.0

Table 2. The years of occurrence of the 230 acute rheumatic fever cases studied, showing the case rate for residents of southeastern Santiago served by the Sótero del Río Hospital.

Year	No. of cases	Rate per 100,000 inhabitants
1976	54	9.15
1977	72	12.20
1978	29	4.91
1979	24	4.06
1980	22	3.73
1981	29	4.91
Total	230	6.50 per year

Table 3. Distribution of the 230 study cases among the municipalities of the Southeastern Santiago Health Area served by the Sótero del Río Hospital.

Municipality	No. of cases	% of cases	Rate per 100,000 inhabitants
La Granja	97	42.2	31.9
La Florida	61	26.5	43.1
Puente Alto	61	26.5	48.1
Pirque	2	0.9	23.0
San José	2	0.9	19.4
Others	7	3.0	—
Total	230	100	38.9

Table 4. Seasonal distribution of the 230 study cases.

Season	Cases	
	No.	%
Summer	36	15.7
Fall	67	29.1
Winter	65	28.3
Spring	62	27.0
Total	230	100

Table 5. Distribution of the 230 study cases by the patient's socioeconomic status.

Patient's socioeconomic status	Cases	
	No.	%
Class I	53	23.0
Class II	62	27.0
Class III	75	32.6
Class IV	19	8.3
No data	21	9.1
Total	230	100

15 years of age, and the degree of crowding in the home (the number of residents per bedroom and per bed). Each episode involving the same patient was considered separately.

Overall, the study population was found to have a slight predominance of women and a marked predominance of people in relatively young age groups. The number of admissions tended to decline during the study period. Most of the cases came from the more urban communities in the study area (the highest rate occurring in Puente Alto); and the rate of illness episodes was found to be comparable in the fall, winter, and spring, and to decline significantly in the summer. Regarding the subjects' socioeconomic status, most were found to fall into the next to the lowest category (III); the most commonly determined levels of room and bed occupancy were in the ranges of 2.1-4.0 people per bedroom and 1.1-2.0 people per bed. No clear associations were found between any of these variables.

Medical Histories

Table 6 shows the number of cases studied that had a definite or positive prior history of streptococcal infection. The diagnosis was regarded as definite if the patient had experienced scarlet fever or odynophagia accompanied by fever. Of the 18 patients with definite case histories of previous streptococcal infection, 14 had consulted a physician and 10 of these had received treatment appropriate for eliminating the infection (11).

Table 7 provides a breakdown of cases where the patient's history indicated one or more past episodes of acute rheumatic fever. Of the 48 cases where definite prior episodes appear to have occurred, two involved episodes occurring before age five, 42 involved episodes occurring between five and 14 years of age, and four involved episodes that occurred after age 15. In 22 cases the last previous episode occurred more than five years before the present one. None of these patients was receiving prophylactic treatment at the time of the latter episode; however,

Table 6. Distribution of the 230 study cases according to whether the patient's history indicated that the case in question involved previous streptococcal infection.

History data	Cases	
	No	%
Definite prior streptococcal infection	18 ^a	7.8
Doubtful but possible prior infection	93	40.4
No evidence of prior streptococcal infection	119	51.7
Total	230	100

^aIncludes one case of scarlet fever and 17 cases of febrile odynophagia.

Table 7. Distribution of the 230 study cases according to whether the patient's history indicated one or more previous episodes of acute rheumatic fever.

History data	Cases	
	No.	%
Definite previous episode(s):	48	20.9
1 previous episode	32	13.9
2 previous episodes	5	2.2
3 previous episodes	7	3.0
4 or more previous episodes	4	1.7
Doubtful previous episode(s)	6	2.6
No previous episode	176	76.5
Total	230	100

in four cases any prophylactic treatment that would have been indicated in accordance with Health Ministry standards (12) would have been completed before the latest attack occurred.

Data on prior prophylaxis indicated by patient histories are shown in Table 8. It is noteworthy that six patients had their present illness episode despite receiving regular prophylactic treatment up to the month preceding that attack; four of these patients had cases of chorea and two had rheumatic carditis.

Regarding the interval between the appearance of symptoms and hospitalization, some

30% of the patients were hospitalized within seven days of the appearance of symptoms, 43% between seven and 21 days after the appearance of symptoms, and the remaining 27% over 28 days after the appearance of symptoms.

Table 8. Prophylaxis provided during previous episodes in the 48 instances where the patient's history indicated that one or more previous episodes occurred.

Prophylaxis provided	Cases	
	No	%
Regular prophylaxis (penicillin) ^a	6	12.5
Irregular prophylaxis (penicillin) ^b	29	60.4
Sulfa drug prophylaxis ^c	1	2.0
No prophylaxis	12	25.0
Total	48	100

^aProphylaxis with benzathine penicillin at regular 28-day intervals.

^bProphylaxis with benzathine penicillin that was deemed irregular because the patient came one or more days late or missed clinic appointments altogether.

^cProphylaxis with daily doses of sulfadiazine.

Clinical and Laboratory Findings

Data obtained from examination of the patients and performance of the aforementioned laboratory tests are shown in Table 9. In addition, the numbers of cases meeting the modified Jones criteria, together with the reasons why 23 cases clinically classified as acute rheumatic fever failed to meet these criteria, are indicated in Table 10. It should also be noted that on the basis of the available evidence, 57 (24.7%) of the study cases were classified as definite recurrences, 157 (68.3%) were classified as definite first episodes, and 16 (7%) were classified as doubtful episodes.

Table 9. Numbers of the 230 study cases exhibiting major Jones manifestations, minor Jones manifestations, and clinical or laboratory evidence of streptococcal infection.

	Cases	
	No.	%
<i>Cases with the following major Jones manifestations:</i>		
Carditis	102/230	44.3
Polyarthritits	162/230	70.4
Chorea	35/230	15.2
Erythema marginatum	3/230	1.3
Subcutaneous nodules	9/230	3.9
<i>Cases with the following minor Jones manifestations:</i>		
Elevated erythrocyte sedimentation rate	201/228	88.2
Fever	160/230	69.6
Polyarthralgia	159/230	69.1
Prolonged PR interval	49/217	22.6
Leukocytosis	84/228	36.8
History of acute rheumatic fever	48/230	20.9
Presence of rheumatic heart disease	45/230	19.6
<i>Cases with clinical or laboratory evidence of streptococcal infection:</i>		
Clinical evidence	1/230	0.4
Bacteriologic evidence	16/218	7.3
Serologic evidence ^a	215/217	99.0

^aPositive serologic evidence of streptococcal infection was considered to be elevation or a significant change in the titers obtained in response to at least one of the following tests: anti-streptolysin O (ASO), anti-DNase B (ADB), and anti-streptozyme (ASTZ).

Table 10. Study cases meeting or failing to meet Jones' modified criteria, together with reasons why 23 cases did not meet these criteria.

	Cases	
	No.	%
Cases meeting Jones' modified criteria	207	90.0
Cases not meeting Jones' modified criteria	23	10.0
<i>Reasons for not meeting the criteria:</i>		
<i>Doubtful carditis</i>	3	1.3
<i>Lack of any major manifestation</i>	5	2.2
<i>Insufficient evidence of streptococcal infection</i>	13	5.7
<i>Lack of evidence of streptococcal infection</i>	2	0.9
Total	230	100

Discussion and Conclusions

The distribution by age and sex of the study subjects agrees fairly well with that indicated in classical descriptions (13, 14). The significant decline observed in the annual rate of hospitalization for acute rheumatic fever is consistent with Ministry of Health data for the rest of the Santiago Metropolitan Region (15).

The authors have no explanation to offer for the differences observed between the rate of admission of patients from Puente Alto and the rate of admission of patients from other communities.

It is considered noteworthy that no significant seasonal variations were observed except for the sharp decline of cases in the summer.

In the absence of information about the socioeconomic status of the general population in the region from which the study subjects came, no meaningful epidemiologic conclusions about the study subjects' socioeconomic status can be drawn.

So far as the patients' medical histories are concerned, few of these provided firm evidence of prior streptococcal infection. However, this is not altogether surprising in view of the stringency of the criteria applied (prior scarlet fever or odynophagia accompanied by fever). This stringency seems justified, especially since the prior history data were generally provided by a member of the patient's family—a circumstance that led Jones to accept only a prior history of scarlet fever as definite evidence of previous streptococcal infection (4).

Overall, the number of patients found to have a history of definite or possible prior episodes of acute rheumatic fever (54) agrees fairly well with the number deemed to have had a confirmed recurrence on the basis of other evidence (57). This therefore appears to be a more reliable datum than that related to prior streptococcal infections.

Regarding prophylaxis, it is noteworthy that four patients who experienced recurrences had such a long time elapse between their two bouts of illness that even if prophylaxis had been prescribed in accordance with the Health Ministry's

rules, when the later attack occurred they would have been unprotected.

In addition, there were many cases in which the indicated prophylaxis was not properly completed, and other cases in which it was properly carried out but failed. For one reason or another, prophylaxis failed in 36 of the recurrent cases. In most of these cases, the failure may be explained partly by the fact that no prophylactic control program concerned with overseeing prophylaxis was operating in the area at the time prophylaxis was prescribed. Also, in four out of six instances of "true" failure of a prophylactic regimen,⁵ the patient had chorea, a circumstance that is not surprising (16).

The most frequent major Jones manifestation observed was polyarthritides (in 70.4% of the cases), followed by carditis (44.3%). There was also a high incidence of chorea (15.2%). The most frequent minor Jones manifestation was an elevated erythrocyte sedimentation rate. Among the other minor manifestations, the low percentage of cases with fever (69.6%) seems noteworthy; and even if all cases with chorea are eliminated, the percentage of cases with fever still remains relatively low (at 82%). No association was found between cases without fever and pre-hospitalization latency of the illness, a development that could otherwise have offered an explanation for the lack of fever.

Evidence of streptococcal infection, as a supplemental finding needed for compliance with the modified Jones criteria (4), was based essentially on serologic findings. These findings were 99% positive in 217 cases where at least one of the three tests employed showed a response accepted as evidence of streptococcal infection.

The bacteriologic evidence obtained was very sparse. There are three possible explanations for this: the inherent difficulty of the technique used; pre-hospitalization latency (especially since 70% of the subjects were admitted a week or more after the appearance of symptoms); and a possibly indiscriminate use of antibiotics during the latency period.

Clinical evidence of prior streptococcal infection, as accepted by Jones, was obtained in only one case—from a patient with a history of scarlet fever. The other 17 cases (where the patient had a history of febrile odynophagia) did not provide sufficient clinical evidence of prior streptococcal infection to meet the Jones criteria (see Table 6).

In sum, the modified Jones criteria were met in 207 (90%) of the 230 cases studied. The major element lacking in most cases where the criteria were not met (see Table 10) was inadequate information about streptococcal infection, because in 13 cases a complete set of serologic tests was not available or no pharyngeal smear had been taken.

Regarding the age of patients with recurrent episodes, 23 of the 57 cases involving recurrent episodes occurred among patients under 15 years of age and 34 occurred among older patients. This means that 16.3% of the 141 cases in patients under 15 were recurrent cases and 38.2% of the 89 cases in patients 15 years of age or older were recurrent cases. Our data, which indicate a significant association between the recurrences and cases of carditis ($p < 0.01$), agree with published data (6, 13, 14). Similarly, our data relating age to the frequency of recurrences agree with published data (6, 13, 14).

⁵Patients undergoing prophylaxis are required to attend a special prophylactic clinic every 28 days, where they receive an injection of benzathine penicillin G. This procedure lasts for a long time (anywhere from five years to life). Punctuality in keeping the appointments is essential, since prophylactically adequate serum levels of the drug last about 28 days (14).

Some patients carry out this procedure very rigorously. If despite this rigor they relapse, these relapses are considered true failures (In our case this happened with six patients. The other failures occurred in patients whose prophylaxis was irregular, largely due to lack of appropriate monitoring and supervision.

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SUMMARY

To help enlarge the fund of information available on rheumatic fever in Chile, 230 cases of acute rheumatic fever were investigated. All of these cases afflicted patients who were admitted to the Sótero del Río Hospital serving Santiago's Southeastern Metropolitan Health Service Area during the period 1976-1981.

Most of the patients were admitted during the initial years of the study, suggesting a marked decline in acute rheumatic fever cases over time. There was also a slight predominance of female over male patients. No significant seasonal variations were observed except for a marked drop in admissions during the summer months.

Very few of the patients had any definite previous diagnosis of streptococcal infection, although roughly 20% were found to have previously experienced acute

rheumatic fever. In general, few of these earlier cases had received adequate prophylactic treatment; but there were also a number of cases where adequate prophylaxis (based on Health Ministry standards) appeared to have failed to prevent recurrence of the disease.

Many of the patients were admitted to the hospital over a week after their symptoms had appeared. A relatively high percentage of the study patients had chorea and a relatively low percentage had fever at the time of admission. However, no association was found between pre-admission latency of the illness and lack of fever. Overall, 90% of the cases studied met the modified Jones criteria for diagnosis of rheumatic fever. Most of those that failed to meet these criteria did so for lack of sufficient evidence of streptococcal infection.

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