

EPIDEMIOLOGY AND PROPHYLAXIS OF RHEUMATIC FEVER IN DELHI—A FIVE YEAR FOLLOW-UP

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INTRODUCTION

Rheumatic fever and its sequel viz. rheumatic heart disease are serious public health problems in India as well as in many of the developing countries in the Near-East, Middle-East, Far-East and Latin America, although it has declined considerably in affluent countries. The prevalence of rheumatic heart disease in India as assessed from, all sources has been published elsewhere.^{1,2,3} In accordance with the principles for control enunciated by World Health Organization, 3 programmes are currently under way:

1. A secondary prophylaxis project, established in 1966, which is expected to serve as a model for the whole country and permit extension to other areas. This project seeks to demonstrate the feasibility of control, the cost of prophylaxis (manpower and administrative costs), the patient response e.g. missed appointments, drop-outs etc, the natural history of the disease and the applicability of the Jones criteria in a tropical country, bacteriological and immunological research in streptococcal epidemiology, training of technical personnel and physicians among others.
2. An epidemiological survey in vulnerable groups e.g. school children covering 5 centres in the country including Delhi, in which city 40,000 school children out of a total school-going population of 350,000 are involved.
3. A rheumatic fever registry started recently under the Indian Council of Medical Research.

MATERIAL AND METHODS

A total of 994 patients have been registered to date. These have been divided into two groups i.e. those on regular prophylaxis with benzathine penicillin once a month, and those receiving penicillin and other antibiotics as and when necessary for throat infection and vitamin B injections once a month. The cases were all referred from other hospitals and from general practitioners on the suspicion of rheumatic fever and/or rheumatic carditis. Cases are assigned to the prophylaxis and control programme on the first three and second three days of the week respectively. All patients undergo a thorough clinical examination including ECGs, Chest X-ray, routine hemogram, and ESR. Throat and nasal swabs are taken for culture and blood collected for ASO and AH titrations once a month. ASO titrations are carried out by the log dilution method of Robinson, Crawford and Roholt.⁴ AH titrations are carried out by Quinn's method.⁵ Streptolysin-0 is prepared in our laboratory. Other drugs such as Digoxin, diuretics, aspirin, steroids etc. are given as and when required.

RESULTS

Of the 994 patients, at the present time only 577 in the two groups are being followed up regularly. 71 patients died (7.1%), 256 patients dropped out (25.8%) and 90 patients (9.1%) were very irregular in their attendance at the clinic (Table I). This pattern has

been fairly constant over the five-year period. The age distribution of these patients shows that the majority are in the 10-14 and 15-19 year age groups. This is because of later age presentation of cases in India and because of the study being a cumulative one (Table II). Females outnumber males in the study. The lowest income groups, earning less than Rs. 250/- p.m. predominate as expected (Table III).

INITIAL DIAGNOSIS (Table V)

The initial diagnosis in the 577 referred patients was chronic valvular disease without any evidence of acute rheumatic activity in the largest number, although referred as active. Arthritis was present in the majority of the remaining, followed by chorea. During the first attack and at recurrences the largest number of patients experienced arthralgia as the main symptom followed by sore throat and fever. The next important manifestations were arthritis and acute carditis. Subcutaneous nodules and erythema marginatum were not seen at all.

MODIFIED JONES CRITERIA (Table VI)

The Jones criteria were applicable in about 54% of patients and of these there were only 14% with 2 major criteria. The vast majority had 1 major and 2 minor criteria, the latter obtained only from laboratory tests. This is of some interest because the Jones criteria are considered infrequent in tropical countries. The importance of laboratory tests in the diagnosis is evident.

GRADES (Table VII)

The patients were graded into three groups according to the evidence of acute manifestations and of pre-existing heart disease.⁷ The largest number of patients have been followed up for a period below one year, a lesser number for two years and over. The largest number of patients were in group 'C'. Patients do not seek medical advice until the disease is very advanced usually with congestive failure and reactivation. This makes the problem of follow-up even more difficult than elsewhere.

RATE OF INFECTION AND RHEUMATIC RECURRENCES (Tables VIII and IX)

As judged by streptococcal infections there was a higher rate of clinical infection, positive throat cultures and raised ASO Titres in the controls when judged for the entire group and also for the groups followed up for more than one year, the difference being of statistical significance ($p=0.01$ in both cases) and being more striking for those followed up over one year. The rates of rheumatic recurrences were also higher in the control group as against the prophylaxis group for both types of patients. A comparison of the rate of streptococcal infection and of rheumatic recurrence shows that the rates are very high in our population as compared to previous studies (Table X). Although the reasons are yet to be fully worked out, the following are thought responsible:—

Poor housing and overcrowding, with cross-infection, although not necessarily by Group A streptococci. As in Egypt, injections twice a month may be necessary.

The so-called recurrences may not be actual recurrences, as the yardsticks used to measure them are somewhat nebulous.

TYPES OF STREPTOCOCCAL INFECTION

With regard to the types of streptococcal infections encountered the control group had a higher percentage of all streptococcal isolates and higher ASO

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TABLE I
DISPOSITION OF 994 PATIENTS INCLUDED IN THE STUDY

	Prophylaxis			Control			Grand Total	%
	Male	Female	Total	Male	Female	Total		
REGULAR	142	185	327	123	127	250	577	58.0
IRREGULAR	25	11	36	31	23	54	90	9.1
DROPOUTS	55	64	119	71	66	137	256	25.8
EXPIRED	17	24	41	12	18	30	71	7.1
TOTAL	239	284	523	237	234	471	994	100.0

TABLE II
AGE DISTRIBUTION OF 577 PATIENTS

Age Group	Male	Female	Total	%
upto 5 years	2	3	5	1.0
5 - 9 years	48	26	74	12.9
10 - 14 years	110	146	256	44.9
15 - 19 years	105	137	242	42.2
TOTAL	265	312	577	100.0

TABLE III
SOCIO-ECONOMIC STATUS OF 577 PATIENTS

Income	No. of Patients	%
Rs. 100 and below	141	23.7
Rs. 101-250	261	45.6
Rs. 251-500	107	18.9
Rs. 501-750	37	6.4
Rs. 751-1000	26	4.5
Rs. 1000 and above	5	0.9
TOTAL	577	100.0

TABLE IV
INITIAL DIAGNOSIS IN 577 PATIENTS

Diagnosis	Male	Female	Total	%
Arthritis	47	42	89	13.7
Carditis	8	6	14	2.5
Chorea	7	16	23	3.9
Chronic Valvular Disease	203	248	451	79.9
TOTAL	265	312	577	100.0

TABLE VI
APPLICABILITY OF JONES CRITERIA

	Number	Percentage %
Total No. of Patients	577	100
Patients not Satisfying Jones Criteria	274	45.2
Patients Satisfying Jones Criteria	303	54.8
Patients with Two Major Criteria	82	14.2
Patients with One Major and Two Minor Criteria	221	40.6

TABLE V
RHEUMATIC MANIFESTATIONS

Signs & symptoms	Prophylaxis Group				Control Group			
	First attack		Recurrence		First attack		Recurrence	
	No.	%	No.	%	No.	%	No.	%
Arthritis	208	45.0	164	36.0	211	49.3	172	38.0
Acute carditis	79	17.0	73	16.0	76	17.0	70	15.5
Chorea	24	5.0	18	4.0	14	3.0	10	2.0
Sub-cutaneous nodules	4	1.0	Nil	0.0	3	0.7	Nil	0.0
Polyarthralgia	213	46.0	192	42.0	267	59.0	290	64.0
Fever	215	47.0	216	47.0	184	40.0	176	39.0
Sore Throat	197	42.0	236	51.5	191	42.0	220	48.6
Erythema Marginatum	Nil	0.0	Nil	0.0	Nil	0.0	Nil	0.0

TABLE VII
LENGTH OF FOLLOW-UP AND INITIAL STATUS

Period of Follow up	Group A		Group B		Group C		Total		Grand Total
	Prophy-laxis	Control	Prophy-laxis	Control	Prophy-laxis	Control	Prophy-laxis	Control	
0 - 1 yr.	19	13	7	6	97	113	123	132	225
1 - 2 yr.	9	15	3	2	68	55	80	72	152
2 - 3 yr.	7	4	2	1	50	27	59	32	91
3 - 4 yr.	1	0	1	0	32	11	34	11	45
4 - 5 yr.	11	0	0	0	20	3	31	3	34
TOTAL	47	32	13	9	267	209	327	250	577

GROUP A—No or Questionable Carditis
No Pre-Existing Heart Disease
GROUP B—Carditis present : No Pre-Existing Heart Disease
GROUP C—With definite or questionable Pre-Existing Heart Disease

TABLE VIII
STREPTOCOCCAL INFECTIONS AND RECURRENCES ENTIRE GROUP

	Prophylaxis Group	Control Group
Patient Years	516.8	350.2
Clinical Infections	1.08/Pt. Year	1.73/Pt. Year
Positive Throat Cultures	0.14	0.25
Raised ASO Titres	0.23	0.34
Recurrences	0.02	0.06

TABLE IX
STREPTOCOCCAL INFECTIONS AND RECURRENCES (FOLLOW-UP OVER 1 YEAR)

	Prophylaxis Group	Control Group
Patient Years	480.2	330.6
Clinical Infections	0.97/Pt. Year	1.11/Pt. Year
Positive Throat Culture	0.14/Pt. Year	0.23/Pt. Year
Raised ASO	0.23/Pt. Year	0.34/Pt. Year
Recurrences	0.02/Pt. Year	0.08/Pt. Year

TABLE X
PROFILE OF STREPTOCOCCAL ISOLATIONS AND ASO TITRES

	Prophylaxis Group	Control Group	Total
No. of Specimens	2988	1746	4734
Nos. and Percentage of Isolations all β.H. Streptococci	471 (15.9%)	344 (19.0%)	815 (17.4%)
Group A Streptococci	46 (10.2%)	96 (23.8%)	142 (17.9%)
No. of ASO Titres Above (233 Units)	130 (5.4%)	144 (9.6%)	274 (15.0%)

TABLE XI
GROUPS OF β HEMOLYTIC STREPTOCOCCI ISOLATED

B-Hemolytic Streptococci	Prophy-laxis	%	Control	%
Total Isolations	471		304	
Group A	41	8.7	89	29.3
Group B	22	4.7	21	6.9
C	13	2.8	21	6.9
F	36	7.6	19	6.3
G	182	66.6	132	41.6
R	1	0.2	1	0.3
Non-Groupable	44	9.4	27	8.8

TABLE XII
CAUSES OF DEATH IN 71 PATIENTS

Causes	Prophy-laxis	Control	Total
Progression of Heart Disease	15	9	24
Acute Carditis	7	4	11
Pulmonary Oedema	3	3	6
Pulmonary Embolism	5	2	7
Other Unrelated Causes	1	0	1
Causes Unknown	0	3	3
Died at Home	10	9	19
TOTAL	41	30	71

TABLE XIII
STREPTOCOCCAL INFECTIONS RATES A COMPARISON WITH OTHER STUDIES

Series	Pt. Years	Streptococcal Infection Rate (Per Pt. Year)
Massell's ¹² (1960)	214	0.05
Feinstein's ¹⁴ (1965)	560	0.06
Present Series (1966-71)	480.2	0.14

titres. Of the other groups of streptococci isolated group 'G' appear to have accounted for 314 out of 775 isolations (41.8%). The ASO titre rise was higher for group A than for non-group A isolates.⁶

Apart from the major criteria, recurrences in many patients were judged, in the absence of major criteria by arthralgia accompanied by fever or raised sedimentation rate and rise in ASO titres in the presence of pre-existing heart disease. It was also judged sometimes in the presence of evidence of streptococcal infection by change in heart size, development of new murmurs and development of congestive cardiac failure which are not always satisfactory yardsticks.

CAUSES OF DEATH

The causes of death in 71 patients are shown in Table XI. The majority of them died because of progression of heart disease which was severe from the beginning. 7 patients died following surgery for mitral stenosis.

PILOT SCHOOL SURVEY

A pilot school survey conducted among 2,544 school children within the age group 5-15 years in Delhi revealed an incidence of six per one thousand, of rheumatic heart disease. The results of the national survey are awaited.

DISCUSSION

There is evidence of a high prevalence of rheumatic heart disease in Delhi. This is specially so in vulnerable groups such as school children in whom the incidence is higher than reported elsewhere either in recent or more distant times.^{8,9,10} There is also a high dropout rate (26%) and wastage of material which cannot be avoided in developing countries. Patients present with severe heart disease on the very first visit for several reasons. One is lack of medical facilities and transportation, poverty and indifference to early symptoms. Also responsible for this is the infrequency of major symptoms such as arthritis and chorea which leaves the patient unattended until severe cardiac symptoms supervene. Feinstein et al¹¹ have reported a high percentage of initial carditis as well as residual heart disease in patients without polyarthritis or other joint manifestations as opposed to those with florid joint manifestations. In the present series the large number of patients with chronic valvular disease and polyarthralgia are pointers in the same direction. The Jones criteria were applicable only in about 55% of the patients. Only 2 major criteria were found in 14%. In the remainder the diagnosis was made in the presence of chronic valvular disease on the basis of 1 minor manifestation such as polyarthralgia and laboratory data such as raised antistreptolysin-O and erythrocyte sedimentation rates. This points to the importance of having adequate laboratory facilities in the control of rheumatic fever in developing countries.

The effect of prophylaxis is offset by the presence of severe initial carditis which runs its course in spite of prophylaxis. The amounts of residual disease, in the presence of prophylaxis is yet to be worked out in those followed up for a sufficiently long period. There is a high rate of streptococcal infection in spite of prophylaxis as judged by ASO titres and throat cultures. However all streptococcal isolations are not Group A and it has been shown that ASO titres are not as high in non Group A. Group 'G' appears to be an important cause of re-infection.

The rate of streptococcal infection is significantly higher in the control group as opposed to the prophylaxis group. The infection rate is much higher than in other studies elsewhere.^{12,13} (Table XIII). With regard to rheumatic recurrences it was often difficult to judge their presence owing to lack of major criteria. In this study the recurrence rate is also significantly higher than in other comparable studies.^{13,14} Taranta et al¹⁵ found a high rate of recurrence in those with

pre-existing heart disease being more in those with cardiomegaly than in those without it. This might be another reason for the high rate of recurrence in the present series, who were mostly in Group C of the classification used.

TABLE XIV
RHEUMATIC RECURRENCES COMPARISON
WITH OTHER STUDIES

Series	No. Patients Studies	Recurrences Rate
Stollenman (1954) ¹³	258	Nil
Feinstein (1959) ¹⁴	315	0.003/Pt. Year
Present Series (1966-71)	327	0.02/Pt. Year

Causes of death were in the great majority due to progression of initial heart disease and not due to recurrence. This has also been the case in Feinstein's studies.¹⁶ It has been stated that on prophylaxis there is a high rate of disappearance of murmurs and resolution of heart disease.¹⁷ This is yet to be worked out in the present study.

SUMMARY

1. Of 994 patients registered over a 5 year period 577 have been followed up regularly. There was a dropout rate of about 25% and death rate of 7.1%.
2. The majority were from the poorest social class and in the age group, 10-19 years, because of late presentation indifference to early symptoms and absence of florid joint manifestations.
3. Chronic valvular disease was present in the majority of cases on entry into the study and the Jones criteria were applicable in about 54% of patients. Only 18% had 2 major criteria, Febrile polyarthralgia was found to be the most important symptom both at first attack and during recurrences.
4. The majority of patients were in group 'C' i.e. with pre-existing heart disease and carditis on entry into the study. This makes them less suitable for prophylaxis.
5. Streptococcal infections were definitely lower in the prophylaxis group as compared to controls both for these followed up over one year and for the entire group as were rheumatic recurrences. The rates however, were higher than those for studies elsewhere and the reasons are discussed.
6. A pilot school survey showed a 6 per 1000 incidence of rheumatic heart disease in Delhi.
7. It would appear that in the control of rheumatic fever in the tropics the following measures are the most important.
 - (a) Maintenance of a Registry of rheumatic fever in each city or area and surveillance of known cases and prophylaxis.
 - (b) A School Health Programme to detect early rheumatic heart disease from the primary school period and prophylaxis of individuals before they develop severe heart disease.

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