Clinical Profile of Rheumatoid Arthritis Patients Reporting to a Tertiary Care Center – Data From Southwestern Part of India

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ABSTRACT

Introduction: Rheumatoid arthritis is characterized by a persistent joint inflammation along with cartilage and bone damage with significant limitation of activity, reduction in the quality of life and often systemic complications. There have been lot of advances in diagnostic and treatment modalities available for RA in the recent years with better access to tertiary care centers in the country. Study aimed to analyse the present day clinical profile of patients of RA reporting to a tertiary care centre in south western part of India.

Material and methods: This prospective observational, hospital based study was carried out in a tertiary care teaching hospital over a period of six months. All diagnosed consecutive cases of RA visiting our OPD or admitted in wards were evaluated. RA was diagnosed based on American College of Rheumatology Criteria-201. Detailed clinical history and examination along with haematological, biochemical parameters and inflammatory markers were analysed.

Results: Total 92 cases of RA qualified for the study. 81.5% study population was female. 26% of the study population had 1st degree relative suffering from the same disease 36 (39.1%) of the patients had high disease activity. Most common joint involved was MCP joint Most common joint deformity was ulnar deviation of digits, most common radiological finding was joint space narrowing.

Conclusion: RA has female preponderance with a significant proportion having positive family history. Most common joints involved are the MCP joints and the most common deformity was ulnar deviation of digits. There are significant proportions of patients who present with high disease activity. Anaemia, thrombocytosis and extrarticular manifestations are common. Most of the patients are on DMRDs with methotrexate being the most commonly used drug.

Keywords: Rheumatoid Arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic auto immune disease. The course of the disease is variable. A substantial percentage of population presents with persistent pain, stiffness, progressive joint destruction, functional disability, and progressive morbidity and mortality.[1] Disease is characterised by a persistent joint inflammation along with cartilage and bone damage with significant limitation of activity, reduction in the quality of life and often systemic complications.[2] There have been lot of advances in diagnostic and treatment modalities available for RA in the recent years with better access to tertiary care centres in the country. Study aimed to analyse the present day clinical profile of patients of RA reporting to a tertiary care centre in south western part of India.

MATERIAL AND METHODS

The study was prospective observational, hospitalbased, carried out in a tertiary care teaching hospital in India. Study was done over a period of six months from Jan 2018 to July 2018 after approval from institutional ethical committee. All diagnosed consecutive cases of RA visiting our OPD or admitted in wards were evaluated as per a pre designed questionnaire. Allpatients were diagnosed based on American College of Rheumatology Criteria-2010 for RA.[3] Patients with any other joint disease, patients unwilling for the study, fractures in acute stage or known malignancy were excluded.

Data was obtained with special reference to:

Clinical history and presentation including articular and extra articular involvement with disease duration.

Baseline haematological, biochemical, inflammatory markers i.e. Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and radiological investigations as indicated were done. ESR was measured using Westergren method and CRP was measured using Nephelometry (Beckman Coulter IMMAGE 800 Immunochemistry System). Anti-cyclic citrullinated peptide (anti-CCP) and rheumatoid factor (RF) estimation were done in all patients.

Disease activity was assessedby determination of the DAS 28 score (Disease activity score-28 joint count), DAS-CRP (Disease activity score-28 joint count C reactive protein), CDAI (Clinical Disease activity Index) and SDAI (Simplified disease activity Index).[4,5,6]

In DAS 28 and DAS-CRP score High disease activity was defined as a score >5.1, moderate activity as a score >3.2 and ≤5.1, low activity as a score ≤3.2 and >2.6, and remission as a score less than 2.6.In SDAI; High disease activity was defined as a sum>40, moderate activity as >20 and ≤40, low activity as >3.3 and <20 and remission as score ≤3.3. In CDAI; High disease activity was defined as a sum>22, moderate activity as >10 and ≤22, low activity as >2.8 and

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<10 and remission as score ≤2.8.

RESULTS

There were total 92 cases of RA who qualified for the study. 81.5% study population was female. 26% of the study population had 1st degree relative suffering from the same disease (Table 1). The prevalent medication in most patients was therapy with 2 DMARDs (Disease modifying anti rheumatic drugs) +Steroid and the most widely prescribed drug was Methotrexate which was exhibited to 91% of the study population till date(Table2).

We found 69.6% of the study population having anaemia, 11% had leucocytosis, 3.3% had leukopenia, 23% had thrombocytosis and 3% had thrombocytopenia. Another important finding was that ESR was raised in all the patients and CRP was raised in 40% of the patients. Anti-cyclic citrullinated peptide (anti-CCP) was positive for 91% of the patients, Rheumatoid Factor (RF) was positive for 79% of the patients and 9% of the patients had seronegative RA.(Table 3).

Clinically 33% of patients had --- fever, 100% had joint pains, 94% had joint swelling and morning stiffness was present in 97% of the patients. 64% of the patients had joint deformity and 76% of the patients had limitation of movement. Carpell tunnel syndrome was present in 5%, splenomegaly in 11% and lymphadenopathy in 7.6%.(Table 4)

Most common joint involved was of Metacarpophalangeal

		Study population(n=92)		High Disease Activity(n=36)	
		Frequency	Percentage	Frequency	Percentage
Sex	Male	17	18.5	6	16.6
	Female	75	81.5	30	83.3
Family History	Present	24	26.1	12	33.3

Table-1: Demographic Factors

	Study population(n=92)		High Disease Activity(n=36)	
	Frequency	Percentage	Frequency	Percentage
Steroids	61	66.3	28	87.5
Leflunomide	13	14.1	6	16.6
Sulfasalazine	36	39.1	20	55.5
Azathioprine	2	2.2	1	2.7
Hydroxychloroquine	80	87.0	32	88.8
Methotrexate	84	91.3	34	94.4

Table-2: Medications

	Study population(n=92)		High Disease Activity(n=36)	
	Frequency	Percentage	Frequency	Percentage
Anaemia	64	69.6	33	91.6
Leucocytosis	10	10.9	7	19.4
Leucopenia	3	3.3	2	5.5
Raised ESR	92	100.0	36	100
Thrombocytosis	21	22.8	14	38.8
Thrombocytopenia	3	3.3	1	2.7
Raised CRP	37	40.2	23	63.8
Anti-CCP	84	91.3	32	88.8
RF	73	79.3	28	77.7
Seronegative RA	8	8.6	4	11,1

Table-3: Laboratory features

	Study population(n=92)		High Disease Activity(n=36)	
	Frequency	Percentage	Frequency	Percentage
Fever	30	32.6	19	52.7
Joint Pains	92	100.0	36	100
Joint Swelling	87	94.6	35	97.2
Morning Stiffness	90	97.8	36	100
Joint Deformity	59	64.1	34	94.4
Limitation of Movement	70	76.1	36	100
Carpell Tunnel Syndrome	5	5.4	4	11.1
Lymphadenopathy	7	7.6	5	13.8
Splenomegaly	10	10.9	5	13.8

Table-4: Clinical features

	Study population(n=92)		High Disease Activity(n=36)	
	Frequency	Percentage	Frequency	Percentage
PIP	78	84.8	34	94.4
MCP	88	95.7	34	94.4
Wrist	81	88.0	36	100
Elbow	52	56.5	28	77.7
Shoulder	29	31.5	19	52.7
Subtalar	23	25.0	16	44.4
Ankle	20	21.7	14	38.8
Knee	28	30.4	20	55.5
Cervical Spine	11	12.0	8	22.2

Table-5: Joint Involvement

	Study population(n=92)		High Disease Activity(n=36)	
	Frequency	Percentage	Frequency	Percentage
Swan Neck Deformity	21	22.8	17	47.2
Boutonniere Deformity	13	14.1	9	25
Z Deformity	21	22.8	15	41.6
Ulnar Deviation of Digits	36	39.1	28	77.7
Eversion of subtalar Joints	9	9.8	7	19.4
Plantar Subluxation of Metatarsal Heads	6	6.5	5	13.8
Hallux Valgus	7	7.6	6	16.6

Table-6: Joint Deformities

	Study population(n=92)		High Disease Activity(n=36)	
	Frequency	Percentage	Frequency	Percentage
Juxtarticular Osteopenia	54	58.7	33	91.6
Soft Tissue Swelling	46	50.0	27	75
Joint Space Narrowing	57	62.0	34	94.4
Joint Erosions	54	58.7	31	86.1
Intrarticular Loose Bodies	2	2.2	2	5.5
Joint Subluxation	6	6.5	4	11.1

Table-7: Radiological findings

	Study population(n=92)		High Disease Activity(n=36)	
	Frequency	Percentage	Frequency	Percentage
Rheumatoid Nodules	9	9.8	8	22.2
Valvular heart disease	4	4.3	3	8.3
Sjogren Syndrome	4	4.3	2	5.5
Episcleritis	3	3.3	3	8.3
Periodontitis	4	4.3	4	11.1
Pleuritis	7	7.6	7	19.4
CAD	9	9.8	8	22.2

Table-8: Extra articular manifestations

(MCP) joints (95.7%), followed by wrist joint (88%), Proximal Interphalangeal (PIP) joint (84.8%) and elbow joint (56.5%). Shoulder, knee, subtalar and ankle joints were affected in a decreasing frequency of involvement. Cervical spine was also involved in 12% of the patients (Table 5).

Most common joint deformity was ulnar deviation of digits (39%), followed by Swan Neck deformity (22.8%), Z deformity (22.8%) and Boutonniere deformity (14.1%) (Table 6).

Most common radiological changes on X ray were joint space narrowing (62%) followed by juxta articular Osteopenia (58.7%), joint erosions (58.7%), and soft tissue swelling (50%). There were 6.5% of patients who had joint subluxation. (Table 7).

Extra articular manifestations included presence of rheumatoid nodules in 10% of the patients. Pleuritis was present in 7.6% of the patients and 9.8% of the patients had CAD. Around 4% of the patients had valvular involvement, Sjogren syndrome and periodontitis.(Table 8).

Clinical profile of patients with high disease activity

On analysis of results we found that 36 (39.1%) of the patients had high disease activity with at least one parameter satisfying the criteria i.e DAS 28, DAS CRP, CDAI or SDAI. 83.3% of these patients were females, 33.33% had positive

family history, 91.6% had anaemia, 19.4% had leucocytosis, 5% had leucopenia, 100% had raised ESR, 38.8% had thrombocytosis, 1 case had thrombocytopenia, 63.8% had raised CRP. 88% were positive for anti-CCP and 78% were positive for RF. (Table-3)

Clinically 52.7% of patients had fever, 100% had joint pains, 97% had joint swelling and morning stiffness was present in 100% of the patients. Carpell tunnel syndrome was present in 11.1%, splenomegaly and lymphadenopathy in 13.8% of patients. All patients had limitation of movements and 94.4% patients had joint deformities. (Table-4)

Most common joint involved was wrist joint (100%), followed by the MCP and PIP joints (94.4%),and elbow joint (77.7%). Most common joint deformity was ulnar deviation of digits (77.7%), followed by Swan Neck deformity (47.2%), Z deformity (41.6%) and Boutonniere deformity (25%). Most common radiological changes on X ray were joint space narrowing (94.4%) followed by juxta articular Osteopenia (91.6%), joint erosions (81.6%), and soft tissue swelling (75%).

Extra articular manifestations included presence of rheumatoid nodules in 22% of the patients. Pleuritis was present in 19.4% of the patients and 22% of the patients had CAD.

DISCUSSION

RA is a chronic disease with autoimmune origin and variable course mainly presenting with joint involvement leading to considerable morbidity and systemic complications.The clinical picture of RA is mainly related to the involvement of peripheral joints with symmetrical involvement of hands, wrist, knee and feet. Significant extra articular involvement of organs like skin, heart, lungs and eyes can be present. Prodromal symptoms such as fatigue, weight loss, transient pain in muscles and joints, sweating, paresthesia and migrant swelling are often present before the onset of symptoms and signs.[7]

Involvement can be seen of any synovial joint. If the disease is uncontrolled, the associated co morbidities include cardiovascular disease (CVD), infections, depression and gastrointestinal disease.[8] Pathologically RA synovitis is characterized by leukocytic infiltrate, proliferative synovial membrane, and a neo vascularization that give rise to synovial hypertrophy. Early identification of synovitis is of importance as it represents the location of the rheumatoid joint inflammatory process and a target for therapeutic intervention.[9]

Prevalence of RA varies from region to region but the overall reported trends in the change in incidence and sex distribution are nearly the same in most populations.[10] Most epidemiological studies have been done in Western countries, showing a prevalence in the range of 0.5–1.0% in white individuals.[11] The prevalence differs between different ethnic groups. High prevalence of 5–6% has been reported in Native American populations.[12] The prevalence of RA in Kinshasa, Democratic Republic of the Congo, is 0.6% in the general black population and 0.9% in black individuals aged >18 years.[13] The differences are linked to a complex interaction of genetic and environmental factors and till date most of the factors remain speculations.[10]

Studies in India reported a prevalence range from 0.28% to 0.7%. In a study conducted in the year 1996 in the Bhigwan village of Pune district using surveys developed by WHO and International League of associations for Rheumatology (WHO-ILAR) Community Oriented Program for Control of Rheumatic Diseases (COPCORD) reported a prevalence of 0.51% for RA diagnosed with ACR criteria and 0.6% for RA diagnosed clinically.[14] In Jammu, a prevalence of 0.7% was reported by Mahajan et al.[15] In Ballabhgarh (Haryana) prevalence reported was 0.7%.[16]

Third COPCORD study was carried out in urban area of Pune. They recorded a prevalence of 0.28% for RA diagnosed with ACR criteria and 0.45% for RA diagnosed clinically. There was a prevalence of 3.5% of RA among those with rheumatic musculoskeletal diseases.[17]

Treatment methodology has evolved over time with application of newer diagnostic and therapeutic modalities. Currently the main aim is to detect RA early and treat it aggressively as maximum damage occurs in initial two years. We undertook this study to evaluate the clinical profile and disease activity assessment by validated disease indices of patients of RA reporting to a tertiary care centre.

Maximum number of patients in our study comprised of females i.e.81.5% of the population which was in comparison to the study by Diggikar et al. and Premkumar et al in which female study population was 84% and 77.3% respectively.[18,19] In fact worldwide the tread remains same with female predominantly effected by the disease. This has been postulated as related to hormonal status or differences in gender related life style.[20] However a correct explanation for the gender differences is still awaited and further research in understanding genetic and epigenetic influences will probably lead the pathway.

26% of the study population and 33.3% of the subset of patients with high disease activity had a positive family history of RA. Positive family history increases the risk of RA by three to five times; as it was estimated that genetics account for 40 to 65% of cases of seropositive RA, but only around 20% for seronegative RA.[4] Family history was positive in 28% of the patients in the study by Diggikar et al. and 14.8% in the cross sectional study by Vij et al.[18,21]

On analysis we found that 36 (39.1%) of the patients had high disease activity with at least one parameter satisfying the criteria i.e DAS 28, DAS CRP, CDAI or SDAI. In a similar study carried out in a western region of india, the percentage of patients with high disease activity having DAS28 score of more than 5.1 were 44.3%.[21] The clinical parameters of these patients were much worse with more frequent joint involvement, clinical symptomatology and signs and extra articular manifestations of the disease. The above methods used for disease activity scoring have been widely accepted. However there is still discordance between them. It has been proposed that the DAS28-ESR and the CDAI/SDAI weights their individual components differently, which sometimes

caused discordant assessments of RA disease activity.[22] We have used all the scoring systems and if found high score in any one of them we labelled the patient as having high disease activity.

Anaemia was found in 69% of the population and 91.6% in the subset of patients of high disease activity, which was similar to observational study carried out by Goyal et al. on 59 patients of RA in India which showed 67.8% of the patients had anaemia and 90% in the subset of patients of high disease activity.[23] The cause of anemia in RA is mainly due to anemia of chronic disease caused by the inflammatory mediators effecting hematopoesis.[24] However in our country deficiency disorders also compound it.

Thrombocytosis has also been reported in various studies. A study by Hutchison et al. demonstrated 39 out of 75 patients with RA had thrombocytosis.[25] Diggikar et al. demonstrated thrombocytosis in 26% of the patients[18] whereas in our study 22.8% of the patients had thrombocytosis with 38.8% in the subset of patients of high disease activity. Thrombocytosis has been associated with disease activity with a positive correlation.[26] Hutchinson et al. (1976) have noted the association between extreme thrombocytosis and extra-articular manifestations of the disease, in particular pulmonary involvement, peiipheral neuropathy, and vasculitis. Relapses of arthritis may frequently be associated with the appearance of thrombocytosis, while remissions are usually accompanied by a decreased platelet count.

In the study conducted by Joshi et al. 62% of the RA patients were seropositive for RF while 100% were seropositive for anti-CCP.[17] In our study anti CCP and RF was positive in 91 and 79% of patients (88% anti-CCP and 78% RF positivity in the subset of patients of high disease activity), as compared to 94 and 76% in a study by Diggikar et al.[18] 74% of patients had a positive RF in the study by Goyal et al.[23] In a case control study done by Gupta et al at a tertiary care centre in Delhi where 63 patients with RA and 51 patients with non-RA rheumatic diseases having joint pain were studied, 54 of 63 RA patients (85.71%) were positive for anti-CCP antibodies and in the non-RA group, anti-CCP antibody was positive in only 5 of 51 patients (9.8%).[27]

Our study reported raised ESR in all patients and raised CRP in 40% of the patients (63% of the patients had raised CRP in the subset with high disease activity) as compared to raised ESR and CRP levels in 86% and 84% of the patients respectively in the study by Diggikar et al.[18] The difference in percentage of patients with raised CRP could be because of the difference in methodology used which was Nephelometry in our study as compared to ELISA in other studies. A study by Sokka et al. demonstrated normal ESR,CRP or RF in 35-45% of patients in Finnish and American population.[28]

Fever, joint pain, joint swelling, morning stiffness, deformity, limitation of movement, carpel tunnel syndrome, splenomegaly ware present in a similar number of patients as per a study from a similar region by Diggikar et al.[18]

Most common joint deformity was ulnar deviation of digits, followed by Swan Neck deformity, Z deformity and Boutonniere deformity as depicted in Table 6. In a subset of population with high disease activity the joint deformity was much worse with 77.7% having ulnar deviation of digits and 47.2% having Swan neck deformity. Similar results were seen in a similar study by Diggikar et al.[18]

In our study the most common joint involvement was MCP joint (95.7%), wrist joint (88%) and PIP joint (84.8%) with involvement of knee and ankle in 30.4% and 21.7% of the patients respectively. Most common joint involved in patients with high disease activity was wrist joint (100%) followed by MCP and PIP joint (94.4%). The significant difference was in the percentage of wrist involvement being 88% in our study and being 66% in a study from the similar region by Premkumar et al.[19] Similar results on the percentage of joint involvement were demonstrated by Jacoby et al in 100 patients with the most common joint being MCP joint (87%), wrist joint (82%) and PIP joint (63%) with knee and ankle involvement in 56% and 53% of patients.[29]

In a study by Jeffery RC., extra-articular manifestations were seen in around 40% of patients with RA. 30% of the patients had rheumatoid nodules, 75% had pulmonary involvement and 50% had cardiac involvement on post mortem with most common involvement being pleurisy and CAD.[30] In our study extra articular manifestations included presence of rheumatoid nodules in 10%, pleuritis in 7.6% and CAD in 9.8% of the patients. In patients with high disease activity rheumatoid nodules were seen in 22%, pleuritis in 19.4% and CAD in 22% of the patients. Similar results were found in a study by Diggikar et al.[18]

Most common radiological changes on X ray were joint space narrowing (62%) followed by juxta articular Osteopenia (58.7%), joint erosions (58.7%) and soft tissue swelling (50%). 6.5% of patients had joint subluxation. In patients with high disease activity, joint space narrowing was seen in 94.4%, juxta articular osteopenia was seen in 91.6% and joint erosions in 86% of the patients. Joint subluxation was seen in 11% of the patients. The results of our study were similar to the study conducted by Diggikar etal. in 100 diagnosed cases of RA. In their study they had found juxta articular osteopenia in 74%, soft tissue swelling in 74%, joint space narrowing in 60% and joint erosions in 40% of the patients.

In a study by Fletcher et al. as old as in 1952 where analysis of radiological features in 200 diagnosed cases of RA was done, joint space narrowing was seen in 75% of the patients, joint erosions in 76% and joint subluxation in 21% of the patients at that time. Hence the morbidity associated with disease does not seem to have changed much in the developing world.[31]

Therapy of RA presently has focus on early and aggressive management to prevent joint damage. Frequent modification of therapy is being done along with initiation of combination therapy.[32] Methotrexate is the DMARD (Disease modifying anti rheumatic drug) of choice in management of patients with RA. Effective combinations include triple therapy (Methotrexate + Sulfasalazine + Hydroxychloroquine), Methotrexate + Leflunomide, methotrexate +biological. Chronic therapy with low dose steroids is also used to control disease activity in patients with inadequate response

to DMARD therapy. In our study most of the patients were on therapy with 2 DMARDs + low dose steroid therapy. Methotrexate was the most widely prescribed drug.

CONCLUSION

Morbidity associated with RA remains highly prevalent. The disease has female preponderance with a significant proportion having positive family history. Most common joints involved are the MCP and the wrists and the most common deformity we found ulnar deviation of digits. There are significant proportions of patients who present with high disease activity. Anaemia, thrombocytosis and extrarticular manifestations are common. Most of the patients are on DMRDs with methotrexate being the most commonly used drug.

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