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RHEUMATIC FEVER IN DEVELOPING COUNTRIES - PRESENTATION, DIAGNOSTIC CRITERIA AND SOCIOECONOMIC ASPECTS

by

Dr M.A. Najeeb

Acute Rheumatic Fever is basically a socioeconomic disease and has become almost extinct in the developed countries with the exception of certain pockets in some city slums. The disease has also become milder in these countries. Medical and non-medical factors have both been given credit for this change. The decline had occurred before the antibiotic era due to improvements in socioeconomic conditions and also due to changes in prevalence and virulence of rheumatogenic streptococcal strains. The remark that 'Rheumatic fever was on the way out but it received a definite push from medicine' is pertinent in this context. The trend predated the antibiotic era but there was a precipitous decline after 1945, which may have been the result of combined effect of improved living conditions, better medical care and antibiotics.This bonanza has however remained confined to a chosen few countries. The vast majority of the African, Asian and Latin American nations have actually become poorer during the past two centuries as a result of many factors, one of them being population explosion, and although they are being labelled as developing countries in fact the pace of their development is quite imperceptible. They are now in a hurry to catch up with the developed world and their existing socioeconomic and medical problems are being compounded by rapid industrialization and its attendant urbanisation. They are therefore in a predicament worse than that faced by the West at any point of time. They still have a large share of the communicable disease among them and there is a steep rise in the incidence of non-communicable diseases like coronary heart disease, hypertention, diabetes and cancer.

The diagnosis of rheumatic fever has become more common in these countries over the past few decades. It is possible that it was not adequately recognised during earlier times due to lack of proper medical facilities, but the increase in the incidence is to a large extent real.There is a mass scale immigration of population from rural areas to crowded city slums with overcrowding not only in homes but also in the make-shift schools and other congregational centres. Although poverty is said to be a direct determinent of the prevalence of rheumatic fever in any community, the actual manifestation of poverty that is responsible is overcrowding in substandard housing conditions. The relative immunity enjoyed by the rural population - whose percapita income is generally lower than their urban counterparts - may be due to this factor, while the higher incidence of rheumatic fever among soldiers who are well fed and well clothed is because of their overcrowded living quarters promoting the spread of streptococcal infection through close personal contact. Again the enhanced incidence of rheumatic fever during the winter months is due to the huddling together under one quilt of several children at night.The myth about ARF being a disease of temperate climates has been blown up. It is found to be equally rampant now among the tropical and subtropical countries.

Rheumatic fever is indeed very common in these countries today. Population studies in one of them showed a prevalence rate as high as 47/100,000 and a rate of 140/100,000 for the 5 - 9 year age group. The hospital incidence ranges from 1 - 3% of admissions at all ages and from 6 - 7% of hospital admissions upto 12 years of age. The prevalence of rheumatic heart disease varies from 5 - 30% of all cases of cardiopathy and 1 - 10% of children may be suffering from rheumatic cardiopathy. The wide variability is due to the particular sample of population

studied. Most data is hospital based. Community and school population studies again may be highly biased because of selection. The picture is not very different in Pakistan. A school study in Islamabad of children belonging to educated, relatively well off families living in satisfactory accommodation and studying in good schools showed a prevalence rate of 1.5 per thousand as against 11 per thousand in a remote poor mountain village of Chitral with make-shift schools. In fact school studies are highly misleading in our population because only 50% of our children go to school. Majority of the children in a hospital based study of 249 patients in National Institute of Cardiovascular Diseases, Karachi, had never attended a school.Population studies of two closely knit ethnic communities in Pakistan showed a prevalence rate of 5.9 per thousand.

It has been suggested that in the absence of reliable epidemiological data on rheumatic fever, the rheumatic to congenital heart disease ratio may indicate as to how prevalent rheumatic fever is at a given time. Congenital heart disease occurs at a constant rate of 8 - 10 per thousand live births in Pakistan, thus the incidence ratio of rheumatic heart disease to congenital heart disease may be a sensitive index reflecting prevalence of rheumatic heart disease in both hospital and population studies. This ratio was found to be 3 : 5 in the two ethnic community studies referred to earlier.

The presentation of acute rheumatic fever has been thought to be different in the tropics. It has been said that chronic valvular disease is very much more common than acute rheumatic fever and that acute rheumatic fever when seen presents an unusually mild or sub-clinical picture. The age of onset of acute rheumatic fever and rheumatic heart disease especially mitral stenosis is not the same as in the developed countries. There is also a prevailing opinion that Jones Criteria are not sufficiently sensitive because the clinical manifestations may differ significantly from those found in the Western countries. It has been suggested that arthralgia may be considered to be a major criterion in these areas. To test some of the hopothesis and misconceptions it is proposed to present a survey of the data base available in Pakistan. The studies included in this survey are:-

I) One year study of 59 episodes of ARF admitted to a postgraduate medical centre in Karachi. There were 29 male and 28 female patients in the group. Their average age when first seen was 13.3 ± 3.6 years the range being 5 - 22 years. Thirty three (58%) were seen apparently in their first attack of rheumatic fever, 23 gave a history of a previous febrile arthritis. When ages of patients in both observed and historical first attack were combined the average age at the first attack was 11.7 ± 3.5 years in 56 patients. Twenty seven of the 57 patients required more than 30 days to seek hospitalisation, 23 of these had carditis. Patients who had carditis without arthritis required an average of 88 ± 65 days for admission, while those with carditis and arthritis on admission required only 28 ± 16 days. The clinical manifestations were as under:-

i)	Carditis.	(43) 73%	Leukocytosis.	30%
ii)	Arthritis with Carditis.	(31) 53%	Raised ESR.	85%
	Isolated Arthritis.	(11) 19%	H/O. sore throat.	31%
iii)	Chorea.	(4) 7%	Raised ASOT 250 units or above.	90%
	Isolated Chorea.	(2)3.4%		
iv)	Skin Lesions.	(2)3.4%		
v)	Subcut. Nodules.	(2)3.4%		

Out of the 43 patients with carditis isolated mitral valvulitis was present in 26 and combined mitral and aortic disease in 16, one patients had isolated pericarditis. Twenty six

patients had significant cardiomegaly and 17 had frank congestive cardiac failure. Nine patients had pericarditis. It was found that in terms of age, sex, cardiopathy, duration of illness and history of previous streptococcal infection these patients did not differ remarkably from the Western series.

II) Fifty four cases of ARF admitted to an army hospital over a period of 2 years from an adult male population of a Pakistan army base were studied. Their age group ranged between 18 - 45 years, 28 cases (52%) were between the ages of 18 - 22 years, 24 cases (44%) between 23 - 45 years, one patient was aged 38 and another 45 years. The onset of illness was acute in 46 cases (85%) who sought admission after 3 days and 8 cases (15%) had an insiduous onset reaching the hospital in 5 - 7 days. The first symptom noticed was fever alone in 8 cases (15%),fever with arthritis in 45 cases (83%) and abdominal pain in one. None of the cases presented with cardiac symptoms.

The Clinical manifestations were as under:-

Polyarthritis.	(54) 100%	Fever.	(54) 100%
Carditis.	(9)16.6%	Arthralgia.	Nil.
Chorea.	Nil.	Leucocytosis.	60%
Erythema marginatum.	Nil.	Raised ESR.	100%
Subcutaneous nodules.	Nil.	H/o. Sore throat.	45%
		Raised ASOT >250 units.	66%
		Positive throat culture.	43%

The diagnosis of 45 cases in this series was based on only one major criterion i.e. polyarthritis plus some minor criteria. This set of manifestations may be found in many other diseases like rheumatoid arthritis, lupus erythematosus,osteomyelitis, leukemia, sickle cell anemia, undulant fever, gonococcal arthritis, and dysenteric arthritis. A careful search was made to elicit signs of these conditions and the combination of criteria was considered sufficient to justify a diagnosis of rheumatic fever.

The diagnosis of carditis was based on a pansystolic apical murmur grade 2/6 or more in 3 cases, an apical middiastolic murmur in 5 and an aortic diastolic murmur in one case. None showed any other manifestation of carditis viz. pericarditis, heart failure or cardiomegaly. Eight of the nine cases with carditis were under the age of 21 years.

III)The mode of presentation was analysed in a retrospective study of 249 children admitted in the National Institute of Cardiovascular Diseases, Karachi, during 1980 - 1985. The mean age at presentation was 9.7 $\pm$ 2.1 years (range 4 - 14 years). Majority of the patients came from poor communities of Karachi city, despite the fact that the Institute gets frequent referrals from the interior of the country. The presenting features of the 249 patients were as under:-

Acute Rheumatic Fever:

Group I.		+ve history, + ve lab	95	(38.2%)
	a)	With Carditis	83	
	b)	Without Carditis	12	
Rheumatic Fever with Carditis:				
Group II.		+ve history -ve lab	134	(53.8%)
	1)	+ve history less than 5 months	20	
	2)	+ve history more than 8 months	74	
	3)	+ve history ?duration	40	

Chronic (Recurrent) Rheumatic Carditis:

Group III.

-ve history -ve lab. 20 (8.0%)

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The group I patients ARF was diagnosed by a history of arthritis/arthralgia, carditis, raised ESR. Sixty nine of the 95 patients had their first episode of ARF and 26 presented with recurrent ARF. Eighty three of the 95 patients had carditis, while 12 out of the 69 first episode ARF did not have evidence of carditis.

The second group of 134 patients had evidence of carditis with a positive history of joint pains and fever but without any rise in ESR or ASOT . The duration of symptoms varied between less than 5 months to over 8 months in 94 and was undetermined in 40.

The third group presented with evidence of valvulitis without any preceding history and with ESR and ASOT within normal ranges.

The most frequent valvular lesion detected was mitral insufficiency (59.8%), isolated mitral stenosis and aortic regurgitation were found in 8.4% and 4% respectively. Mitral stenosis alone or in combination with other lesions was present in 53 (21%) cases in which the mean age was 9.9 ± 2.3 years range 7 - 14 years.

These patients were followed up and it was found that the majority of them remained either unimproved or showed actual deterioration in the severity of cardiopathy. About fifty percent were admitted twice or more often due to recurrent episodes of cardiac decompensation or recurrent acute rheumatic fever. It is apparently due to non-compliance with treatment as well as penicillin prophylaxis.

IV) One year (1985) admission of ARF in the Department of Paediatric Medicine, National Institute of Child Health, Karachi, in which 35 cases were initially suspected but finally 20 cases were proven to be suffering from ARF. The male female ratio was 4:1. Ten cases occurred between the age of 5 - 7 years, 8 between 7 - 10 years and only 2 cases were above the age of 10 years. Eighteen patients (90%) were admitted between 1 - 8 weeks of onset of symptoms. Nine patients (54%) presented during the first episode and 11 (53%) with history of a previous attack.

The clinical manifestations were as under:-

Arthritis.	(6)	30%	Raised ESR.	(14)	70%
Carditis.	(7)	35%	H/o. Sore throat.	(3)	15%
Arthritis and Carditis.	(3)	15%	Raised ASOT ($\geq$333 units).	(4)	20%
Chorea.	(4)	20%			
S.C. Nodules.		0%	Positive throat culture.	(2)	10%
Erythema Marginatum.		0%			

Two cases presented with pericarditis, cardiomegaly, congestive cardiac failure and significant murmurs, while one presented with pericarditis, congestive cardiac failure and significant murmurs. One patient had cardiomegaly, congestive cardiac failure and significant murmurs, three had congestive cardiac failure with significant murmur and another three presented with a significant murmur only.

Mitral incompetence was present in five cases (25 percent). Mitral Stenosis was present in one case only (5 percent). Mitral Stenosis with incompetence was present in two cases (10 percent.).

V) A retrospective study of cases of acute rheumatic fever admitted to adult cardiology wards of National Institute of Cardiovascular Diseases, Karachi, during 1981 - 86 has been carried out. The total number of patients was 140, aged 12 to 44 years - mean age 28 years. Male female

ratio was 48 to 52. Eighty four percent of the patients were from the lower strata of society. Seventy percent gave a history of previous RF/RHD.

The clinical manifestations were:-

Carditis.	(115) 82.14%	Fever.	(82) 58.6%
Polyarthritis.	(56) 40 %	Arthralgia.	(31) 22 %
S.C. Nodules.	(7) 5 %	Previous RF/RHD.	(98) 70 %
E. Marginatum.	(4) 2. 8%	Leucocytosis.	(22) 15.7%
Chorea.	(3) 2. 1%	Raised ESR.	(111) 79.3%
		H/o.Sore throat.	(65) 46 %
		Raised ASOT.	(140)100 %

All the patients in this group had evidence of chronic rheumatic valvular diseases. Mitral stenosis alone was present in 46 (33%) mitral regurgitation in 18 (13%) and aortic regurgitation in 11 (8%). Mitral stenosis with mitral regurgitation was found in 26 (18.5%), mitral stenosis with aortic regurgitation in 7 (5%), mitral regurgitation with aortic regurgitation in 14 (10%) and mitral stenosis, mitral regurgitation and aortic regurgitation in 18 (13%). The most frequent valve involved was mitral and the most frequent lesion was mitral stenosis. Manifestations of cardiac failure were present in 54 (38.6%) and evidence of pericarditis in 14 (10%). Thirty percent of the cases in this series gave no definite history of a previous attack suggestive of acute rheumatic fever or chronic rheumatic carditis, but all the rest had a history of one or more recurrences of ARF or cardiac decompensation. The duration of their presenting symptoms before admission to hospital varied from weeks to months. The majority of these patients had failed to comply with penicillin prophylaxis.

This is a heterogenous group of studies, but it does indicate the main trends in the modes of presentation and diagnostic criteria having valid applications in the diagnosis of acute rheumatic fever and rheumatic heart disease in our geographic setting. There is an apparent variation in the mode of presentations in these cases as compared to those seen in the developed countries. ARF occurs at an earlier age in the developing countries and an onset between 3 - 5 years of age is not uncommon. RHD is common under the age of 20. The reason for this increased susceptibility may be a higher incidence of streptococcal infections with greater rheumatogenicity and virulence, lack of immunity which may be heightened by malnutrition and as yet undetermined genetic predisposition. The clinical features of rheumatic fever including those of carditis become modified and the laboratory parameters have returned to normal by the time they seek medical advice. Moreover the history of preceding symptoms and its timing is often not precisely recalled. Most of the patients in our series therefore presented with symptoms resulting from carditis namely cardiac decompensation rather than fever and joint pains. The main reason for this variation is the delay in reaching a medical facility from the initial onset of symptoms. This delay may extend over several months in which active rheumatic process continues. These patients may be regarded as having'chronic'rheumatic fever.

However this variation in presentation does not mean that the symptomatology is fundamentally different - it has indeed been modified because of lack of early detection thus depriving the patient of medical care which may have changed the sequence of events. It may therefore be justifiably asserted that the mode of presentation and diagnostic criteria for ARF do not differ essentially from the series reported in the West a few decades ago when the environmental and medical conditions prevailing there were comparable to the ones found in the tropical countries now. The disease pattern in the West at present has been modified due to several factors including the environmental and medical changes and the changes in the prevalence and virulence of streptococcal infection although in a recent outbreak of rheumatic fever in U.S. this trend was reversed and there was an extraordinary high percentage of patients who had carditis many of them with congestive failure. The experience from our studies provides ample indications that Jones Criteria (revised 1965) are generally sensitive to diagnose most of the cases of ARF. It

must however be emphasised that the criteria are not a set of rules and should be used as guidelines. 'Two major or one major and two minor manifestations' are considered definite evidence but a degree of probability could be assigned to each case on the basis of a combination of symptoms and signs and laboratory data during the initial episode and its follow up. The main controversy has been regarding the incidence of involvement of joints and carditis.

The variation in joint manifestations is due to sampling biases, disregard of arthritis as a serious ailment by the parents, delay in presentation and inadequate medical care available. If arthralgia is accepted as a major criterion as suggested by some workers, it will result in overdiagnosis leading to undesirable disability and hardship. In cases of true polyarthralgia with fever elevated ESR and ASOT, a diagnosis of probable rheumatic fever should be made initially and a meticulous follow up instituted over a period of time. Diagnosis of rheumatic fever in the adults over the age of 20 years is problematic because of the virtual absence of the major criteria viz.carditis, chorea, erythema marginatum and subcut. nodules. That is why some authors have suggested that the diagnosis of rheumatic fever in such cases be substituted by the term post-streptococcal arthritis. But this appears hardly justifiable. The diagnosis in these cases should remain rheumatic fever or may be rheumatic arthritis.

The incidence of carditis in Pakistan like the other tropical countries is substantially higher than U.S.A. and U.K. It ranges from 87% in a cardiac hospital to 64.5% in a children and 73% in an adult general hospital. The most common manifestation of cardiopathy is valvulitis. In the majority of patients it is of severe degree leading to congestive failure with a very high morbidity and mortality. This enhanced incidence of cardiopathy is mainly attributable to the higher prevalence and virulence of streptococcal infection, delay in presentation, protracted course and multiple subclinical recurrences. Although the majority gave a history of previous rheumatic episodes, 8 - 30% among them were unable to recollect any such occurrence. This insiduous onset carditis like chorea, is the only manifestation of ARF and the diagnosis of ARF in these situations has to be made without fulfilling the revised Jones Criteria - because 'two major or one major and two minor criteria' are not available in these cases. Care should be taken to identify metabolic myocarditis, endomyocardial fibrosis presenting as mitral insufficiency, and myocarditis/pericarditis of viral orgin. Isolated or dominant mitral stenosis may occur within two years of the onset of the acute attack and is therefore frequent between the ages of 10 - 20 years. The question, whether these stenotic lesions are due to congenital malformation or acquired rheumatic lesion, is important in this setting, and a detailed echocardiographic study and at times intraoperative observation may provide the answer. The acceleration or telescoping of the mitral stenosis in the juvenile age group is due to the same factors responsible for the enhanced incidence of the cardiopathy. On the other hand the picture in the adult group from the army was diagonally different wherein carditis was very uncommon, and less severe. It conformed to the accepted pattern of inverse relationship between arthritis and carditis in which the older the patient the less frequent and also perhaps milder the carditis, while arthritis was commoner and more florid.

Chorea , subcutaneous nodules and erythema marginatum were as uncommon as elsewhere, the incidence being higher in the younger age group. Subcutaneous nodules and erythema marginatum were usually associated with carditis.

Fever was present in all cases presenting as rheumatic polyarthritis. It was often recalled as a part of the picture of other modes of presentation. It is invariably the only symptom of a recurrence of ARF that the patient may remember. Prolonged fever may also be due to infective endocarditis which is a major complication of rheumatic heart disease and frequently causes confusion in the differential diagnosis of a recurrence. It is however not infrequent for the febrile episode to be ascribed to malaria or enteric fever which are so common in the tropics.

It was not possible to assess the diagnostic value of the P-R interval, since detailed E.C.G. correlation could not be done routinely in each case in most of the studies, although an E.C.G. was done once or more often in all of them.

The laboratory evidence in ARF is only indirect, but it is of value because it indicates the presence of streptococcal infection either by isolation of Group A streptococci from throat swab or by positive streptococcal antibody tests for preceding streptococcal infection. Since ARF is an inflammatory disease, the erythrocyte sedimentation rate & C-reactive protein are useful, although non-specific, detectors of the presence of an inflammatory process. ESR is done almost universally and ASOT is becoming available in most of the places, but facilities for tests for other streptococcal antibodies like antistreptozyme test (ASTZ), CRP testing and throat swab culture are not easily accessible to many developing populations. The results of the tests carried out in our studies though showing wide variations are generally in accord with similar studies elsewhere. Anaemia is otherwise so common in the socioeconomic group suffering from ARF that it may be difficult to apportion the contribution of suppression of erythropoiesis by the inflammatory process.

The course of illness in acute rheumatic fever is generally said to be dependent on the main clinical manifestation. It is short when arthritis alone is the major manifestation, longer in cases of chorea and the longest in the presence of carditis when it may extend over six months or more. In our series there is a large number of so-called chronic rheumatic fever cases because of the higher incidence and increased severity of carditis and the increased frequency of clinical and sub-clinical recurrences. Many of them have a reappearance of the manifestations of acute phase in less than 3 months after the previous attack, which is not a recurrence, but should be considered as a continuation of the same attack. The persistence of arthritis, a sleeping pulse more than 100/min., subcutaneous nodules, appearance of new organic murmurs or increase in cardiac size and congestive failure all signify rheumatic activity. It may be emphasized here that Jones Criteria may not always be satisfied in a recurrence of ARF in cases of established RHD because evidence of fresh carditis - a major manifestation - may not be possible to recognise with pre-existing RHD.

It is contended that secondary prophylaxis is the best and most practical means of prevention at present, but this contention is belied by the available data. The current attempts at secondary prevention have virtually failed to produce consistent results. This may be due to half hearted, sporadic and ill-organised nature of the efforts, alongwith the formidable problem of noncompliance whether the programme is hospital-based or is dependent on the skeletal primary health care system available in the developing countries. Moreover it appears highly probable that once carditis has taken root, its natural course is unrelenting despite secondary prophylaxis. Primary prevention therefore is the only means of eradicating ARF which is a completely preventable malady.

The majority of patients of ARF/RHD were from the lowest urban socioeconomic group but the main determinent was overcrowding. In the four groups from Karachi the bulk of the patients belonged to squatter settlements with large families living in temporary one-room huts. Mass migration of population during 1947 at the time of emergence of Pakistan, followed by the continued in-flow due to the concentration of industry in Karachi resulted in this state of affairs. The group of patients from an army cantonment underscores the same factor viz. overcrowding as the main factor in the causation of ARF although their general living standard was certainly better than the lower income groups of the country. Since the availability and quality of medical care are dependent on the socioeconomic milieu, it may well be argued that no improvement in the former is possible without upgrading the general standard of living. This relationship however may not be as direct as it seems. It is certainly possible to institute public health measures with gratifying results without waiting for the percapita income to rise. Governmental agencies, public health planners and administrators, the medical profession and interested private organisations therefore cannot take refuge behind this premise and absolve themselves of their responsibility. In fact their responsibility becomes heavier under the circumstances. The pace of social development in the poor countries undoubtedly needs acceleration, but public health measures against ARF including primary and secondary prevention programmes should be launched now, without waiting for better environmental conditions.

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