ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 04 | April - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

TO STUDY THE PREVALENCE AND RISK FACTORS OF OSTEOPOROSIS IN CASES WITH RHEUMATOID ARTHRITIS

Rheumatology

Dr Rama Siva Naik* Medicine Resident, Department of Medicine, INHS Asvini, Mumbai, Maharashtra *Corresponding Author

Surg Cdr (Dr) Ramakant Associate Professor Rheumatology, Department of Medicine, INHS Asvini, Mumbai, Maharashtra

Col (Dr) Gautam Mullick Professor Rheumatology, Department of Medicine, INHS Asvini, Mumbai, Maharashtra

Surg Capt (Dr) R Anantha Krishnan Professor cardiologist & HOD, Department of Medicine, INHS Asvini, Mumbai, Maharashtra

ABSTRACT

Back ground and Aims: Rheumatoid arthritis (RA) is a chronic and systemic autoimmune disease leading to inflammatory polyarthritis and continuous joint destruction. The prevalence of osteoporosis in RA patients is reported to be approximately twice that in the general population. The present study was planned to find the prevalence and risk factors of osteoporosis in cases of Rheumatoid arthritis. **Materials & Methods:** A hospital based observational study was done which included 50 diagnosed cases of RA. After detailed history regarding demography and risk factors and general examination, bone mineral densitometry (BMD) was done in all cases. **Results:** Prevalence of osteoporosis among RA cases was observed as 32%. Mean age of cases with osteoporosis was significantly higher than casers without osteoporosis. No association was observed between presence of osteoporosis with Rheumatoid factor positivity or anti-CCP antibodies and also with CRP and ESR levels. Mean BMI was significantly lower among cases with osteoporosis (21.12 vs 23.45 Kg/m2; $p<0.01$). A significant association was observed between presence of osteoporosis and RA severity. **Conclusion:** Osteoporosis affects every one in three cases with RA. Advanced age, low body mass index and increased severity of RA, were observed to be significantly associated with risk of osteoporosis.

KEYWORDS

BMI-Body Mass Index, BD-Bone Density, OP-Osteoporosis, RA-Rheumatoid Arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic and systemic autoimmune disease which can result in constant inflammatory polyarthritis and continuous joint destruction, leading to damaged mobility and increased disability [1]. The prevalence of RA worldwide is about 0.5% to 1% [2,3] and in India, it is about 0.65 % to 0.75% [4]. The etiology of RA is still unclear and remain to be clarified, and both genetic and environment factors contribute to its etiology [5].

Several contributors to RA pathogenesis have been identified in recent years: genetic factors, cigarette smoking, autoantibodies, infectious agents, as well as nutritional and hormonal factors [6]. Ultimately, an interplay between these endogenous and exogenous factors has been postulated to break immunological tolerance and trigger the immunological response [7]. The immunological activation of RA leads to infiltration of the synovium by an orchestra of immune cells like T and B cells, macrophages, dendritic cells and fibroblast-like synoviocytes, contributing to the proliferation of cell tissue (i.e. pannus formation) and neovascularization [8]. These immunological processes perpetuate systemic inflammatory responses, leading to a chronic, disabling disease which results in the inability to work and an impaired quality of life [9].

Osteoporosis is defined as a "skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture". The diagnosis of OP is made by measuring bone marrow density by dual energy x ray absorptiometry of the lumbar vertebrae or hip (neck of femur), which according to World Health Organization (WHO) classification: $T > -1$ is normal, $-1 > T > -2.5$ is osteopenia and $T < -2.5$ is OP [10]. Osteoporosis is a well-known extra-articular complication in patients with rheumatoid arthritis (RA) [11]. It is more common in patients with RA than in the general population, due to active systemic inflammation, the use of corticosteroids and lack of mobility [12,13]. As a result, patients with RA are at increased risk of fractures, an outcome that impairs quality of life and leads to mortality [14,15].

The prevalence of osteoporosis in RA patients is reported to be approximately twice that in the general population [14]. The frequency of generalized osteoporosis in patients with RA ranges from 12.3 to 38.9 % in the lumbar spine and from 6.3 to 36.3 % in the hip [14,15]. Above all, there is at least a two-fold increase in the risk of vertebral fracture (VFs) in RA patients and a higher risk, up to six-fold, has been reported in patients with long-standing disease [16].

The risk factors for osteoporosis and osteoporotic fractures in RA patients are age, disability, low body mass index (BMI), previous non-vertebral fracture, long-standing disease, and glucocorticoids. In particular, regardless of additional risk factors, patients taking glucocorticoids should be screened for osteoporosis. Although awareness of osteoporosis by healthcare professionals has increased in recent years, it remains underdiagnosed and undertreated [17].

The increased risk of osteoporosis in RA patients is well reported [11,12] and may be linked to differences in the distribution and interactions of genetic and environmental factors [18]. However, little information is available on the frequency of osteoporosis and bone mineral density (BMD) measurement rates in RA patients and the associated risk factors in Indian population. The present study was thus planned to find the prevalence and risk factors of osteoporosis in cases of rheumatoid arthritis.

MATERIALS AND METHODS

Design, Participants

A hospital based observational study was conducted at Department of Medicine & Rheumatology in INHS Asvini, Mumbai. Final sample size was 50 diagnosed cases (ACR-2010 criteria [19]) of Rheumatoid arthritis coming to our hospital.

Procedures

After detailed history regarding demography, risk factors and general examination, Bone mineral densitometry (BMD) was done in all cases by Dual-energy X-ray absorptiometry DEXA method.

Osteoporosis was defined as T-score lower than -2.5 in lumbar spine (L2-L4) or hip (Neck of femur). The patients were divided in two groups according to their bone mineral densitometry results, patients with OP (T-score $\leq$-2.5 in femoral neck or L2-L4 spine) and without OP. The data about OP and potential related factors such as age, gender, co-morbidities, factors related to RA such as disease activity score (DAS 28), use of steroids and methotrexate, seropositivity for RF and anti CCP were noted.

Statistical analysis

All the data was noted down in a pre-designed study proforma. Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi-Square test. Quantitative data was represented using Mean ± SD. Analysis of Quantitative data between the two groups was done using unpaired t-test if data passed 'Normality test' and by Mann-Whitney Test if data failed 'Normality test'. A p-value < 0.05 was taken as level of significance. Results were graphically represented where deemed necessary. SPSS Version 21.0 was used for analysis.

RESULTS

Mean age of the study cases was 49.22 years with 36% in the age range of 31 to 50 years and 40% in the age range of 51 to 70 years. In present study, 80% of the patients of rheumatoid arthritis were females. Associated co-morbidities included diabetes (22%), hypertension (8%) and hypothyroidism (8%). History of prolonged steroid use was given by 20% cases. Rheumatoid factor positivity was observed in most of the cases (90%) while anti-ccp was positive in 44% cases. Raised ESR and CRP was seen in 52% and 74% cases respectively. Moderate to high disease activity at presentation was observed in 42% and 54% cases. Only 1 case (2%) had low activity and 1 (2%) was in remission. Prevalence of osteoporosis among RA cases was observed as 32% (**Table 1**).

Mean age of cases with osteoporosis was significantly higher than cases without osteoporosis (59.25 vs 53.82 years; p<0.01). Incidence of osteoporosis was comparable between males and females (30% vs 32.5%; p-0.51). No significant association was observed between presence of osteoporosis and associated co-morbidities (p-0.24). Incidence of osteoporosis among cases with history of prolonged steroid use was 30% as compared to 17.5% in cases without history of steroid use (p-0.16). No association was observed between presence of osteoporosis with Rheumatoid factor positivity or anti-CCP antibodies (p>0.05). Mean CRP and ESR levels were comparable among cases with and without osteoporosis (p>0.05). Mean BMI was significantly lower among cases with osteoporosis (21.12 vs 23.45 Kg/m^2; p<0.01). A significant association was observed between presence of osteoporosis and disease severity. Prevalence of osteoporosis was 48.1% in cases with severe disease as compared to 14.3% and 0% in cases with moderate and low severity respectively (**Table 2**).

Tables

Table 1. Distribution of patients as per baseline data

Variable		N	%
Age (yrs)	</= 30	9	18.0%
	31-50	18	36.0%
	51-70	20	40.0%
	>70	3	6.0%
Gender	Male	10	20.0%
	Female	40	80.0%
Co-morbidities	DM	11	22.0%
	HTN	9	18.0%
	Hypothyroidism	4	8.0%
Steroids	No	40	80.0%
	Yes	10	20.0%
Investigations	RF positive	45	90.0%
	Anti-ccp positive	22	44.0%
	Raised ESR	26	52.0%
	CRP Positive	37	74.0%
Disease severity (DAS Score)	Remission	1	2.0%
	Low	1	2.0%
	Moderate	21	42.0%
	High	27	54.0%
Osteoporosis	No	34	68.0%
	Yes	16	32.0%

Table 2. Risk Factors for osteoporosis in cases of Rheumatoid arthritis

Variable		N	Osteoporosis (N/ % or Mean / SD)				P -value
			Yes		No		
Age (yrs)	</= 30	9	1	11.1%	8	88.9%	0.016
	31-50	18	4	22.2%	14	77.8%	
	51-70	20	8	40.0%	12	60.0%	
	>70	3	3	100.0 %	0	0.0%	
Gender	Male	10	3	30.0%	7	70.0%	0.51
	Female	40	13	32.5%	27	67.5%	
Co-morbidities	DM	11	3	27.3%	8	72.7%	0.24
	HTN	9	3	33.3%	6	66.7%	
	Hypothyroidism	4	2	50.0%	2	50.0%	
Steroids	No	40	7	17.5%	33	82.5%	0.16
	Yes	10	3	30.0%	7	70.0%	
Investigations	RF positive	45	15	33.3%	30	66.7%	0.54
	Anti-ccp positive	22	10	45.5%	12	54.5%	0.12
	ESR		41.88	26.21	49.69	34.14	0.41
	CRP		27.25	30.63	50.78	48.32	0.075
	BMI		21.12	2.45	23.45	3.12	0.01
Disease severity (DAS Score)	Remission	1	0	0.0%	1	100.0%	<0.01
	Low	1	0	0.0%	1	100.0%	
	Moderate	21	3	14.3%	18	85.7%	
	High	27	13	48.1%	14	51.9%	

DISCUSSION

The prevalence of OP in the general population ranges from 9 to 38% for women and 1 to 8% for men depending on the countries [20]. On the other hand, the prevalence of OP in RA is around 30% (up to 50% in post-menopausal women), which might be a two-fold increase over the general population [21].

In present study, on DEXA analysis, prevalence of osteoporosis among RA cases was observed as 32%. Barbara H et al. [22] study observed that osteoporosis was present in 91 out of 304 (29.9%) patients at either the spine or total hip compared with 157/903 (17.4%) of age- and gender-matched controls. Of 1322 postmenopausal woman patients with RA studied by Lee JH et al. [23], 619 patients (46.8 %) were in the osteoporosis group (T-score ≤ −2.5 SD). Moshayedi et al. [24] in a systemic review observed the prevalence of OP among RA as 27.6% (95%CI 23.9–31.3%).

OP and RA share some common risk factors such as female gender (female: male ratio in RA: 3–4:1) and smoking. Other general OP risk factors such as age, low body mass index (BMI), menopause, diabetes or thyroid disorders [25-27] are equally applicable to patients with RA and to the general population.

In present study, mean age of cases with osteoporosis was significantly higher than cases without osteoporosis (59.25 vs 53.82 years; p<0.01). However, the incidence was comparable between males and females (30% vs 32.5%; p-0.51). Incidence of osteoporosis among cases with history of prolonged steroid use was 30% as compared to 17.5% in cases without history of steroid use, The difference was however statistically non-significant (p-0.16). No association was observed between presence of osteoporosis with co-morbidities, RF positivity or anti-CCP antibodies or ESR and CRP levels (p>0.05). Mean BMI was significantly lower among cases with osteoporosis (21.12 vs 23.45 Kg/m^2; p<0.01). A significant association was observed between presence of osteoporosis and disease severity. Prevalence of osteoporosis was 48.1% in cases with severe disease as compared to 14.3% and 0% in cases with moderate and low severity respectively.

Barbara H et al. [22] observed that In RA patients, osteoporosis was associated with female gender ($P = 0.002$), age ($P < 0.001$), time since menopause ($P < 0.001$), BMI ($P < 0.001$), ESR ($P = 0.006$), Larsen score ($P = 0.011$) and co-morbidities ($P = 0.020$), but logistic regression analysis showed that only age and BMI were independent predictors. Lee JH et al. [23] observed Advanced age (≥70 years; OR = 2.28, 95 % CI: 1.40–3.58), lower body mass index (<25 ; OR = 2.14, 95 % CI:1.52–3.02), longer disease duration (≥10 years; OR = 1.46, 95 % CI: 1.07–2.00), higher cumulative glucocorticoid dose (OR = 1.03, 95 % CI: 1.01–1.05), and higher severity of disease (OR = 1.37, 95 % CI:1.11–1.69) were independent risk factors for osteoporosis. Lindner L et al. [28] study observed that cases with high disease activity and patients who took glucocorticoids (GC) were more often affected by osteoporosis than patients in remission or without GC. Athimni S, et al. [29] observed that Advanced age, glucocorticoid use and high DAS 28, CRP were independent risk factors for OP (respectively p=0.04, p=0.02 and p=0.01). Body mass index, smoking, disease duration high

Health Assessment Questionnaire (HAQ) score (p=0.545) and smoking (p=0.326) were not associated with high risk of OP.

CONCLUSION

Study concluded that prevalence of osteoporosis in RA remains high in the modern era despite aggressive management and the use of biologic therapy. Osteoporosis affects every one in three cases with RA. Advanced age, low body mass index and increased severity of RA, were observed to be significantly associated with risk of osteoporosis. We thus conclude that assessment of osteoporosis should be done in all RA patients so that decrease in bone density can be identified at an early stage and appropriate preventive and control measures can be taken.

REFERENCES

1. Li Q, Laumonnier Y, Syrovets T, Simmet T. Yeast two-hybrid screening of proteins interacting with plasmin receptor subunit: C-terminal fragment of annexin A2. Acta Pharmacol Sin. 2011;32:1411–8. 10.
2. Sokka T, Abelson B, Pincus T. Mortality in rheumatoid arthritis: 2008 update. Clin Exp Rheumatol. 2008; 26(5 Suppl. 51):S35–61.
3. Wallberg-Jonsson S, Ohman ML, Dahlqvist SR. Cardiovascular morbidity and mortality in patients with seropositive rheumatoid arthritis in Northern Sweden. J Rheumatol. 1997; 24:445–51.
4. Malaviya AN, Kapoor SK, Singh RR, Kumar A, Pande I. "Prevalence of rheumatoid arthritis in the adult Indian population". Rheumatol Int. 1993; 13(4):131–4.
5. Choy E. Understanding the dynamics: pathways involved in the pathogenesis of rheumatoid arthritis. Rheumatology. 2012; 51(Suppl. 5):v3–11.
6. van Halm V, Peters M, Voskuyl A, Boers M, Lems W, et al. Rheumatoid arthritis versus diabetes as a risk factor for cardiovascular disease - cross sectional study - He CARRÉ Investigation. Annals of the Rheumatic Diseases. In press 2008. Ann Rheum Dis. 2005 64: 1595-1601.
7. Roos A, Bakker SJL, Links TP, Gans ROB, :ol ِenbuttel BHR (2007) Hyroid Function Is Associated with Components of the Metabolic Syndrome in Euthyroid Subjects. J Clin Endocrinol Metab. 2007; 92: 491-496.
8. Sidiropoulos P, Karvounaris S, Boumpas D. Metabolic syndrome in rheumatic diseases: epidemiology, pathophysiology, and clinical implications. Arthritis Research & Herapy. 2008; 10: 207.
9. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, et al. He American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum. 1988; 31: 315-324.
10. Meng J, Li Y, Yuan X, Lu Y. Evaluating osteoporotic fracture risk with the Fracture Risk Assessment Tool in Chinese patients with rheumatoid arthritis. Medicine. 2017 May; 96(18).
11. Deodhar AA, Woolf AD. Bone mass measurement and bone metabolism in rheumatoid arthritis: a review. Br J Rheumatol. 1996; 35:309–22.
12. Kleyer A, Schett G. Arthritis and bone loss: a hen and egg story. Curr Opin Rheumatol. 2014; 26:80–4.
13. Ørstavik RE, Haugeberg G, Uhlig T, Mowinckel P, Kvien TK, Falch JA, et al. Vertebral deformities in rheumatoid arthritis: a comparison with population based controls. Arch Intern Med. 2004; 164:420–5.
14. Haugeberg G, Uhlig T, Falch JA, Halse JI, Kvien TK. Bone mineral density and frequency of osteoporosis in female patients with rheumatoid arthritis: results from 394 patients in the Oslo County Rheumatoid Arthritis register. Arthritis Rheum. 2000; 43:522–30.
15. Sinigaglia L, Nervetti A, Mela Q, Bianchi G, Del Puente A, Di Munno O, et al. A multicentre cross sectional study on bone mineral density in rheumatoid arthritis. Italian Study Group on Bone Mass in Rheumatoid Arthritis. J Rheumatol. 2000; 27:2582–9.
16. Van Staa T, Geusens P, Bijlsma JW, Leufkens HG, Cooper C. Clinical assessment of the long-term risk of fracture in patients with rheumatoid arthritis. Arthritis Rheum. 2006;54:3104–12.
17. Molokhia M, McKeigue P. Risk for rheumatic disease in relation to ethnicity and admixture. Arthritis Res. 2000;2:115–25.
18. Tobon GJ, Youinou P, Saraux A. The environment, geo-epidemiology, and autoimmune disease: Rheumatoid arthritis. Autoimmune Rev. 2010; 9:A288–92.
19. Kourilovitch M, Galarza-Maldonado C, Ortiz-Prado E. Diagnosis and classification of rheumatoid arthritis. Journal of autoimmunity. 2014; 48:26-30.
20. Wade SW, Strader C, Fitxpatrick LA, Anthony MS, O'Malley CD. Estimating prevalence of osteoporosis: examples from industrialized countries. Arch Osteoporosis. (2014) 9:182.
21. Hauser B, Riches PL, Wilson JF, Horne AE, Ralston SH. Prevalence and clinical prediction of osteoporosis in a contemporary cohort of patients with rheumatoid arthritis. Rheumatology. 2014); 3:1759–66.
22. Barbara Hauser, Philip L. Riches, James F. Wilson, Annamarie E. Horne, Stuart H. Ralston, Prevalence and clinical prediction of osteoporosis in a contemporary cohort of patients with rheumatoid arthritis, Rheumatology. 2014; 53(10): 1759–1766.
23. Lee JH, Sung YK, Choi CB, Cho SK, Bang SY, Choe JY, Hong SJ, Jun JB, Kim TH, Lee J, Lee HS. The frequency of and risk factors for osteoporosis in Korean patients with rheumatoid arthritis. BMC Musculoskeletal Disorders. 2016; 17(1):1-7.
24. Moshayedi, S., Tasorian, B. & Almasi-Hashiani, A. The prevalence of osteoporosis in rheumatoid arthritis patient: a systematic review and meta-analysis. Sci Rep. 2022; 12: 15844.
25. Adami G, Saag KG. Osteoporosis pathophysiology, epidemiology, and screening in rheumatoid arthritis. Curr Rheumatol Rep. 2019; 21:34.
26. Haugeberg G, Green MJ, Quinn MA, Marzo-Ortega H, Proudman S, Karim Z, et al. Hand bone loss in early undifferentiated arthritis: evaluating bone mineral density loss before the development of rheumatoid arthritis. Ann Rheum Dis. 2006; 65:736–40.
27. Lindner L, Callhoff J, Alten R, Krause A, Ochs W, Zink A, et al. Osteoporosis in patients with rheumatoid arthritis: trends in the German National Database 2007–2017. Rheumatol Int. 2020; 12:2005–12.
28. Lindner L, Callhoff J, Alten R, Krause A, Ochs W, Zink A, Albrecht K. Osteoporosis in patients with rheumatoid arthritis: trends in the German National Database 2007-2017. Rheumatol Int. 2020; 40(12):2005-2012.
29. Athimni S, Bouden S, Tekaya AB, Dghais A, Saidane O, Tekaya R, Mahmoud I, Abdelmoula L. AB0611 Osteoporosis In Rheumatoid Arthritis: A Necessary Evil? 2021: 1341-1341.