



Frequency of distribution of joint involvement in rheumatoid arthritis patients.

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INTRODUCTION

Rheumatoid arthritis is an autoimmune disease, usually chronic and inflammatory in nature and most of time without any etiology. It has both systemic as well as articular manifestations that usually lead to deformities over the course of disease.¹ Generally, it affects 0.5-1% of population worldwide. All over the world, the prevalence of RA remained constant regardless of racial or geographical presentation. Most of patients with rheumatoid arthritis are positive for either rheumatoid factor or anti-citrullinated peptide antibodies or both, which can be present years before the onset of symptoms.^{2,3} These antibodies have very important role in pathogenesis and phenotype of rheumatoid arthritis. A few patients tested negative for RA factor and anti-CCP antibodies, both or either, indicating that presence of RA factor and anti-CCP antibodies is not prerequisite for presence of rheumatoid

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ABSTRACT... Objectives: To determine the frequency of joint distribution in rheumatoid arthritis presenting at Independent University Hospital Faisalabad. Assessment of joint involvement in RA patients is not only important to determine the disease activity but also to assess the future joint damage. **Study Design:** Cross Sectional Study. **Setting:** Independent University Hospital Faisalabad. **Period:** July 2019 to Jan 2020. **Material & Methods:** 384 consecutive RA patients fulfilling inclusion and exclusion criteria, of either sex between age of 17- 60 years were enrolled from Rheumatology division of Independent University Hospital Faisalabad from July 2019 to Jan 2020. Frequency of joint distribution was assessed. Chi square test was used to compare the frequency of joint distribution among different treatment groups, age groups and gender, disease duration. A p-value of < 0.05 was considered statistically significant. **Results:** In this study 384 patients with RA were studied. Joint distribution was determined according to pattern of joint involved at presentation. More patients (178) were noted in oligoarticular group, with predominant small joint involvement 111 (28.9%). 173 patients were noted in poly-articular group with 102 (26.6%) were in predominant small joint involvement. **Conclusion:** Pattern of joint distribution in RA patients is very important especially if there is monoarthritis or oligoarthritis, along with its association with gender, age of onset, disease duration, investigations.

Key words: Monoarthritis, Oligoarthritis, Rheumatoid Arthritis.

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arthritis.¹² This indicates that pathogenesis of RA is complex, most of the time genetic, environmental, systemic and local mechanical factors influence the phenotype and joint distribution.^{4,5,6,7}

Joint involvement and distribution in RA patients have been determined by counting the number of swollen and tender joints.⁸ Assessment of joint involvement in RA patients is not only important to determine the disease activity but also to assess the future joint damage. Different methods were used to determine the number and involvement of joints in RA. Disease activity score (DAS) assesses 28 joints of the body including small and large joints of both upper and lower limb which includes bilateral wrist, 1st to 5th metacarpal (MCP) joints and proximal interphalangeal (PIP) joints, elbow, shoulder, and knee joints.^{13,14} Most of time patients with RA present with symmetrical polyarthritis affecting the small joints of the hands

and feet, but mono and oligoarthritis are also frequent. Polyarthritis patients usually present with features of worse prognosis.^{9,16}

In western countries, studies specific for phenotype and joint distributions in RA patients are very rarely done.¹⁰ One study showed the proportion of patients with monoarthritis was 38.3%, 34.1% had oligoarthritis (2–4 swollen joints), and 27.6% had arthritis of 5 joint or more (polyarthritis). Patients with mono, oligo or polyarthritis have different joint involvement. Oligo and monoarthritis most frequently have knees and ankle involvement, while polyarthritis patients have mostly involvement of the small joints of hands and feet.⁹ A large study conducted in Mexico, Africa, Netherlands and India, showed that more polyarticular presentation in Mexico and Africa, while oligo or monoarthritis presentation more common in India and Netherlands.¹²

Early assessment and early intervention with disease modifying anti-rheumatic drugs of patients presenting with either mono or oligoarthritis, have a significant impact on patient health, preventing systemic involvement, joint deformity and arresting later presentation with polyarthritis. All these effects have very significant impact on economy, social behavior, and family life of patients.¹¹

The main aim of the study was to determine either mono or oligo or polyarthritis distribution of joints in RA patients because most of the early presentations of monoarthritis or oligoarthritis or polyarthritis were neglected and not investigated and they started treatment until they develop either joint damage or extra-articular manifestations. So early assessment for mono or oligoarthritis and then early treatment can prevent further joint damage and morbidity.

OBJECTIVES

To determine the frequency of joint distribution in Rheumatoid Arthritis patients presenting at independent university hospital Faisalabad.

MATERIAL & METHODS

This cross-sectional study was carried out at

Rheumatology clinic of Independent University Hospital Faisalabad July 2019 to Jan 2020. Consecutive Three hundred and eighty-four adult patients with baseline RA fulfilling the 2010 criteria of American College of Rheumatology, visiting the Rheumatology clinic Independent University Hospital Faisalabad and fulfilling the selection criteria, were selected through Non-Probability Convenient Sampling technique for this study. This study was proved by the Institutional Review Board of the hospital (IUH/IRB/000024). Inclusion criteria were patients aged between 17 to 60 years of either gender who were diagnosed cases of rheumatoid arthritis. Patients with Spondyloarthropathy or diagnosed cases of Osteoarthritis, also other autoimmune diseases like Systemic Lupus Erythematosus, Systemic Sclerosis and diagnosed cases of infective or metabolic causes of arthritis were excluded. A sample size of 384 was estimated by using 95% confidence level, 5% margin of error, with expected frequency of MetS 50% (conservative approach) among RA patients. Patients were explained about the purpose, risk/benefit of the study and pre-tested proforma was filled. Demographic data and history including age, gender, hospital registration number, and disease duration and treatment history and primary investigations like Quantitative RA factor, Anti-CCP antibodies, Blood complete with ESR, CRP was noted. All patients were assessed clinically for the number of tender and swollen joints. Tenderness and swelling were assessed by bimanual method, Small and large joint involvement was also noted. Patients with joints of hands including wrist and feet were labelled as small joints, while elbow, shoulder, hip, knees, ankles were labelled as large joints.

Patients with single joint involvement was labelled as mono-arthritis, 2-4 joint involvement was labelled as oligo-arthritis, and 5 or more than 5 joint involvement was labelled as polyarthritis. Disease duration with onset of symptoms of inflammation with pain or stiffness or restricted joint motion less than 6 weeks, from 6 weeks to 2 years or more than 2 years was also noted. Treatment history was also noted. Patients taking no treatment or taking DMARDs treatment with methotrexate, leflunomide, sulfasalazine, hydroxychloroquine,

either alone or in combinations was also noted. Also, disease score with either remission, low, moderate, or high was calculated by DAS-28 formula using mobile application of Rheuma helper. It is an electronic formula in which we have put number of tender and swollen joint count along with patient general health score by visual analog scale (VAS) and ESR or CRP. DAS-28 score was calculated as remission, low, moderate or high disease. A score less than 2.6 was remission, > 2.6 - 3.2 was low, <3.2 – 5.1 was moderate, > 5.1 was high disease activity.

Data were entered and analyzed on computer using IBM SPSS Statistics version 23.0 software program. Data for age, disease duration, disease score were described by using Mean \pm SD. Data for gender, joint distributions, investigations and treatment history were described by using frequency and percentages. Frequency of joint distribution was described by percentage as per given criteria. Chi square test was used to compare the frequency of joint distribution among different treatments groups, disease duration, age groups and disease score. A p-value \leq 0.05 was considered statistically significant.

Operational Definitions

Mono-arthritis

Single joint involvement

Oligo-arthritis

2-4 joint involvement

Poly arthritis

When 5 or more than 5 joints are involved.

ACR criteria for classification of RA⁷

A score of 6/10 is needed for classification of a patient as having definite RA)

Joint involvement

- | | |
|---|---|
| A. 1 large joint: | 0 |
| B. 2-10 large joints: | 1 |
| C. 1-3 small joints (with or without involvement of large joints): | 2 |
| D. 4-10 small joints (with or without involvement of large joints): | 3 |
| E. 10 joints (at least 1 small joint): | 5 |

Serology

(at least 1 test result is needed for classification)

- | | |
|--|---|
| A. Negative RF and negative ACPA: | 0 |
| B. Low-positive RF or low-positive ACPA: | 2 |
| C. High-positive RF or high-positive ACPA: | 3 |

Acute-phase reactants

(At least 1 test result is needed for classification)

- | | |
|----------------------------------|---|
| A. Normal CRP and normal ESR: | 0 |
| B. Abnormal CRP or abnormal ESR: | 1 |

Duration of Symptoms

- | | |
|-----------------------|---|
| A. Less than 6 weeks: | 0 |
| B. 6 weeks or more: | 1 |

RESULTS

In this study 384 patients with RA were studied. Mean age of the patients was 39.67 ± 10.6 years with age range of 17 to 60 years. Out of 384, 298 (77.6%) were females, and 86 (22.4%) were males as shown in Figure-1.

The distribution of RA patients according to age is presented in Table-I. A comparative large number of patients 192(50.0%) were from age group 26-50 years while 135 (35.2%) patients were from age group of less or equal 25 years and only 57 (14.8%) were from the age group of greater or equal 51 years.

The distribution of joint involvement was shown in Table-II. More patients (178) were noted in oligoarticular group, with predominant small joint involvement 111 (28.9%). 173 patients were noted in poly-articular group with 102 (26.6%) were in predominant small joint involvement. Only 33 (8.6%) patients were from monoarthritis group.

A relatively higher number of patients 146 (38.0%) were taking only methotrexate as DMARD therapy along with symptomatic treatment. 91 (23.7%) patients presented to us were taking no treatment as shown in Table-III.

Also 130 (33.9%) were in low disease activity, 150 (39.1%) were in moderate and 104 (27.1%) in high disease activity as shown in Table-IV. Most of the patients 249 (64.8%) were positive for both

quantitative RA factor and Anti-CCP antibodies, and only 19 (4.9%) were negative for both quantitative RA factor and Anti-CCP antibodies as shown in Table-V.

Chi-square test showed that joint distribution in RA patients is significantly associated with the disease duration, treatment history, and disease score whereas there was no significant difference

in joint distribution among relevant investigations of disease, gender and age distribution as shown in Table-VI.

It was also found that the large Proportion of patients of RA with oligo or polyarthritis were taking methotrexate, while greater number of patients with mono-arthritis were taking sulfasalazine.

Age (years)				
	Frequency	Percent	Valid Percent	Cumulative Percent
Less and Equal 25	135	35.2	35.2	35.2
26-50	192	50.0	50.0	85.2
Greater and Equal 51	57	14.8	14.8	100.0
Total	384	100.0	100.0	

Table-I.

Joint Distribution				
	Frequency	Percent	Valid Percent	Cumulative Percent
Monoarthritis	33	8.6	8.6	8.6
Oligoarthritis (predominant Large joint)	67	17.4	17.4	26.0
Oligoarthritis (predominant Small joint)	111	28.9	28.9	54.9
Predominant small joint	102	26.6	26.6	81.5
Predominant large joint	71	18.5	18.5	100.0
Total	384	100.0	100.0	

Table-II.

Treatment History				
	Frequency	Percent	Valid Percent	Cumulative Percent
no taking treatment	91	23.7	23.7	23.7
methotrexate	146	38.0	38.0	61.7
leflunomide	41	10.7	10.7	72.4
sulfasalazine	28	7.3	7.3	79.7
combination	78	20.3	20.3	100.0
Total	384	100.0	100.0	

Table-III.

Disease Score				
	Frequency	Percent	Valid Percent	Cumulative Percent
low	130	33.9	33.9	33.9
moderate	150	39.1	39.1	72.9
high	104	27.1	27.1	100.0
Total	384	100.0	100.0	

Table-IV.

Investigation				
	Frequency	Percent	Valid Percent	Cumulative Percent
RA factor positive	52	13.5	13.5	13.5
anti-CCP antibodies positive	64	16.7	16.7	30.2
both positive	249	64.8	64.8	95.1
both negative	19	4.9	4.9	100.0
Total	384	100.0	100.0	

Table-V.

Variables	Joint Distribution					Total	P-value
	Mo-noartis	Oligoarthritis (predominant large joint)	Oligoarthritis (predominant small joint)	Predominant small joint	Predominant large joint		
Duration							
Less than 6 weeks	9(27.3%)	0(0%)	10(9.0%)	9(8.8%)	10(14.1%)	38(9.9%)	0.00
6 weeks to 2 years	24(72.7%)	58(86.6%)	83(74.8%)	57(55.9%)	18(25.4%)	240(62.5%)	
> 2 years	0(0.0%)	9(13.4%)	18(16.2%)	36(35.3%)	43(60.6%)	106(27.6%)	
Total	33(100.0%)	67(100.0%)	111(100.0%)	102(100.0%)	71(100.0%)	384(100.0%)	
Treatment History							
No taking treatment	19(57.60%)	5(7.50%)	38(34.20%)	19(18.60%)	10(14.10%)	91(23.70%)	0.00
Methotrexate	0(00.0%)	53(79.10%)	32(28.80%)	38(37.30%)	23(32.40%)	146(38.00%)	
Leflunamide	0(00.0%)	9(13.40%)	14(12.60%)	18(17.60%)	0(00.0%)	41(10.70%)	
Sulfasalazine	14(42.40%)	0(00.0%)	14(12.60%)	0(00.0%)	0(00.0%)	28(7.30%)	
Combination	0(00.0%)	0(00.0%)	13(11.70%)	27(26.50%)	38(53.50%)	78(20.30%)	
Total	33(100.00%)	67(100.00%)	111(100.00%)	102(100.00%)	71(100.00%)	384(100.00%)	
Disease Score							
Low	23(69.7%)	43(64.2%)	28(25.2%)	18(17.6%)	18(25.4%)	130(33.9%)	0.00
Moderate	10(30.3%)	24(35.8%)	60(54.1%)	23(22.5%)	33(46.5%)	150(39.1%)	
High	0(0.0%)	0(0.0%)	23(20.7%)	61(59.8%)	20(28.2%)	104(27.1%)	
Total	33(100.0%)	67(100.0%)	111(100.0%)	102(100.0%)	71(100.0%)	384(100.0%)	
Investigation							
RA factor positive	0(0.0%)	0(0.0%)	32(28.8%)	20(19.6%)	0(0.0%)	52(13.5%)	0.00
Anti-ccp antibodies positive	0(0.0%)	32(47.8%)	23(20.7%)	0(0.0%)	9(12.7%)	64(16.7%)	
Both positive	33(100.0%)	25(37.3%)	56(50.5%)	82(80.4%)	53(74.6%)	249(64.8%)	
Both negative	0(0.0%)	10(14.9%)	0(0.0%)	0(0.0%)	9(12.7%)	19(4.9%)	
Total	33(100.0%)	67(100.0%)	111(100.0%)	102(100.0%)	71(100.0%)	384(100.0%)	
Gender							
Male	09(27.3%)	53(79.3%)	0(0.0%)	5(4.9%)	19(26.8%)	86(22.4%)	0.00
Female	24(72.7%)	14(20.9%)	111(100.0%)	97(95.1%)	52(73.2%)	298(77.6%)	
Total	33(100.0%)	67(100.0%)	111(100.0%)	102(100.0%)	71(100.0%)	384(100.0%)	
Investigation							
Less and equal 25	20(60.6%)	21(31.3%)	56(50.5%)	18(17.6%)	20(28.2%)	135(35.2%)	0.00
26-50	13(39.4%)	31(46.3%)	47(42.3%)	59(57.8%)	42(59.2%)	192(50.0%)	
Greater and equal 51	0(0.0%)	15(22.4%)	8(7.2%)	25(24.5%)	9(12.7%)	57(14.8%)	
Total	33(100.0%)	67(100.0%)	111(100.0%)	102(100.0%)	71(100.0%)	384(100.0%)	

Table-VI. Cross tabulation.

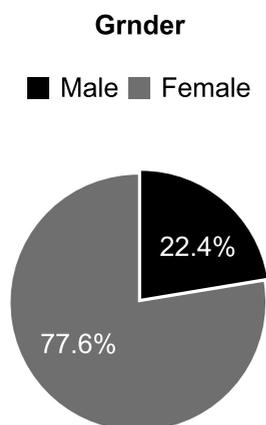


Figure-1.

DISCUSSION

Rheumatoid arthritis is a joint damaging autoimmune disease and most of time this damage occurred very early during the course of disease. So early quantitative measurement of joint involvement and disease activity is very important to save the joints.¹⁵

Regarding presentation in our study, 62.5% (240) patients presented with disease duration of 6 weeks to 2 years while only 9.9% (38) patients have early presentation of less than 6 weeks. Reason for this late presentation might be due to late referral, ignoring the early arthritis, or insidious presentation of the disease. A study conducted in Norway have median duration of disease of 30 days,⁹ while a Dutch study have disease duration of less than 2 years because most of patients with RA had insidious onset and usually no clinical features present for tender and swollen joints in early phase of disease.¹⁷

Few studies have done to determine the joint distribution in RA. In our study, oligoarthritis with predominant small joint involvement was more common, followed by polyarthritis with predominant small joints and then large joints. A similar findings were noted in another study showed that mono and oligoarthritis more frequent than polyarthritis in early presentation of disease⁹, and small joint involvement was less common in oligoarthritis, which is contrary to our findings which showed small joints involvement

more common even in early presentation. A study conducted in 2017 showed that large joint involvement was more common in India, Mexico, south Africa, while small joint was more common in Netherland.¹² This difference might be due to selection bias, life style with Asians have more knee bending and physical labor as compared to Europeans or this difference might be true due to the pathogenetic mechanisms and genetic factors that influence the phenotype, so more work is needed to evaluate this difference.

Most of patients in our study were positive for autoantibodies either RA factor or Anti-CCP antibodies while only 4.9% (19) patients were negative for both antibodies. When comparing to other countries, number of patients with RA studied for joint distribution have higher auto-antibodies positivity in India as compared to Netherland.¹² A lot of factors have studied for this difference which include smoking, environmental factors, diet, oral hygiene. All these factors affect joint distribution I RA but needs more work.^{18,19}

33 – 70% of our patients have low to moderate disease activity, which included predominant 54.1% (60) patients in oligoarticular group with small joint involvement and 64.2% (43) patients of oligoarticular large joint group have low disease activity. 59.8% (61) have high disease activity which belonged to polyarticular small joint group. Another study showed that most of patients with large joint involvement have low to moderate disease activity, while patients with polyarticular involvement have high disease activity, another finding noted in this study was that patients with large joint involvement usually have late onset disease, while small joint involvement have early onset disease.²⁰

In our study 23.7% (90) patients presented with arthritis were not taking treatment, in which 57.6 (19) were monoarthritis, 34.2% (38) were oligoarthritis. Which is very significant ratio (P-value <0.00). 38.0% (146) patients using methotrexate which is also very significant proportion (P-value <0.00) at presentation that includes both oligoarthritis, and polyarthritis. Also significant number of patients using leflunomide (10.70%),

and 20.30% using in combination therapy. A study conducted in Sweden showed that most of patients with late onset disease that were usually oligoarticular and large joint involvement were not taking treatment with DMARDs, and patients with polyarthritis and small joint involvement were taking treatment with DMARDs and biologics.²⁰ So, most of patients with either monoarthritis, or oligoarthritis were neglected for specific treatment with anti-rheumatic drugs which leads to high disease activity, early joint damage and severe extraarticular manifestations. One of the most common causes for this delayed treatment in monoarthritis or oligoarthritis especially in old age is wide differential and non-specific presentation which are not properly assessed for typical inflammatory signs for RA.

Initial studies showed that late presentation and mono or oligoarthritis usually have mild disease and low disease activity²¹, but recent studies showed clearly that late presentation or oligo or monoarthritis has equal or worse disease activity as compared to early presentation or polyarthritis.^{22,23} So most of guidelines including European league against rheumatism (EULAR)²⁴, American college of rheumatology (ACR)²⁵ clearly defined that treatment must be started as early as possible from the start of disease, especially with methotrexate and low dose corticosteroids if disease activity is moderate or high.

In our study disease activity was associated with pattern of joint distribution. High activity was more common in polyarticular arthritis, also oligoarthritis with predominant small joint involvement, whereas low disease activity was noted in most of monoarthritis and oligoarthritis with large joint involvement. A study conducted on Japanese population showed similar findings that joint involvement increases as the disease activity increases but pattern of joint distribution was not affected by disease activity.²⁶

Our study was not without limitations. Its cross-sectional design limits its ability to describe comparison with control. Similarly results cannot be generalized because of small sample size. Also, logistic regression analyses were not performed to distinguish covariates associated

with the determinant – joint distribution in RA. Also, doses and effect of therapy was not noted during study whether treatment improves joint distribution and disease activity. Also, comparison with other inflammatory and non-inflammatory (osteoarthritis) rheumatic disorders were not performed. Finally, this is first study in Pakistan to assess frequency of joint distribution in RA, so it is not possible to compare our results in local population.

CONCLUSION

A brief review of above discussion has an urge to understand the significance of relationship between RA and its articular presentation especially joint distribution. Frequency of joint distribution was comparable with the rest of world with minor differences. After brief review, one can conclude that assessment for joint distribution and its pattern has very important role in management of RA, can lead to better control of disease, prevent joint damage and its comorbidities and prevent extra-articular manifestations of disease.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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1	Zafar Ali Zafar	Introduction, Data analysis and discussion writing.	
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3	Muhammad Absar Alam	Data collection.	
4	Touseef Anwar	Data collection, review.	
5	Muhammad Sarfraz	Methodology.	
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