DOI: 10.7860/JCDR/2022/58811.17098

Original Article

Internal Medicine Section

Assessment of Current Trends in Demographic and Clinical Characteristics of Male Patients with Rheumatoid Arthritis: A Retrospective Study

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ABSTRACT

Introduction: Role of gender in development of an autoimmune dysfunction in Rheumatoid Arthritis (RA) is very complex and therefore novel concept of gender medicine has come into limelight.

Aim: To assess current trends in demographic and clinical characteristics of male patients with RA.

Materials and Methods: This retrospective study was conducted among patients with RA attending Outpatient Department of Rheumatology at Santokba Durlabhji Memorial Hospital cum medical Research Institute, Jaipur and Centre for Arthritis and Autoimmune Rheumatic Disorders, Jaipur, Rajasthan, India, during April 2015 to April 2021. Men who qualified the European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) criteria for RA were included in this study. The medical records of patients were reviewed for collecting demographic and clinical characteristics, disease activity, disease duration, deformities, extra articular manifestations, and co-morbid illness.

Results: A total of 179 men were enrolled, and the mean age was 45.3±11.1 years. The majority of patients had severe disease with more than two years of disease duration. Subcutaneous nodule (27.8%) was most frequently observed extra-articular manifestations. Rheumatoid factor positivity and cyclic citrullinated peptide were prevalent in 107 and 110 patients, respectively. Osteoporosis (21.1%) and hypertension (19.2%) were the most common co-morbidities and majority of patients reported wrist deformities.

Conclusion: Overall observations indicate the presence of subcutaneous nodule as the common extra-articular manifestation with more than 2 years of disease duration, osteoporosis and hypertension as the most common co-morbidities; and high prevalence of wrist deformities in male patients with RA.

Keywords: Hypertension, Osteoporosis, Subcutaneous nodule

INTRODUCTION

Gender differences in Rheumatoid Arthritis (RA) is a well-established fact and women are more prone to develop RA than men [1-4]. Sex hormones play an important role in the pathogenesis of RA. The severity of RA correlates inversely with androgen levels, therefore there is lower severity of RA in men. Although RA affects more women than men evidence from several studies indicates that long-term conditions of disease impact differently on men compared to women [5]. The significance of studying RA in men suggests that RA in men has significantly higher risk and may predispose men to poor outcomes, such as pain and disability and early mortality [6].

However, the role of gender in the development of an autoimmune dysfunction in RA is very complex and it is crucial to gain comprehensive knowledge about impact of each gender on disease prevalence, aetiology, disease progression and outcomes of therapeutic interventions. Therefore, in today's modern era, a novel concept of gender medicine has come into limelight. Focusing on the impact of gender differences on human physiology, pathophysiology, and clinical features of diseases, analysing the complex interrelation and integration of gender and psychological and cultural behaviour [7].

Gender has been shown to affect the physiological, biological, functional, clinical, social presentation, history, and response to medications in rheumatic disease [8,9]. Male health has emerged as a new paradigmfocused on the dramatic disparities in occurrence, clinical signs, outcome, and therapeutic efficacy [10]. Applying this model to RA may allow the identification of gender based outcomes such as activity indices and radiographic damage [11].

Studies evaluating demographic and clinical characteristics of male patients with RA are scarce [6,12,13] and there is a need to better investigate the possible factors contributing to the sexual dimorphism in RA. Thus, the present study aimed to assess current trends in demographic and clinical characteristics, disease activity, disease duration, deformities, extra-articular manifestations, and co-morbid illness among male patients with RA.

MATERIALS AND METHODS

This retrospective study was conducted among patients with RA attending Outpatient Department of Rheumatology Santokba Durlabhji Memorial Hospital cum medical Research Institute, Jaipur and Centre for Arthritis and Autoimmune Rheumatic Disorders, Jaipur, Rajasthan, India, during April 2015 to April 2021. The study was approved by the Institutional Ethics Committee (IEC/2022/16).

Inclusion and Exclusion criteria: All male patients qualifying the European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) criteria for RA [14] were included in the study. The ACR/EULAR negative patients were excluded from the study.

The medical records of patients were reviewed for collecting demographic details that included age, gender, medical history of family, associated co-morbidities including osteoporosis, hypertension, diabetes mellitus, hypothyroidism, anaemia, dyslipidaemia, and pattern of joint affected prescribed.

The pretreatment parameters including tender joint count, swollen joint count, Visual Analogue Scale Score (VAS), Disease Activity Score (DAS) [15], disease activity, and cyclic citrullinated peptide were evaluated.

STATISTICAL ANALYSIS

Data were analysed using Statistical Package for the Social Sciences (SPSS) version 23.0. Descriptive statistics was used to describe categorical variables (frequency and percentages) and continuous variables {mean and Standard Deviation (SD)} or median and range (depending on the normality of data).

RESULTS

A total of 179 men were enrolled in this study. The mean age of study population was 45.3±11.1 years and 9.4% of patients had family history of RA. The average number of swollen and tender joints affected were 4.8% and 6%, respectively. In extra-articular manifestations, subcutaneous nodule (27.8%), Sjögren's syndrome (22.2%) and interstitial lung disease (22.2%) were common. The mean visual analogue scale was 37.3 and mean disease activity score was 5.2. More than half (51.7%) of patients had severe disease activity score (15/28) [Table/Fig-1]. Majority of patients (47.9%) reported longer disease duration (more than 2 years). Total 107 patients had Rheumatoid Factor (RF) positive and 110 patients showed presence of cyclic citrullinated peptide.

Parameters	n,%
Age (years) (Mean±SD) (n=124)	45.3±11.1
Family history (n=160)	15 (9.4)
Extra-articular (n=36)	
Sjögren's syndrome	8 (22.2)
Subcutaneous nodule	10 (27.8)
Interstitial lung disease	8 (22.2)
Peripheral neuropathy	1 (2.8)
Vasculitis	3 (8.3)
Others	6 (16.7)
Symptoms	
Swollen joints (Mean±SD) (n=124)	4.9±4.8
Tender joints (Mean±SD) (n=124)	8.9±6.0
Measures	
Visual analogue scale (Mean±SD) (n=124)	37.3±20.6
Disease activity score (Mean±SD) (n=124)	5.2±1.4
Disease activity (n=29)	
Low	1 (3.4)
Moderate	9 (31.0)
Severe	15 (51.7)
Inactive	4 (13.8)
Disease duration (n=167)	
<3 months	8 (4.8)
3 to 6 months	20 (11.9)
6 months to 2 years	59 (35.4)
>2 years	80 (47.9)
Erosion (n=35)	16 (45.7)
Erythrocytes sedimentation rate (Mean±SD) (n=124)	46.9±24.1
Rheumatoid factor (IU/mL) (n=170)	107 (62.9)
Cyclic citrullinated peptide (U/mL) (n=168)	110 (65.4)
Antinuclear antibodies (n=11)	3 (27.2)

[Table/Fig-1]: Patients' clinical characteristics.
Others-Coronary artery disease, cystoid macular edema, interstitial lung disease, Myelopathy, rheumatoid arthritis

[Table/Fig-2] presents distribution of co-morbidities observed among patients. Osteoporosis (21.1%) and hypertension (19.2%) were the most common co-morbidities observed. Among the joint deformities observed, bilateral deformities were prevalent than unilateral ones. Among these, the majority of patients reported wrist deformities (62.5% and 17.1%) [Table/Fig-3].

Co-morbidities	n,%
Hypertension	20 (19.2)
Diabetes mellitus	11 (10.5)
Dyslipidaemia	4 (3.8)
Osteoporosis	22 (21.1)
Anaemia	4 (3.8)
Coronary artery disease	2 (1.9)
Others	41 (39.4)

[Table/Fig-2]: Prevalence of comorbidities in patients with rheumatoid arthritis (N=104).
Others- Aortic regurgitation, azoospermia, cataract, cervical spine,eczema, fibromyalgia, myasthenia, hypothyroid renal dysfunction, carcinoma stomach, herpes zoster, post chikungunya arthritis, verrucae vulgaris, tinea corporis, nodular sclerosis, maculopathy, neuropathy

Deformities	Bilateral (n,%)	Unilateral (n,%)
Hand	9 (10.2)	0
Wrist	55 (62.5)	15 (17.1)
Elbow	12 (13.6)	8 (9.1)
Knee	17 (19.3)	3 (3.4)
Foot	4 (4.5)	0
Others	6 (6.8)	3 (3.4)

[Table/Fig-3]: Joint deformities (n=88).
Patients had more than one deformity; Others-Baber's cyst, cervical spine, hallax valgus, ulnar deviation, shoulder, swan neck

DISCUSSION

Past literature has established the evidence in support of the concept that gender has major impact on several pathogenic and epidemiologic aspects of RA, resulting in differences between affected males and females. Accordingly, there will be different patterns of disease onset and presentation, disease activity, response to treatments, disability, radiographic progression, and extra-articular manifestations/co-morbidities in men and women [16]. Gender may have indirect effect on increased RA susceptibility through environmental/behavioural factors, such as smoking, known to be implicated in seropositive RA [17].

Extensive literature search revealed that there is no Indian study which assessed pattern of disease epidemiology and pathogenicity in male patients alone. Therefore, the present study is of its first kind that evaluated trend of RA epidemiology in men. The key findings were: i) presence of subcutaneous nodule, Sjögren's syndrome and interstitial lung disease as the common extra-articular manifestations; ii) majority of patients having severe disease and with more than 2 years of disease duration; iii) patients having RF positive and presence of cyclic citrullinated peptide were prevalent; iv) osteoporosis and hypertension were the most common co-morbidities; and v) wrist deformities were prevalent among both bilateral and unilateral joint deformities.

There are no similar studies to compare these results. However, landmark studies which evaluated gender differences in epidemiology of RA demonstrated that men were slightly more likely to be RF positive, to have arthritis in large joints, to develop early radiographic damage, and to have a different pattern of extra-articular manifestations (more nodules and lung and pericardial disease) [18,19].

Although RA is more common in women, extra-articular manifestations of RA are more common in men. Generally, the constitutional factors such as male gender, a disease associated HLA genes, high titers of rheumatoid factor, and environmental factors such as a history of smoking were predictors of extra-articular manifestations and complications [20]. In the present study, subcutaneous nodule, interstitial lung disease, and Sjögren's syndrome were common extra-articular manifestations associated with the male gender. In a recent study, men with RA from a population-based incident case cohort were presented with more concomitant extra-articular manifestations and had a higher incidence of interstitial lung disease and dermal

vasculitis complications than women [21]. In accordance with the previous study, the present study also revealed that male gender was recognised as a risk factor for developing interstitial lung disease [22]. Similarly, a recently published national register-based cohort revealed a significant male propensity towards extra-articular manifestation presentation than women [23]. These findings strongly suggest that men affected by RA have more severe disease.

RA patients with other co-morbidities may play a major role in the outcome of the disease [24]. During the past few years, it has been concluded that RA is an independent risk factor for the development of Cardiovascular (CV) disease. Moreover, CV is one of the leading causes of mortality in patients with RA [25]. Similarly in the present study, have found important differences in the co-morbidity profile of male patients. Men presented with a higher prevalence of HTN. Women with RA are more prone to develop osteoporosis. Quite to the contrary, this study observed higher rates of osteoporosis among men patients [26,27]. These findings suggest the importance of HTN and osteoporosis prevention and detection particularly in male patients.

Several hand and wrist deformities have been described as secondary to RA [28]. A study found that men with RA on average have higher grip force [29]. Nordenskiold UM and Grimby G, found that themajority of women (80.0%) with RA with a disease duration of 5-32 years (mean 12) had wrist deformity compared to healthy women [30]. Men showed significantly less disease activity in terms of including swollen joint count, tender joint count, pain, and patient global status [31]. However, in the present study wrist deformities were prevalent among both bilateral and unilateral joint deformities among men patients.

Limitation(s)

This study did not record the impact of RA on the quality of life of the patients which could have added valuable data while inferring the observations. Additionally, the small sample size has restricted its applicability to a general population.

CONCLUSION(S)

Overall observations indicate the presence of subcutaneous nodule as the common extra-articular manifestation with more than two years of disease duration, prevalence of RF positive and cyclic citrullinated peptide, osteoporosis and hypertension as the most common co-morbidities; and wrist deformities as prevalent joint deformities in male patients with RA. It is evident that male have greater activity of RA and associated co-morbidities such as hypertension and osteoporosis. Due to this, it is important to implement screening protocol and multidisciplinary management approach. Lastly, while considering gender differences, one has to take into account the fact that disease activity may be influenced by gender. The present study sheds light on the importance of the increased risk of osteoporosis in male patients with RA, but further researches are needed to confirm the findings.

REFERENCES

[1] Lleo A, Battezzati PM, Selmi C, Gershwin ME, Podda M. Is autoimmunity a matter of sex? Autoimmun Rev 2008;7:626-630. Doi: https://doi.org/10.1016/j.autrev.2008.06.009. PMid:18603021.

[2] Pennell LM, Galligan CL, Fish EN. Sex affects immunity. J Autoimmun. 2012;38: J282-J291. Doi: https://doi.org/10.1016/j.jaut.2011.11.013. PMid:22225601.

[3] Smolen JS, Aletaha D, Mcinnes IB. Rheumatoid arthritis. Lancet. 2016; 388:2023-2038. Doi: https://doi.org/10.1016/S0140-6736(16)30173-8.

[4] Myasoedova E, Crowson CS, Kremers HM, Therneau TM, Gabriel SE. Is the incidence of rheumatoid arthritis rising?: Results from Olmsted County, Minnesota, 1955-2007. Arthritis Rheumatol. 2010;62:1576-82. Doi: https://doi.org/10.1002/art.27425. PMid:20191579.

[5] Del Mar García-Calvente M, Hidalgo-Ruzzante N, del Río-Lozano M, Marcos-Marcos J, Martínez-Morante E, Maroto-Navarro G, et al., Exhausted women, tough men: A qualitative study on gender differences in health, vulnerability and coping with illness in Spain. Sociol Health Illn. 2012;34:911-926. Doi: https://doi.org/10.1111/j.1467-9566.2011.01440.x. PMid:22443288.

[6] Lack S, Noddings R, Hewlett S. Men's experiences of rheumatoid arthritis: An inductive thematic analysis. Musculoskeletal Care. 2011;9(2):102-12. Doi: https://doi.org/10.1002/msc.203. PMid:21365737.

[7] Baggio G, Corsini A, Floreani A, Giannini S, Zagonel V. Gender medicine: A task for the third millennium. Clin Chem Lab Med. 2013;51:713-27. Doi: https://doi.org/10.1515/cclm-2012-0849.

[8] Voulgari PV, Katsimbri P, Alamanos Y, Drosos AA. Gender and age differences in systemic lupus erythematosus. A study of 489 Greek patients with a review of the literature. Lupus. 2002;11:722-29. Doi: https://doi.org/10.1191/0961203302lu253oa. PMid:12475002.

[9] Eder L, Thavaneswaran A, Chandran V, Gladman DD. Gender difference in disease expression, radiographic damage and disability among patients with psoriatic arthritis. Ann Rheum Dis. 2013;72:578-82. Doi: https://doi.org/10.1136/annrheumdis-2012-201357. PMid:22589379.

[10] Elterman DS, Pelman RS. Male health: A new paradigm, strategies for care delivery, advocacy, education and research. Revista Médica Clínica Las Condes. 2014;25:35-39. Doi: https://doi.org/10.1016/S0716-8640(14)70008-2.

[11] Aurrecoechea E, IlorcadiazJ ,Diezlizuain ML, Mcgwin G, Calvo-alen J. Impact of gender in the quality of life of patients with rheumatoid arthritis. J Arthritis. 2015;4:01-07.

[12] Flurey CA, Hewlett S, Rodham K, White A, Noddings R, Kirwan JR. "You obviously just have to put on a brave face": A qualitative study of the experiences and coping styles of men with rheumatoid arthritis. Arthritis Care Res (Hoboken). 2017;69(3):330-37. Doi: https://doi.org/10.1002/acr.22951. PMid:27273926.

[13] Beaton C, Hodge F, Nyamathi A, Weinreb A, Mays V, Maliski S. Male Veterans Coping With the Pendulum Swing of Rheumatiod Arthritis Pain: A Qualitative Study. Calif J Health Promot. 2012;10:44-55. Doi: https://doi.org/10.32398/cjhp.v10i1.1495. PMid:25530733.

[14] Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum. 1988;31:315-24. Doi: https://doi.org/10.1002/art.1780310302. PMid:3358796.

[15] van der Heijde DM, van 't Hof MA, van Riel PL, Theunisse LA, Lubberts EW, van Leeuwen MA. Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. Ann Rheum Dis. 1990;49:916-20. Doi: https://doi.org/10.1136/ard.49.11.916. PMid:2256738.

[16] Favalli EG, Biggioggero M, Crotti C, Becciolini A, Raimondo MG, Meroni PL. Sex and management of rheumatoid arthritis. Clinical Reviews in Allergy & Immunology. 2019; 56:333-345. Doi: https://doi.org/10.1007/s12016-018-8672-5. PMid:29372537.

[17] Krishnan E, Sokka T, Hannonen P. Smoking-gender interaction and risk for rheumatoid arthritis. Arthritis Res Ther. 2003;5:R158-R162. Doi: https://doi.org/10.1186/ar750. PMid:12723987.

[18] Weyand CM, Schmidt D, Wagner U, Goronzy JJ. The influence of sex on the phenotype of rheumatoid arthritis. Arthritis Rheum. 1998;41: 817-822. Doi: https://doi.org/10.1002/1529-0131(199805)41:5%3C817::AID-ART7%3E3.0.CO;2-S.

[19] Gossec L, Baro-Riba J, Bozonnat M-C, Daurès JP, Sany J, Eliaou JF, et al. Influence of sex on disease severity in patients with rheumatoid arthritis. J Rheumatol. 2005;32:1448-51.

[20] Turesson C, O'Fallon WM, Crowson CS, Gabriel SE, Matteson EL. Extra-articular disease manifestations in rheumatoid arthritis: incidence trends and risk factors over 46 years. Ann Rheum Dis. 2003;62(8):722-27. Doi: https://doi.org/10.1002/1529-0131(199805)41:5%3C817::AID-ART7%3E3.0.CO;2-S. PMid:12860726.

[21] Ramírez Sepúlveda JI, Kvarnström M, Eriksson P, Mandl T, Norheim KB, Johnsen SJ, et al. Long-term follow-up in primary Sjögren's syndrome reveals differences in clinical presentation between female and male patients. Biol Sex Differ. 2017;8(1):25. Doi: https://doi.org/10.1186/s13293-017-0146-6. PMid:2878969.

[22] Boitiaux JF, Debray MP, Nicaise-Roland P, Adle-Biassette H, Danel C, Clérici C, et al. Idiopathic interstitial lung disease with anti-SSA antibody. Rheumatology (Oxford). 2011;50(12):2245-50. Doi: https://doi.org/10.1093/rheumatology/ker267. PMid:21984768.

[23] Bengtsson K, Forsblad-d'Elia H, Deminger A, Klingberg E, Dehlin M, Exarchou S, et al. Incidence of extra-articular manifestations in ankylosing spondylitis, psoriatic arthritis and undifferentiated spondyloarthritis: results from a national register-based cohort study. Rheumatology (Oxford). 2021;60(6):2725-34. Doi: https://doi.org/10.1093/rheumatology/keaa692. PMid:33216939.

[24] Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Ann Rheum Dis. 2014;73:62-68. Doi: https://doi.org/10.1136/annrheumdis-2013-204223. PMid:24095940.

[25] Chodara AM, Wattiaux A, Bartels CM. Managing cardiovascular disease risk in rheumatoid arthritis: clinical updates and three strategic approaches. Curr Rheumatol Rep. 2017;19:16. Doi: https://doi.org/10.1007/s11926-017-0643-y. PMid:28361332.

[26] Michaud K, Wolfe F. Comorbidities in rheumatoid arthritis. Best Pract Res Clin Rheumatol. 2007;21:885-906. DoiL https://doi.org/10.1016/j.berh.2007.06.002. PMid:17870034.

[27] Radner H, Smolen JS, Aletaha D. Impact of comorbidity on physical function in patients with rheumatoid arthritis. Ann Rheum Dis. 2010;69:536-41. Doi: https://doi.org/10.1136/ard.2009.118430. PMid:19825848.

[28] Mohammed RHA, Bhutta BS. Hand and Wrist Rheumatoid Arthritis. [Updated 2022 Feb 9]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.Available from:https://www.ncbi.nlm.nih.gov/books/NBK560890/. Last accessed on: August 19, 2022.

[29] BjörkM, Thyberg I, Haglund L, Skogh T. Hand function in women and men with early rheumatoid arthritis. A prospective study over three years (the Swedish TIRA project). Scandinavian Journal of Rheumatology. 2006;35(1):15-19. Doi: https://doi.org/10.1080/03009740510026562. PMid:16467035.

[30] Nordenskiold UM, Grimby G. Grip force in patients withrheumatoid arthritis and fibromyalgia and in healthy subjects. A study with the Grippit instrument. Scand J Rheumatol. 1993;22:14-19. Doi: https://doi.org/10.3109/03009749309095105. PMid:8434241.

[31] Intriago M, Maldonado G, Cárdenas J, Ríos C. Clinical characteristics in patients with rheumatoid arthritis: Differences between genders. Scientific World Journal. 2019;2019:8103812. Doi: https://doi.org/10.1155/2019/8103812. PMid:31354388.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 02, 2022
- Manual Googling: Aug 22, 2022
- iThenticate Software: Aug 31, 2022 (13%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jul 01, 2022**
Date of Peer Review: **Aug 12, 2022**
Date of Acceptance: **Sep 01, 2022**
Date of Publishing: **Oct 01, 2022**