

Clinical and Immunogenetic Profile of Rheumatoid Arthritis Patients in Kashmir

Buth BA, and Bisati SD

Abstract

Two hundred and five patients of Rheumatoid arthritis, seen over a period of 4 years were studied. The majority of the patients had relatively mild disease at the time of presentation. The disease is seen more commonly in females, and frequent in fourth decade. Small joints are mostly affected and commonest radiological finding was soft tissue swelling and osteoporosis. Extra articular manifestations are uncommon and vasculitis is very rare. Mid expiratory flow rate is the commonest lung function abnormality. 68 patients of classic and definitive Rheumatoid arthritis patients were typed for four HLA-Loci, A,B,C and DR. Out of these 40 patients (58.82 percent) had DR4 positive test. 52 patients (76.47 percent) were Rheumatoid factor positive. Out of 142 control subjects 7 cases (4.9 percent) were RF positive and 31.69 percent were DR4 positive.

Introduction

Rheumatoid arthritis is a chronic multisystem disease, although there are a variety of systemic manifestations, the characteristic feature of the disease is persistent inflammatory synovitis, usually involving peripheral joints in symmetric distribution.

Rheumatoid arthritis is highest in incidence among arthritides, and exact the great toll in crippling. This comprise a group of diseases of high morbidity and low mortality, with high potential for crippling disability among a relatively younger age group.

Despite advances in our understanding of the immunological process, leading to articular inflammation and connective tissue destruction, the cause of this malady remains an engima. Indeed it is still not clear whether Rheumatoid arthritis is one disease with multiple etiologies or a symptom complex produced by a single causative factor. A wide clinical spectrum of Rheumatoid arthritis is recognized, thus the patients selected may not represent

a true cross section of disease presentation or clinical profile. In addition environmental, social, genetic and economic factors may play a role in the expression of the disease. Thus a pattern of illness may appear particularly severe in rather homogeneous isolated populations.

Family studies indicate a genetic predisposition. The role of genetic influences in the etiology of Rheumatoid arthritis was established by demonstration of a association with class II major histocompatibility gene complex antigen HLA-DR4.

Severe Rheumatoid arthritis is found at approximately four times the expected rate in first degree relatives of individuals with sero-positive disease.

Since the etiopathogenesis of Rheumatoid arthritis is unknown. Geographical variations in clinically, immunological and immunogenetic pattern may provide some clues towards the etiopathogenesis of this disease. The present study describes these features in patients with Rheumatoid arthritis from Kashmir.

Material and Methods

Over 4 years period (October 1987-October 1991) 205 adult patients with Rheumatoid Arthri-

*Correspondence: Dr. Bashir Ahmad Buth
Department of Physical Medicine and Rehabilitation,
Institute of Medical Sciences, Soura,
Srinagar-190011 Kashmir (India), Post Bag No. 27*

tis attending the out patient department of Institute of Medical Sciences were studied. The diagnosis of Rheumatoid Arthritis was established according to the American Rheumatism Association criteria.

In clinical evaluation special stress was placed on the topography of joint involvement and extrarticular manifestation. The patients in addition were assigned anatomical class according to the criteria of Steinbroker

Serological Studies:

Rheumatoid factor was screened in all the patients and controls using latex kits, Auto-antibodies were studied by standard indirect immunofluorescence technique.

Immunogenetic studies:

68 patients with unequivocal deforming and erosive disease were typed for four major HLA Loci A,B, C and DR. 142 control subjects were also typed for HLA, A,B,C, and DR.

HLA-A, B and C were typed by two stage microlymphocyto-toxicity technique and DR typing was done by Nylong wool separation of B cells and typing method.

Results

Clinical Observation.

The patients were in the age range of 11-55 years and the median age of onset of Rheumatoid arthritis was 37.19 years and the female to male ratio was 3.5 : 1.

The average joint count on the first visit was 7. The joints involved and their frequency is given in Table I.

Table :2

Anatomical Stage at which the patients presented

Stage I	27 (13.17)
Stage II	122 (59.51)
Stage III	36 (17.56)
Stage IV	20 (09.75)
	205

(Figures in brackets show % age)

Extra-articular Manifestations:

There were 32 patients (15.60%) who showed typical Rheumatoid nodule. Detailed pulmonary assessment including lung function test were performed only in 60 representative patients. Of these 47 patients had normal skiagram while 7 showed evidence of pulmonary infiltrates, and 6 had pleural effusion.

The pulmonary function studies revealed a number of abnormalities. These included reduced vital capacity in 21 patients (35%), reduced mid expiratory flow rate in 39 patients (65%) diminished forced expiratory volume in first second in 12 patients (20%).

Cardiac involvement was sought clinically and by electro-cardiogram, 7 patients had prolonged. PR interval and 4 patients had pericarditis and 2 had aortic regurgitation clinically.

8 patients had spleenomegaly and 40 patients are found to have mild to severe anemia.

The anatomical stages assigned in these patients according to Steinbroker et al² is shown in Table II.

Serology:

Using the commerical latex fixation test kit 52 (76.47%) patients had Rheumatoid factor titer range 1:48 to 1:92 by the dilution technique Anti-nuclear antibody was positive in titre of 1:8 or more in 27 patients.

Table III shows the results of HLA typing in 68 classical and definite Rheumatoid arthritis patients and 142 control subjects.

Discussion

There are some important differences in clinical presentation of Rheumatoid Arthritis patients in Kashmir and Northern India on one side and the patients of European origin on the other. First the anatomic Stage at which our patients presented indicates a milder form of joint disease than that seen in the west. The present study also shows that the extent of severity of extra-articular manifestations of Rheumatoid Arthritis in patients from Kashmir and Northern India is less than that seen

in the west. Only 32 (15.60%) of our patients had subcutaneous nodules in contrast to the accepted figures from the white race reported in the range of 20% to 35% systemic vasculitis was not found in any of our patients. Malaviya et al³ have reported subcutaneous nodule in 8.5% patients and Walker, W.C. and Wright,⁴ have reported subcutaneous nodules in 44% male and in 24% of female patients. Though pulmonary function tests were abnormal in a large population of our patients, the paucity of radiologically demonstrable disease is in contrast to the western figures. Eye involvement in the form of episcleritis was noted in 5.8% of our patients. Similar results have been reported by Walker and Wright⁴ Reddy, S.C. et al⁵ Examined 50 patients of Rheumatoid arthritis and reported 33% patients having one or more ocular changes. Cardiac involvement was found in 19% patients. 10.29% patients had electro-cardiographic evidence of cardiac involvement in the form of PR prolongation. Nearly 3% patients had aortic regurgitation. These patients did have any history of Rheumatic heart disease or any other cause of aortic regurgitation. Pericarditis was clinically diagnosed in 5.88% patients and was substantiated by electrocardiogram. These patients had no evidence of any other disease giving rise to pericarditis. Malaviya et al³ found mitral regurgitation in two patients out of total of 258 patients studied. Lebowitz, W.B⁶. reported pericarditis in 50% of patients at autopsy. Pulmonary involvement was seen in 6.34 percent of cases in our patients. Pleural effusion was present in 6 patients and interstitial lung disease was seen in 7 patients in our series, diagnosed clinically, substantiated by radiology and lung function test, which revealed restrictive pattern. Lung function tests revealed reduced vital capacity in 35% patients, reduced mid expiratory flow rate in 65% and diminished forced expiratory volume in first second in 20% patients. Malaviya et al³ have found reduced vital capacity, reduced mid expi-

ratory flow rate and reduced forced expiratory volume in first second in 36% 92% and 30% patients respectively. Walker, W.C. and Wright, V⁴ have reported interstitial pulmonary fibrosis in 1.6% Patients. Splenomegaly was noticed in 8 (11.76%) patients. Walker and Wright⁴ have found splenomegaly in 3 percent patients. The frequency of seropositivity and the association of disease with DR4 is comparable to that reported in caucasians. 40 (58.82%) out of 68 patients in our study were DR4 positive which was highly significant whereas 31.69% control subjects had DR4 positive test. 52 (76.47%) patients were RF positive as compared to 7 (4.9%) control subjects. 31.69% patients were DR4 positive in control group. No significant difference was found in antigen frequencies of HLA-A B and C loci in patients and Control group. The high frequency of HLA-DR4 antigen detected in representative group of Kashmir^{3,7} population correlates well with North Indian population as shown by Malaviya, A.N et al and Mehra NK et al^{3,7} as well as white caucasoid population as shown by others⁸⁻¹³. The HLA-DR4 association of Rheumatoid Arthritis in our study is in conflict with observations of Michol and Woodrow^{14,15} who reported a strong association of DRI with Rheumatoid arthritis in Indians from Liver pool.

Summary & Conclusion

Rheumatoid arthritis affects females about twice as commonly as the males. The onset of disease is most frequent during fourth decade of life in females and fifth decade of life in males. Small joints of hands with exception of distal interphalangeal joints are more frequently involved as compared to other joints. Joint deformities are found most frequently in wrist joints. Extra-articular manifestation are uncommon, vasculites is very rare. Commonest radiological findings are soft tissue swelling and osteoporosis. Reduced mid-expiratory flow rate is the commonest lung func-

Table No. 1
Comparison of Joint Involvement in Rheumatoid Arthritis in patients from Kashmir, Northern India and White Race.

Joints	Frequency of Involvement in present study. (Percent)	Frequency of Involvement in Northern India (Percent)	Frequency of Involvement in White Race. (Percent)
Wrist	73.17	95	82
PIP	76.09	90	63
MCP	71.70	87	87
Knee	76.09	75	50
Ankle	34.14	55	53
MIP	29.26	47	48
Shoulder	29.26	40	47
Elbow	26.82	35	21
Hip	08.29	15	Not mentioned
Cervical spine	07.80	0.8	Not mentioned

PIP = Proximal Interphalangeal Joint
MCP = Metacarpophalangeal Joint.
MTP = Metatar sopal angeal Joint.

Table No. 3
HLA-DR Antigen in the patients & Control subjects

Antigen	Patient (n=68) No %	Control (n=142) No. %	PR	X2	P
DR1	08 (11.76)	16 (11.27)	1.05	0.008	HS
DR2	29 (42.15)	62 (43.66)	0.76	0.019	NS
DR3	09 (13.24)	21 (14.79)	0.878	0.0394	NS
DR4	40 (58.82)	45 (31.69)	3.08	14.03	HS .001
DR5	08 (11.76)	20 (14.08)	0.81	0.2153	NS
DR6	09 (13.24)	24 (16.90)	0.75	0.4687	NS
DR7	13 (19.12)	54 (38.03)	0.385	7.57	.005
DR8	-	09 (06.34)	0	5.22	.025
DR9	02 (02.94)	06 (04.23)	0.686	0.46902	NS
DR10	06 (08.82)	04 (02.82)	3.34	3.34	NS
DQW1	50 (73.53)	102 (71.83)	1.089	0.066	NS
DQW2	19 (27.94)	73 (51.41)	0.366	10.28	.005
DQW3	51 (75.00)	72 (50.70)	2.926	11.18	.005

tion abnormality. Majority of the patients are seropositive. Extracellular manifestations are found in seropositive patients only. HLA-DR4 is found more frequently in rheumatoid arthritis patients as compared to controls.

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