Section: Miscellaneous

Original Research Article

RHEUMATOID ARTHRITIS IN EASTERN INDIA: A COMPREHENSIVE CLINICAL STUDY AT A TERTIARY CARE HOSPITAL

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Received : 12/08/2023
Received in revised form : 10/09/2023
Accepted : 21/09/2023

Keywords:
Auto-immune, Hospital-based, Rheumatoid Arthritis.

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DOI: 10.47009/jamp.2023.5.5.108

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (5); 550-556

Abstract

Background: The symptoms of rheumatoid arthritis include persistent joint inflammation, cartilage, and bone loss, severe activity restriction, a decline in quality of life, and frequently systemic consequences. With improved access to tertiary care facilities across the nation, there have been significant advancements in the diagnostic and therapeutic options for RA in recent years. The study aimed to evaluate the current clinical profile of RA patients visiting a tertiary care facility in eastern India. **Materials and Methods:** This prospective observational, hospital-based investigation was conducted in a tertiary care teaching hospital over six months. All consecutively diagnosed RA cases who visited our OPD or were admitted to the wards were assessed. The American College of Rheumatology Criteria-201 was used to diagnose RA. In addition to analyzing inflammatory markers, a thorough clinical history and examination were also conducted. **Result:** For the study, a total of 103 patients of RA were eligible. In the study population, women made up 82.5 percent. One first-degree relative in 26.2% of the study group had the same illness as them. Of the patients, 40 (38.8%) exhibited severe disease activity. MCP joint was the most often involved joint. The most frequent radiological result was joint space narrowing, and the most frequent joint deformity was an ulnar deviation of the digits. **Conclusion:** Most people with RA were female, and a sizable percentage had a favorable family history. The MCP joints are the most often affected, and ulnar deviation of the fingers is the most prevalent deformity. A sizeable percentage of individuals have severe disease activity when they first arrive. Common symptoms include anemia, thrombocytosis, and extrarticular manifestations. Most patients are on DMRDs, with methotrexate being the most often prescribed medication.

INTRODUCTION

A chronic systemic auto-immune condition, rheumatoid arthritis (RA) is a disease. The disease's progression can vary. A sizeable portion of the population experiences chronic pain, stiffness, deteriorating joints, functional impairment, and rising morbidity and death.[1] A chronic joint infection, cartilage and bone deterioration, considerable activity limitations, a decline in quality of life, and frequent systemic consequences characterize the disease.[2] With improved access to tertiary care facilities nationwide, there have been significant advancements in the diagnostic and therapeutic options for RA in recent years. The study aimed to evaluate the current clinical profile of RA patients visiting a tertiary care facility in eastern India.

MATERIALS AND METHODS

The study was conducted at the MKCG Medical College and Hospital in Berhampur, India, and was prospective observational and hospital-based. The study was conducted for six months, from January 2021 to July 2021, with the institutional ethics committee's consent. All consecutively diagnosed RA cases who visited our OPD or were admitted to the wards were assessed using a pre-made questionnaire. Based on the 2010 American College of Rheumatology Criteria for RA, all patients had their diagnoses made.[3] Patients who had any other

ISSN (O): 2687-5365; ISSN (P): 2753-6556

joint diseases, were hesitant to participate in the trial, had acute fractures, or had a history of malignancy were also disqualified.

Data was collected with particular attention to Clinical history and presentation, extra-articular and articular involvement, and the length of the disease. As stated, Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), and radiographic studies were performed as baseline hematological, biochemical, and inflammatory indicators. The Westergren method was used to measure ESR, while nephelometry was used to measure CRP (Beckman Coulter IMMAGE 800 Immunochemistry System). All patients had estimated levels of rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP). 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 were used to measure disease activity (Simplified disease activity Index).[4-6]

DAS-CRP score and DAS-28 A score >5.1 indicated high disease activity, a score >3.2 and 5.1 indicated moderate disease activity, a score 3.2 and >2.6 showed low disease activity, and a score less than 2.6 indicated remission. According to the SDAI, high disease activity was suggested by a score of>40, moderate disease activity by >20 and 40, low disease activity by >3.3 and 20, and remission by a score of 3.3. A score of >2.8 indicated remission, >2.8 indicated low disease activity, >10 indicated moderate disease activity, and >2.8 indicated low disease activity on the CDAI.

RESULTS

A total of 103 instances of RA met the study's eligibility requirements. In total, 84 women participated in the survey, and 26.2% of the population had a first-degree relative with the same illness [Table 1]. After analyzing the data, we discovered that 40 patients (38.8%) had significant disease activity, and at least one parameter matched the requirements, i.e., DAS 28, DAS CRP, CDAI, or SDAI. 32.5 percent of these patients had a favorable family history, and 82.5 percent were female.

Most patients received treatment with two DMARDs (disease-modifying anti-rheumatic drugs) plus steroids, and methotrexate, which has been prescribed to 92.2 percent of the study population to date, was the drug most frequently used [Table 2].

Anaemia affected 69.6% of the study population, along with leucocytosis, leukopenia, thrombocytosis, and thrombocytopenia in 10.7%, 22.3%, and 33.9% of cases, respectively. Another significant observation was that ESR was elevated in all patients, and CRP was elevated in 39.8%. 91.3 percent of the patients tested positive for anti-cyclic citrullinated peptide (anti-CCP), 79.6 percent tested positive for rheumatoid factor (RF), and 8.7 percent tested seronegative for RA. [Table 3]. Patients with high disease activity showed anemia in 92.5% of cases, leucocytosis in 20%, leucopenia in 5%, elevated ESR in 100% of cases, thrombocytosis in 40% of cases, thrombocytopenia in 1 point, and raised CRP in 65% of cases. Anti-CCP positivity was 87.5 percent, and RF positivity was 77.5 percent.

Clinically, 32% of patients had a fever, 100% experienced joint aches, 94.2 percent had joint swelling, and 98.1 percent had morning stiffness. 75.7% of patients experienced movement restrictions, and 64.1% had joint deformities. 5.8% of people experienced carpal tunnel syndrome, 10.7% had splenomegaly, and 8% had lymphadenopathy. [Table 4] Patients with high-risk activities: Clinically, 100% of patients experienced morning stiffness, 100% of patients had joint aches, 100% of patients had joint swelling, and 52.5 percent of patients had fever. Splenomegaly, lymphadenopathy, and carpal tunnel syndrome were all present in 10%, 15%, and 20% of patients, respectively. Ninety-five percent of patients had joint abnormalities, and all patients had movement restrictions.

The Metacarpophalangeal (MCP) joint was the most often affected joint (95,1%), followed by the Proximal Interphalangeal (PIP) joint (91%) and the Elbow joint (87%) (58 percent). The shoulder, knee, subtalar, and ankle joints were all afflicted, though to varying degrees. The cervical spine was also affected in 12% of the patients [Table 5]. The wrist joint was the most often involved in patients with high-risk activity (100%), followed by the MCP and PIP joints (95%) and the elbow joint (77.5 percent).

The most frequent joint deformity was an ulnar deviation of the digits (38.8%), followed by Swan Neck (22.3%), Z (22.3%), and Boutonniere (13.6%) deformities [Table 6]. The most prevalent joint deformity in high-risk activity patients was ulnar deviation of the fingers (77.5%), followed by Swan Neck (47.5%), Z (42.5%), and Boutonniere deformities (25 percent).

Joint space narrowing (62.1%) was the most prevalent radiological change seen on X-rays, followed by juxta-articular osteopenia (58.3%), joint erosions (58.3%), and soft tissue swelling (58.3%). (49.5 percent). Joint subluxation affected 6.8% of the patient population. [Table 7]. Joint space narrowing (95%) and juxta-articular osteopenia (92.5%), joint erosions (85%), and soft tissue edema (95%) were the most prevalent radiographic alterations in high-risk patients (75 percent).

9.7% of the patients had rheumatoid nodules, which were extra-articular symptoms. 9.7 percent of the patients had CAD, while 7.8 percent had pleuritis. Sjogren syndrome, periodontitis, and valve involvement were present in about 3.9 percent of the patients. [Table 8]. Extra-articular symptoms in patients with high-risk activities included the existence of rheumatoid nodules in 22% of the patients. 22.5 percent of the patients had pleuritis, and 22.5 percent had CAD.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 1: Characteristics of study participants

		Study population(n=103)		High Disease Activity(n=40)	
		Frequency	**Percentage**	**Frequency**	**Percentage**
Sex	Male	19	18.4	7	17.5
	Female	84	81.6	33	82.5
Family History	Present	27	26.2	13	32.5

Table 2: Medications among study participants

	Study population(n=103)		High Disease Activity(n=40)	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Steroids	68	66.0	35	87.5
Leflunomide	14	13.6	7	17.5
Sulfasalazine	40	38.8	22	55
Azathioprine	2	1.9	3	7.5
Hydroxychloroquine	90	87.4	36	90
Methotrexate	95	92.2	38	95

Table 3: Key laboratory parameters of study participants

	Study population(n=103)		High Disease Activity(n=40)	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Anaemia	72	69.9	37	92.5
Leucocytosis	11	10.7	8	20.0
Leucopenia	3	2.9	2	5.0
Raised ESR	103	100.0	40	100.0
Thrombocytosis	23	22.3	16	40.0
Thrombocytopenia	3	2.9	1	2.5
Raised CRP	41	39.8	26	65.0
Anti-CCP	94	91.3	35	87.5
RF	82	79.6	31	77.5
Seronegative RA	9	8.7	4	10.0

Table 4: Clinical features of study participants

	Study population(n=103)		High Disease Activity(n=40)	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Fever	33	32.0	21	52.5
Joint Pains	103	100.0	40	100
Joint Swelling	97	94.2	39	97.5
Morning Stiffness	101	98.1	40	100
Joint Deformity	66	64.1	38	95
Limitation of Movement	78	75.7	40	100
Carpell Tunnel Syndrome	6	5.8	4	10
Lymphadenopathy	8	7.8	6	15
Splenomegaly	11	10.7	6	15

Table 5: Joint Involvement

	Study population(n=103)		High Disease Activity(n=40)	
	Frequency	**Percentage**	**Frequency**	**Percentage**
PIP	87	84.5	38	95
MCP	98	95.1	38	95
Wrist	91	88.3	40	100
Elbow	58	56.3	31	77.5
Shoulder	32	31.1	21	52.5
Subtalar	26	25.2	18	45
Ankle	22	21.4	15	37.5
Knee	31	30.1	22	55
Cervical Spine	12	11.7	9	22.5

Table 6: Joint Deformities among study particiopants

	Study population(n=92)		High Disease Activity(n=36)	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Swan Neck Deformity	23	22.3	19	47.5
Boutonniere Deformity	14	13.6	10	25
Z Deformity	23	22.3	17	42.5
Ulnar Deviation of Digits	40	38.8	31	77.5
Eversion of subtalar Joints	10	9.7	8	20
Plantar Subluxation of Metatarsal Heads	7	6.8	5	12.5
Hallux Valgus	8	7.8	7	17.5

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 7: Radiological findings of study participants

	Study population(n=92)		High Disease Activity(n=36)	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Juxtarticular Osteopenia	60	58.3	37	92.5
Soft Tissue Swelling	51	49.5	30	75
Joint Space Narrowing	64	62.1	38	95
Joint Erosions	60	58.3	34	85
Intraarticular Loose Bodies	2	1.9	2	5
Joint Subluxation	7	6.8	4	10

Table 8: Extra-articular manifestations in study participants

	Study population(n=92)		High Disease Activity(n=36)	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Rheumatoid Nodules	10	9.7	9	22.5
Valvular heart disease	4	3.9	3	7.5
Sjogren Syndrome	4	3.9	2	5
Episcleritis	3	2.9	3	7.5
Periodontitis	4	3.9	4	10
Pleuritis	8	7.8	8	20
CAD	10	9.7	9	22.5

DISCUSSION

RA is a chronic autoimmune disease with a varied course that often affects the joints and causes significant morbidity and systemic consequences. The involvement of peripheral joints with symmetrical involvement of the hands, wrists, knees, and feet dominates the clinical picture of RA. Skin, heart, lungs, and eyes can all have significant extra-articular involvement. Before symptoms and signs appear, prodromal symptoms such as weariness, weight loss, momentary muscle and joint pain, sweat, paresthesia, and migratory edema are frequently present.[7]

Any synovial joint can show involvement. If the condition is left untreated, co-morbidities such as depression, gastrointestinal disorders, infections, and CVD will develop.[8] Leukocytic infiltration, proliferative synovial membrane, and a neo-vascularization that results in synovial hypertrophy are the pathological characteristics of RA synovitis. Early detection of synovitis is crucial because it is a target for therapeutic intervention and the site of the inflammatory process in rheumatic joints.[9]

Although the incidence of RA varies from place to region, most populations have generally reported relatively identical trends in incidence and sex distribution.[10] Most epidemiological research has been conducted in Western nations, and the frequency in white people is between 0.5 and 1.0 percent.[11] The incidence varies among various ethnic groups. Native American populations have been reported to have a high incidence of 5–6 percent.[12] In Kinshasa, Democratic Republic of the Congo, RA affects 0.6 percent of the total black population and 0.9 percent of black people over the age of 18.[13] The differences are attributed to a complex interplay between genetic and environmental factors, the majority of which are still subject to conjecture.[10]

According to studies, the prevalence in India ranged from 0.28 percent to 0.7 percent. Using surveys created by the WHO and International League of Associations for Rheumatology (WHO-ILAR), the Community Oriented Program for Control of Rheumatic Diseases (COPCORD) reported a prevalence of 0.51 percent for RA diagnosed with ACR criteria and 0.6 percent for RA diagnosed clinically in the Bhigwan village of Pune district in 1996.[14] Mahajan et al. observed a prevalence of 0.7 percent in Jammu.[15] The prevalence rate in Ballabhgarh, Haryana, was reported to be 0.7%.[16]

The third COPCORD research was conducted in Pune's urban region. The prevalence of RA diagnosed using ACR criteria was 0.28 percent, while for RA diagnosed clinically, it was 0.45 percent. Among people with rheumatic musculoskeletal disorders, the prevalence of RA was 3.5%.[17] Application of more recent diagnostic and therapeutic technologies has led to an evolution in treatment methodology. The current focus is on early detection and vigorous treatment of RA because the first two years are when most damage happens. We conducted this study to analyze the clinical profile and disease activity in RA patients presenting to a tertiary care facility using validated disease indices.

In contrast to studies by Diggikar et al. and Premkumar et al., in which the proportion of female study participants was 84 percent and 77.3 percent, the majority of patients in our study, 82.5 of the population, were female.[18,19] the trend is still toward more females being affected by the disease globally. This has been theorized to be connected to hormone states or lifestyle variations associated with gender.[20] The correct explanation for gender disparities is still pending, and additional studies into the roles of genetic and epigenetic factors will likely go in that direction. 26.2 percent of the study group had a positive family history of RA, and 38.8 percent of the population had high disease activity. Since genetics are thought to be responsible for between 40 and 65 percent of instances of seropositive RA but only around 20 percent of cases of seronegative RA, having a positive family history raises the chance of developing RA by three to five times.[4] In the study by Diggikar et al., 28% of the patients had a positive

ISSN (O): 2687-5365; ISSN (P): 2753-6556

family history. In the cross-sectional study by Vij et al., 14.8% had a positive family history.[18,2]

Upon investigation, we discovered that 40 patients (38.8%) exhibited significant disease activity, and at least one parameter matched the requirements, i.e., DAS 28, DAS CRP, CDAI, or SDAI. In a related study conducted in western India, 44.3% of patients with significant disease activity had DAS28 scores greater than 5.1.21. These individuals' clinical characteristics were significantly worse, including more frequent joint involvement, clinical symptomatology and symptoms, and extra-articular disease presentations. The techniques mentioned above for calculating disease activity scores are extensively employed. But they continue to disagree with one another. It has been suggested that the CDAI/SDAI and the DAS28-ESR weight their constituent components differently, occasionally resulting in inconsistent estimates of the severity of RA disease.[22] We have used all available grading methods, and if a patient received a high score in any of them, we classified them as having a high disease activity.

Similar to an observational study conducted by Goyal et al. on 59 RA patients in India that revealed anemia in 67.8% of the patients and 90% in the subset of patients with high disease activity, anemia was found in 69.9% of the population and 92.5 percent in the subset of patients with high disease activity in this study.[23] Anemia in RA is mainly brought on by chronic disease-related anemia brought on by inflammatory mediators that affect hematopoiesis.[24] However, it is also exacerbated in our nation by deficiencies problems. Numerous investigations have also detected thrombocytosis. 39 out of 75 RA patients in a study by Hutchison et al. exhibited thrombocytosis.[25] In our study, 22.3 percent of the patients exhibited thrombocytosis, with 40.0 percent of those in the subset of patients with high disease activity. Diggikar et al. found that thrombocytosis occurred in 26 percent of the patients.[18] Disease activity has been positively correlated with thrombocytosis.[26] Extreme thrombocytosis has been linked to extra-articular illness symptoms, such as lung involvement, peripheral neuropathy, and vasculitis, according to Hutchinson et al. (1976). A decreased platelet count typically accompanies remissions from arthritis, but relapses are generally associated with developing thrombocytosis.

Joshi et al. study. Found that whereas 100% of the RA patients tested positive for anti-CCP, only 62% of RA patients tested positive for RF.[17] In contrast to 94 and 76 percent in research by Diggikar et al., anti-CCP and RF positivity was found in 91.3 and 79.6 percent of patients in our study (87.5 percent anti-CCP and 77.5 percent RF positivity in the sample of patients with high disease activity).18 In the Goyal et al. trial, 74% of patients got a positive RF.[23] In a case-control study conducted by Gupta et al. at a tertiary care center in Delhi, where 63 patients with RA and 51 patients with non-RA rheumatic diseases with joint pain were studied, 54 of the 63 RA patients (85.71 percent) had anti-CCP antibodies, while only 5 of the 51 patients in the non-RA group had anti-CCP antibodies (9.8 percent).[27]

In our investigation, all patients had elevated ESR levels, and 39.8% of patients had elevated CRP levels (65% of patients had elevated CRP in the subset with high disease activity), compared to the study by Diggikar et al., where these values were elevated in 86% and 84 % of patients, respectively.[18] Nephelometry was utilized in our study as opposed to ELISA in other investigations, which may account for the discrepancy in the percentage of individuals with elevated CRP. In research by Sokka et al., 35–45% of patients in the Finnish and American populations had normal ESR, CRP, or RF levels.28 According to research from a nearby region by Diggikar et al., splenomegaly, carpal tunnel syndrome, morning stiffness, deformity, joint discomfort, and edema were all present in a similar number of patients.[18]

The most frequent joint deformity was ulnar deviation of the digits, followed by Swan Neck, Z, and Boutonniere deformities. The joint deformity was substantially severe in a subset of the cohort with high disease activity, with 77.5 percent having ulnar deviation of the digits and 47.5 percent having Swan neck deformity. Similar findings were found in a study conducted by Diggikar et al.[18]

The most frequently affected joints in our study were the MCP joint (95,1%), wrist joint (88.3%), and PIP joint (84,5%), with the knee and ankle being involved in 30,1% and 21,4% of patients, respectively. Wrist joint (100%) was most frequently involved in patients with significant disease activity, followed by MCP and PIP joint (95 percent). The percentage of wrist involvement was 88 percent in our study versus 66 percent in a study from the same area by Premkumar et al.; that was a significant difference.[19] Jacoby et al. showed similar results regarding the percentage of joints involved in 100 patients, with the most prevalent joints being the MCP joint (87 percent), wrist joint (82 percent), and PIP joint (63 percent), and the knee and ankle being involved in 56 percent and 53 percent of patients, respectively.[29]

According to research by Jeffery RC, about 40% of RA patients had extra-articular symptoms. On post-mortem examination, 30% of the patients exhibited rheumatoid nodules, 75% had pulmonary involvement, and 50% had cardiac involvement, with pleurisy and CAD being the most frequent.[30] In our investigation, patients with rheumatoid nodules (9.7%), pleuritis (7.8%), and CAD (9.7%) were shown to have extra-articular symptoms. Rheumatoid nodules, pleuritis, and CAD were all seen in 22.5%, 20.5%, and 22.5% of patients with significant disease activity, respectively. In a research by Diggikar et al., comparable outcomes were discovered.[18]

Joint space narrowing (62%) was the most prevalent radiological change seen on X-rays, followed by juxta-articular osteopenia (58.3%), joint erosions (58.3%), and soft tissue swelling (58.3%). (49.5 percent). Joint subluxation affected 6.8% of the

ISSN (O): 2687-5365; ISSN (P): 2753-6556

patient population. Joint space narrowing, juxta-articular osteopenia, and joint erosions were all observed in 92.5 percent, 92.5 percent, and 85 percent of individuals with high disease activity, respectively. 10% of the patients had signs of joint subluxation. Our study's findings were comparable to those of a survey carried out by Diggikar et al. in 100 instances of RA that had been diagnosed. They discovered juxta-articular osteopenia in 74% of the patients, soft tissue edema in 74%, joint space constriction in 60%, and joint erosions in 40%. Joint space narrowing was observed in 75% of patients, joint erosions in 76% of patients, and joint subluxation in 21% of patients in a 1952 study by Fletcher et al. that examined radiological characteristics in 200 diagnosed cases of RA. Consequently, disease morbidity appears to have not altered significantly in the developing world.[31]

The current focus of RA treatment is on early and aggressive care to stop joint deterioration. Therapy is being regularly modified, and combination therapy has been started.[32] The preferred DMARD (disease-modifying anti-rheumatic drug) for treating RA patients is methotrexate. Methotrexate + Leflunomide, Methotrexate + Biological, and Triple Therapy (Methotrexate + Sulfasalazine + Hydroxychloroquine) are all effective combinations. When DMARD therapy fails to produce the desired results in a patient, chronic low-dosage steroid therapy is utilized to control disease activity. Most of the patients in our study were receiving treatment with two DMARDs and low-dose steroid therapy. The most often prescribed medication was methotrexate.

CONCLUSION

The morbidity linked to RA is still widespread. The disease disproportionately affects women; many cases have a favorable family history. The MCP and wrists are the most often affected joints, and the most frequent digit deformity we discovered is ulnar deviation. A sizeable percentage of individuals have severe disease activity when they first arrive. Common symptoms include anemia, thrombocytosis, and extra articular manifestations. Most patients are on DMRDs, with methotrexate being the most often prescribed medication.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556

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ISSN (O): 2687-5365; ISSN (P): 2753-6556