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The prevalence of osteoporosis in rheumatoid arthritis patient: a systematic review and meta-analysis

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Osteoporosis (OP) is one of the most commonly known extra-articular complications of rheumatoid arthritis (RA). Since the prevalence of OP is diverse in different studies and there is no general consensus about it, in this systematic review, we aimed to investigate the global prevalence of OP among RA patients. In this review, three databases including Medline via PubMed, Scopus, and Web of Science (Clarivate analytics) were searched by various keywords. After screening of retrieved papers, the related data of included papers were extracted and analyzed. To assess the risk of methodological bias of included studies, quality assessment checklist for prevalence studies was used. Because of heterogeneity among studies, random-effect model was used to pooled the results of primary studies. In this review, the results of 57 studies were summarized and the total included sample size was 227,812 cases of RA with 64,290 cases of OP. The summary point prevalence of OP among RA was estimated as 27.6% (95%CI 23.9–31.3%). Despite significant advances in prevention, treatment and diagnostic methods in these patients, it still seems that the prevalence of OP in these patients is high and requires better and more timely interventions.

Abbreviations

PRISMA	Preferred reporting items for systematic reviews and meta-analyses
OP	Osteoporosis
RA	Rheumatoid arthritis
CI	Confidence interval
DMARDs	Disease-modifying anti-rheumatic drugs
MeSH	Medical subject headings
BMD	Bone mineral density
WHO	World Health Organization

Rheumatoid arthritis (RA) is one of the most common autoimmune diseases that in the early stages of the disease begins with pain and symmetrical swelling of the small joints of the hands, feet, swelling of the soft tissue around the joint and morning stiffness and fatigue[1–4] and it is characterized by persistent synovitis and progressive destruction of symmetrical multi-joints and intra-articular manifestations including subchondral lesions, decreased bone mass, and reduced generalized bone density[4–7]. The prevalence of RA in the general population is about 1%, but is more common in the 50 s and 60 s and is higher in women than men[8,9].

Osteoporosis (OP) is one of the most known common extra-articular complications of RA[10] and its prevalence in RA patients is almost twice that of the general population[4,11,12]. OP is a systemic skeletal disease characterized by decreased bone mineral density and its complication (increased fragility and fracture due to reduced resistance to torsion and compression)[7,13]. Bone fragility in people with RA includes a combination of systemic inflammation, circulating autoantibodies, and proinflammatory cytokines (IL1, IL6, TNF, etc.)[11,14]. Chronic inflammation in people with RA affects bone metabolism and disrupts the normal resorption cycle and reduces localized and generalized bone mineral density (BMD)[15].

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Search	Query	Results
#5	Search: ((("Arthritis, Rheumatoid"[Mesh] OR "Rheumatoid Arthritis"[tw] OR "Rheumatoid"[tw]) AND ("Osteoporosis"[Mesh] OR "Osteoporosis"[tw] OR "Osteoporo*"[tw] OR " Bone Loss"[tw] OR "Osteopenia"[tw] OR "Bone Density"[Mesh] OR "Bone Density"[tw] OR "Bone Mineral Density"[tw])) AND ("Prevalence"[Mesh] OR "Incidence"[tw] OR "Epidemiology"[Mesh] OR "epidemiology" [Subheading] OR "Incidence"[Mesh] OR "Incidence"[tw])) NOT ("Clinical Trial" [Publication Type] OR "Controlled Clinical Trial" [Publication Type] OR "Clinical Trial, Phase III" [Publication Type]) Filters: Humans, English Sort by: Most Recent	527
#4	Search: "Clinical Trial" [Publication Type] OR "Controlled Clinical Trial" [Publication Type] OR "Clinical Trial, Phase III" [Publication Type] Sort by: Most Recent	897,690
#3	Search: "Prevalence"[Mesh] OR "Incidence"[tw] OR "Epidemiology"[Mesh] OR "epidemiology" [Subheading] OR "Incidence"[Mesh] OR "Incidence"[tw] Sort by: Most Recent	2,895,709
#2	Search: "Osteoporosis"[Mesh] OR "Osteoporosis"[tw] OR "Osteoporo*"[tw] OR " Bone Loss"[tw] OR "Osteopenia"[tw] OR "Bone Density"[Mesh] OR "Bone Density"[tw] OR "Bone Mineral Density"[tw] Sort by: Most Recent	166,724
#1	Search: "Arthritis, Rheumatoid"[Mesh] OR "Rheumatoid Arthritis"[tw] OR "Rheumatoid"[tw] Sort by: Most Recent	162,057

Box 1. The search strategy in PubMed.

Decreased bone mass can also be affected by factors such as disease severity, gender, especially after menopause, decreased vitamin D levels, advanced age, using corticosteroids and disease-modifying anti-rheumatic drugs (DMRADs) and decreased mobility[12,16]. In the US, data show that osteoporotic fractures account for about one-third of RA-related mortality[5]. Fractures increase morbidity and mortality, reduce quality of life, reduce independent functioning of people, especially in old age, and increase economic burden[6,17]. Vertebral fracture is one of the most common fractures due to decreased BMD, which causes limitation of activity, disability, kyphosis and decreased pulmonary function[10,18,19].

The diagnosis of OP is made by measuring bone marrow density by dual x ray absorptiometry of the lumbar vertebrae, which according to World Health Organization (WHO) classification: $T > -1$ is normal, $-1 > T > -2.5$ is osteopenia and $T < -2.5$ is OP[20].

Despite advances in the identification of the destructive mechanism and pharmacological treatment of RA, the complications associated with this disease are still common. So, screening and assessing the prevalence of OP and proper management, especially in relation to timely identification, is essential to prevent fractures. For this reason, in this study, we systematically reviewed the international databases and the results of related papers were pooled regarding the prevalence of OP.

Methods

Study design. This is a systematic review and meta-analysis study. In this study, three international databases were systematically searched using different keywords. The "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)"[21] and "Cochrane Handbook for Systematic Reviews of Interventions"[22] were used to report the results.

Search strategy. To find related articles, a combination of related keywords was used in three databases including Medline via PubMed, Scopus, and Web of Science (Clarivate analytics). The keywords used included a combination of the suggested words by Medical Subject Heading (MeSH) and other related words. The search query used in PubMed was as follows: ((("Arthritis, Rheumatoid"[Mesh] OR "Rheumatoid Arthritis"[tw] OR "Rheumatoid"[tw]) AND ("Osteoporosis"[Mesh] OR "Osteoporosis"[tw] OR "Osteoporo*"[tw] OR " Bone Loss"[tw] OR "Osteopenia"[tw] OR "Bone Density"[Mesh] OR "Bone Density"[tw] OR "Bone Mineral Density"[tw])) AND ("Prevalence"[Mesh] OR "Incidence"[tw] OR "Epidemiology"[Mesh] OR "epidemiology" [Subheading] OR "Incidence"[Mesh] OR "Incidence"[tw])) NOT ("Clinical Trial" [Publication Type] OR "Controlled Clinical Trial" [Publication Type] OR "Clinical Trial, Phase III" [Publication Type]). Finally, the search filtered to human studies and English language studies. The adapted keywords were used to search in Scopus and Web of Science databases. The detailed search strategy was presented in Box 1. Databases were searched by two authors (AAH and SM) on June 22, 2021, and to find gray literatures, Google Scholar, and references of remaining articles manually searched.

Study selection and screening. To find and screen related articles, all retrieved articles were entered into Endnote software, and duplicate articles were first identified and removed. Then, in the next step, the articles were screened in terms of title and abstract, and the irrelevant articles were deleted. In the next step, the full text of the related articles was screened, and the articles that met the inclusion criteria and related data were studied and the required information was extracted from them. All these steps were performed by two authors (SM and AAH) independently and in case of disagreement between the two authors, a decision was made after consultation.

Inclusion and exclusion criteria. Articles with English full-text that were indexed in desired databases up to June 22, 2021 (from 1962 to 2021) were searched and there was no publication time limit. All observational studies in which the prevalence of OP has been reported in patients with RA have been included in the study. All clinical trials, letter to editor, editorials, review articles, commentaries, case reports, case series studies and papers with no relevant data were excluded.

Data extraction.   The required data were extracted from the articles by two authors (SM and AAH) and in case of disagreement, the final decision was made after consultation. The extracted data were entered into a designed checklist in Excel software. This data includes first author's name, year of publication, duration of patient's recruitment, mean age, mean of disease duration, countries, the score of risk of bias, sample size, number of cases with OP and prevalence of OP.

Risk of bias.   To assess the risk of bias of included studies, quality assessment checklist for prevalence studies which was developed by Hoy et al.[23] was used. This checklist consists of nine items, each item has a score of 0 or 1. The score of 0 indicates the low risk and score of 1 indicates the high risk. The total score of checklists ranges from 0 to 9, which categorized in three levels; 0–3, 4–6 and 7–9 as low, moderate and high risk, respectively.

Statistical analysis.   The I^2 statistic with as well as chi-square test was used to assess the heterogeneity across the included studies. The results revealed that there was noteworthy heterogeneity between studies, and a meta-regression to find the source of heterogeneity and a subgroup analysis were done, and because of heterogeneity, the random-effect model was used to pooled the extracted prevalence with "metaprop" command[24]. Egger's linear regression and funnel plot were used to explore the publication bias and trim and fill method was used to estimate the prevalence in case of publication bias. To recognize the effect of each study on the pooled prevalence, a sensitivity analysis was conducted. All analyses were conducted using Stata software version 13 (Stata Corp, College Station, TX, USA).

Ethics approval and consent to participate.   This study was approved by Ethical Committee of Arak University of Medical Sciences (Code: IR.ARAKMU.REC.1399.259).

Result

Study selection and study characteristics.   The process of study selection is presented in the PRISMA flow diagram[25] (Fig. 1). First, after searching the desired databases, we retrieved 2214 primary studies (PubMed/Medline: 527, Scopus: 868, and Web of Science: 819). Then, 495 articles were removed due to duplication and 1719 studies were screened by title and abstract. Next, 658 papers were excluded by irrelevant title and 942 papers were excluded by irrelevant abstract. After that, the full text of 121 remained papers were assessed for eligibility and 62 papers were excluded (no data: 46 papers, unavailable full text: 15 papers and foreign language: 1 paper). Finally, data from 57 articles[1,3,4,7,8,11,13,16,18,20,26–72] were entered into the meta-analysis.

The sample size of imported articles ranged from 37 to 142,955. The oldest article was in 1962 and the most recent article was in 2021, and the reported prevalence of OP among RA patients varied from 3.7% to 62.2%. Further details regarding the selected studies are described in Table 1.

Risk of bias within studies.   The risk of bias of included studies was assessed by the quality assessment checklist for prevalence studies. The results showed that the risk of bias of 75.4% (n = 43), 22.8% (n = 13) and 1.75% (n = 1) of included papers were low, moderate and high, respectively.

Quantitative data synthesis.   In this review, the results of 57 studies were summarized and the total included sample size was 227,812 cases of RA with 64,290 cases of OP. Due to the significant heterogeneity across studies, the random-effect model was used to pool the reported prevalence. The summary point prevalence was estimated as 27.6% (95%CI: 23.9–31.3%) (Table 2; Fig. 2).

Heterogeneity and meta-regression.   The obtained results revealed a significant heterogeneity across primary included studies (heterogeneity chi-square = 18587.5, d.f = 56, p = 0.001, I-square (variation in prevalence attributable to heterogeneity) = 99.7%, estimate of between-study variance Tau-square = 0.019), for this reason, random-effect model was used to pool the reported prevalence. In addition, meta-regression method was used to find the heterogeneity source, and in meta-regression, we included sample size, study reign (continents), date of publication and risk score of studies and in the meta-regression model, none of these variables were significant. Finally, in addition to using a random effect model, subgroup analysis was performed based on study reigns (continents), date of publication and risk score of studies.

Sub-group analysis.   As it was showed in Table 2, according to the subgroup analysis based on the data of publication, the highest prevalence was in studies conducted during 2011–2015 (36.2% (95%CI 24.5–47.8)), followed by 2016–2021 (27.1% (95%CI 20.7–33.4)) and before 2010 (21.6% (95%CI 15.8–27.4)). The prevalence in studies with low and moderate risk score was 29.8% (95%CI 26.2–33.5) and 36.2% (95%CI 24.5–47.8), respectively. Based on the study reign, the highest prevalence of OP was in Africa (46.1% (95%CI 40.8–51.3)), followed by Asia (30.6% (95%CI 23.2–38.0)), Europe (25.6% (95%CI 18.7–32.4)), and the Americas (19.5% (95%CI 15.9–23.1)).

Risk of bias across studies.   Egger's test for small-study effects was performed to check for possibility of publication bias. The obtained results of Egger's test (z = 2.13, p = 0.033) suggested that there is an evidence of publication bias. In addition to Egger's test, the asymmetry in the funnel plot (Fig. 3) emphasized the existence of publication bias. For this reason, trim and fill method was used to estimate the OP prevalence and, the prevalence was estimated to be 23.3% (95%CI 19.7–26.8%) using random-effect model.
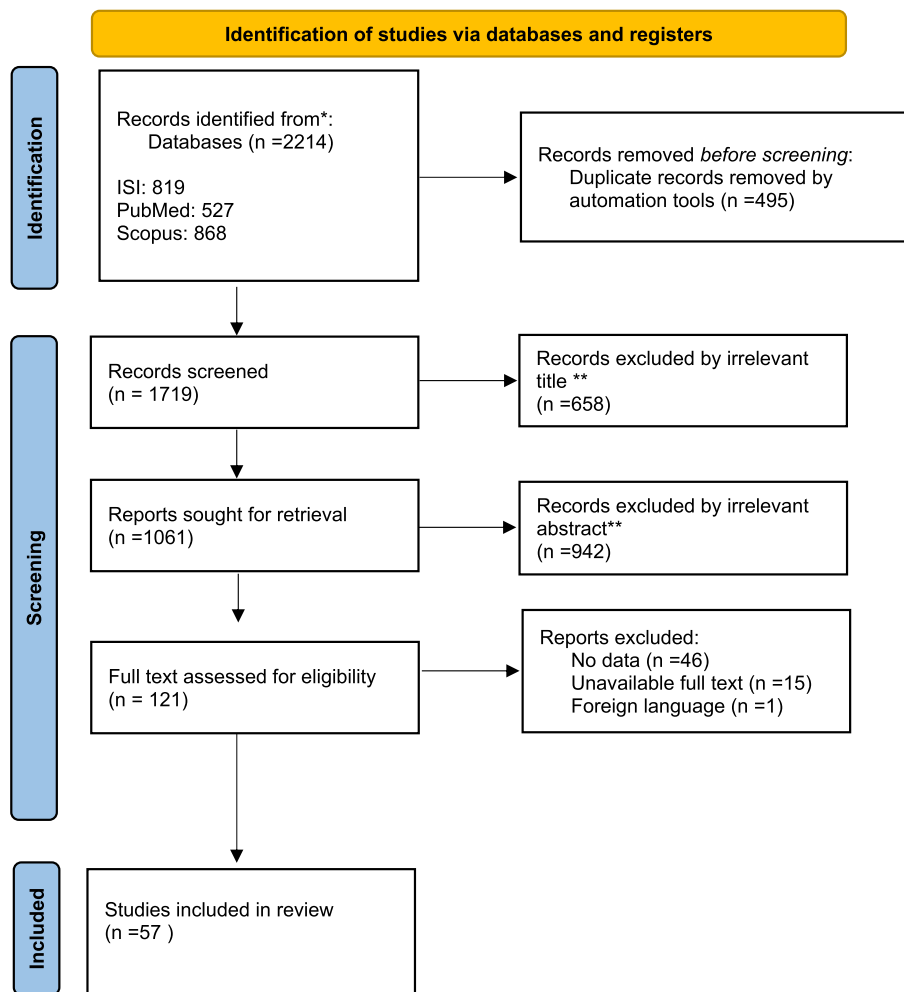
Figure 1. Flow diagram of the literature search for studies included in meta-analysis.

Sensitivity analysis. To investigate the effect of each study on the pooled prevalence, we conducted a sensitivity analysis in which pooled prevalence are estimated omitting one study at a time. The highest pooled prevalence (28.1%, 95%CI 24.4–31.8%) was obtained by omitting the study of Innala et al.[3] and the lowest pooled prevalence (27.0%, 95%CI 23.3–30.7%) was obtained by omitting the study of Hu et al.[43].

Discussion

In this study, 57 primary studies with a total population of 227,812 cases were included in the meta-analysis, and according to the obtained results, OP prevalence among RA patients is 27.6%. The subgroup analysis based on the data of publication suggested that the highest prevalence was found in studies conducted during 2011–2015 (36.2%), followed by 2016–2021 (27.1%). The prevalence in studies with low and moderate risk score was 29.8% and 36.2%, respectively. Based on the study region, the highest prevalence of OP was in Africa (46.1%), followed by Asia (30.6%), Europe (25.6%), and the Americas (19.5%).

RA is a chronic inflammatory disease that, it leads to localized and generalized reduction in bone density and eventually causes OP[73]. Bone fractures are one of the most common complications in RA patients caused by OP and is associated with poor prognosis in old age and low quality of life[74]. According to the results, the prevalence of OP varies in different countries and continents, which can be attributed to the population density and different time of studies, age, economic situation and lack of government attention to the issue. In addition, difference in the quality of providing medical services, access to osteoporosis screening methods, and controlling the risk factors related to it and also preventing the disease play an important role.

A systematic review conducted by Salari et al.[75] in 2021 to estimate the prevalence of OP in the general population. After review of 86 included studies, the worldwide prevalence of OP is estimated as 18.3% and in Asia, Europe, the Americas and Africa it was estimated as 16.7, 18.6, 12.4, and 39.5%, respectively. According to

Id	Author	Year	Countries	Prevalence	Sample size	Mean age	Disease duration	Risk score	References
1	Venter G	2021	Australia	14.7	109	59.5	204	Moderate	[69]
2	Tavassoli S	2021	Iran	8.5	129	56.33	83	Low	[7]
3	Pierini F. S	2021	Argentina	36.5	74	62.1	114	Low	[13]
4	Hu Z	2021	China	54.7	340	59.4	66	Low	[4]
5	Tong J	2019	China	33.6	865	55.6	113	Low	[68]
6	Lindner L	2020	Germany	6	5423	63	168	Low	[51]
7	Hu Z	2020	China	62.1	452	58	67	Low	[43]
8	Yan S	2019	China	4.19	788	56	48	Low	[72]
9	Wafa H	2018	Tunisia	48	173	54.1	98	Low	[71]
10	Tong H	2018	China	35	320	54.1	72	Low	[67]
11	Luque Ramos A	2019	Germany	25.9	2535	62.5		Moderate	[52]
12	Fauny M	2019	France	26.7	105	61.1	144	Low	[30]
13	Phuan-udom R	2018	Thailand	5	232	61.1	155	Moderate	[11]
14	Panopoulos S	2018	Greece	21.4	182	61.6	108	Low	[62]
15	Mohd-Tahir N. A	2017	Malaysia	29	93	61.7	66	Moderate	[59]
16	Kweon S. M	2018	South Korea	19.7	76	64.5	37.5	Low	[47]
17	Kim D	2018	South Korea	33.8	142,955	54.2	24.5	High	[45]
18	Heidari B	2018	Iran	30.8	39	50.6	108	Low	[41]
19	Gabdulina G	2018	Kazakhstan	45.1	406	50.6	61.6	Low	[31]
20	Ene C. G	2018	Romania	32.2	62	49.43		Low	[29]
21	Choi S. T	2018	South Korea	33.4	479	61.5	53	Low	[27]
22	Rossini M	2017	Italian	35	183	64	108	Moderate	[65]
23	Meng J	2017	China	41.07	168	54.3	146.5	Low	[20]
24	Makhdoom A	2017	Pakistan	40.6	229	46.4		Low	[53]
25	Galarza-Delgado D. A	2017	Mexico	19.1	225	55.7	114	Moderate	[32]
26	Singh S	2016	India	5.9	51	45		Low	[1]
27	Lee J. H	2016	South Korea	46.8	1322	63.7	145	Low	[50]
28	Kim D	2016	South Korea	5.5	5376	58.8	117.5	Low	[44]
29	Innala L	2016	Sweden	3.7	726	55.6	80.5	Moderate	[3]
30	Garip Y	2016	Turkey	21.2	160	53.6	145	Low	[33]
31	Bautista-Molano W	2016	Colombia	17.3	1652	58	110.5	Low	[26]
32	Piao H. H	2015	China	21.6	37	64.4		Moderate	[63]
33	Mohammad A	2013	Ireland	59	603	57	180	Low	[58]
34	Lee J. H	2014	South Korea	59.1	545	57	135	Low	[49]
35	Lee J. H	2014	South Korea	51	100	61.2	78	Low	[48]
36	Hauser B	2014	UK	29.9	304	63.5	115	Low	[40]
37	Gron K. L	2014	34 countries	17.6	9874	54.9	97	Moderate	[37]
38	Mobini m	2012	Iran	32.3	121	55.7	121	Low	[57]
39	Lee S. G	2012	South Korea	22.1	299	52.4	32	Low	[16]
40	Gonzalez-Lopez L	2012	Mexico	24.1	191	52	132	Low	[36]
41	Ghazi M	2012	France	55.4	101	56.1	179.5	Low	[34]
42	Vis M	2011	(Norway, UK, Netherlands)	35	102	61	204	Moderate	[70]
43	Dao H. H	2011	Vietnam	27.6	105	56.3	21	Low	[28]
44	Kim S. Y	2010	USA	18	47,034	55		Low	[46]
45	El Maghraoui A	2010	Morocco	44.2	172	49.4	101	Low	[18]
46	Shankar S	2008	India	22	84	33.9	60	Low	[66]
47	Sarkis K. S	2009	Brazil	25.3	83	55	92.5	Low	[8]
48	Richards J. S	2009	USA	18	282	65.4	156	Moderate	[64]
49	Oelzner P	2008	Germany	47.8	551	58.4	144	Low	[61]
50	Haugen I. K	2007	Norway	19.4	194	60.9		Low	[39]
51	Nolla J. M	2006	Spain	13	187	60.34	109	Low	[60]
52	Mikuls T. R	2005	USA	4.7	175	60	109	Low	[56]
Continued									

Id	Author	Year	Countries	Prevalence	Sample size	Mean age	Disease duration	Risk score	References
53	Heidari B	2004	Iran	25	88	52.6	84	Low	42
54	Manrique F	2003	Venezuela	29.4	85	45.3	113	Low	54
55	Haugeberg G	2000	Norway	4.2	394	54.8	156	Moderate	38
56	Gilboe I. M	2000	Norway	5	75	45	95	Low	35
57	Moconkey B	1962		30.3	97	63.1	14.7	Moderate	55

Table 1. Characteristics of the primary studies included in the meta-analysis.

Groups	No of studies	Prevalence rate		Heterogeneity		
		ES (95%CI)	Model	Chi square	P value	I square (%)
Date of publication						
1962–2010	14	21.6% (15.8–27.4)	Random	553.1	0.001	97.6%
2011–2015	12	36.2% (24.5–47.8)	Random	875.9	0.001	98.7%
2016–2021	31	27.1% (20.7–33.4)	Random	15,203.5	0.001	99.8%
Study risk score						
Low risk	43	29.8% (26.2–33.5)	Random	5504.0	0.001	99.2%
Moderate	13	19.3% (13.9–24.7)	Random	705.8	0.001	98.3%
High risk	1	33.9% (33.6–34.1)	Random	–	–	–
Continents						
Asia	26	30.6% (23.2–38.0)	Random	9508.0	0.001	99.7%
Europe	17	25.6% (18.7–32.4)	Random	1803.9	0.001	99.1%
America	9	19.5% (15.9–23.1)	Random	96.1	0.001	91.6%
Africa	2	46.1% (40.8–51.3)	Random	–	–	–
Overall	57	27.6% (23.9–31.3)	Random	18,613.03	0.001	99.69%

Table 2. Summary of meta-analysis results and subgroups analysis.

their study, the estimated prevalence was lower compared to our study, the reason is that people with RA have a higher risk of developing OP than the general population. In our study, similar to the study of Salari et al., the prevalence was lower in the Americas and higher in Africa followed by Asian and European countries.

In a meta-analysis, Ramírez et al.[76] reviewed the results of 45 articles and found that the prevalence of OP in patients with axial spondylarthritis varies from 11.7 to 34.4%. In another meta-analysis study conducted on the general Chinese population, Chen et al. revealed that the prevalence of OP ranged from 1 to 85%[77]. The results of previous studies[78] have shown that the prevalence of OP in people with RA is about 30%. The findings of our study had a similar estimate.

The results of our study and previous studies have shown that the prevalence of OP in people with RA is higher than the general population. Various factors play a role in increasing the prevalence of OP in patients with rheumatoid arthritis, the most important of which are continuous inflammation, glucocorticoid use, reduced physical activity due to old age and disability, and the use of DMARDs[78].

In this study we investigated the results of 227,812 cases of RA with 64,290 cases of OP and it should be highlighted that 142,955 of these cases (63%) are related to the study conducted by Kim D et al.[45] in South Korea, and the prevalence of OP reported as 33.8% in their study.

The incidence of OP is caused by several factors among RA patients. In the pathogenesis of inflammation and reduction of BMD, various factors in immune system, are involved such as hyper-expression and the effect of autoantibodies against citrullinated proteins, pro-inflammatory cytokine secretion, and receptor activator of NF-kappa B ligand derived from T-cell[79]. Immunosuppressive drugs such as glucocorticoids and DMARDs are used to treat RA. Glucocorticoids with their anti-inflammatory effects can prevent local and systemic decrease in BMD. Furthermore, DMARDs are used to achieve remission, and evidence suggests that DMARDs prevent structural damage to cartilage and bone[80,81].

Decreased vitamin D intake is associated with an increased risk of RA, and also, vitamin D deficiency is associated with disease activity in patients with RA[82]. Therefore, vitamin D deficiency can be one of the common causes of RA and OP. The results of a meta-analysis study showed that vitamin D deficiency in RA patients is significantly higher than healthy individuals and serum vitamin D levels are inversely related with disease activity[83].

The results suggest that the prevalence of RA has been declining in recent years, which may be attributed to the increase of human knowledge about drugs that suppress RA and timely imaging studies for early diagnosis and adequate treatment. Among the four continents (i.e., Africa, Asia, the Americas and Europe), Asia has the most prevalent of OP followed by Europe. In most studies, due to the higher risk of women with RA, the majority of the population was women and most of them were in menopausal ages and is associated with estrogen
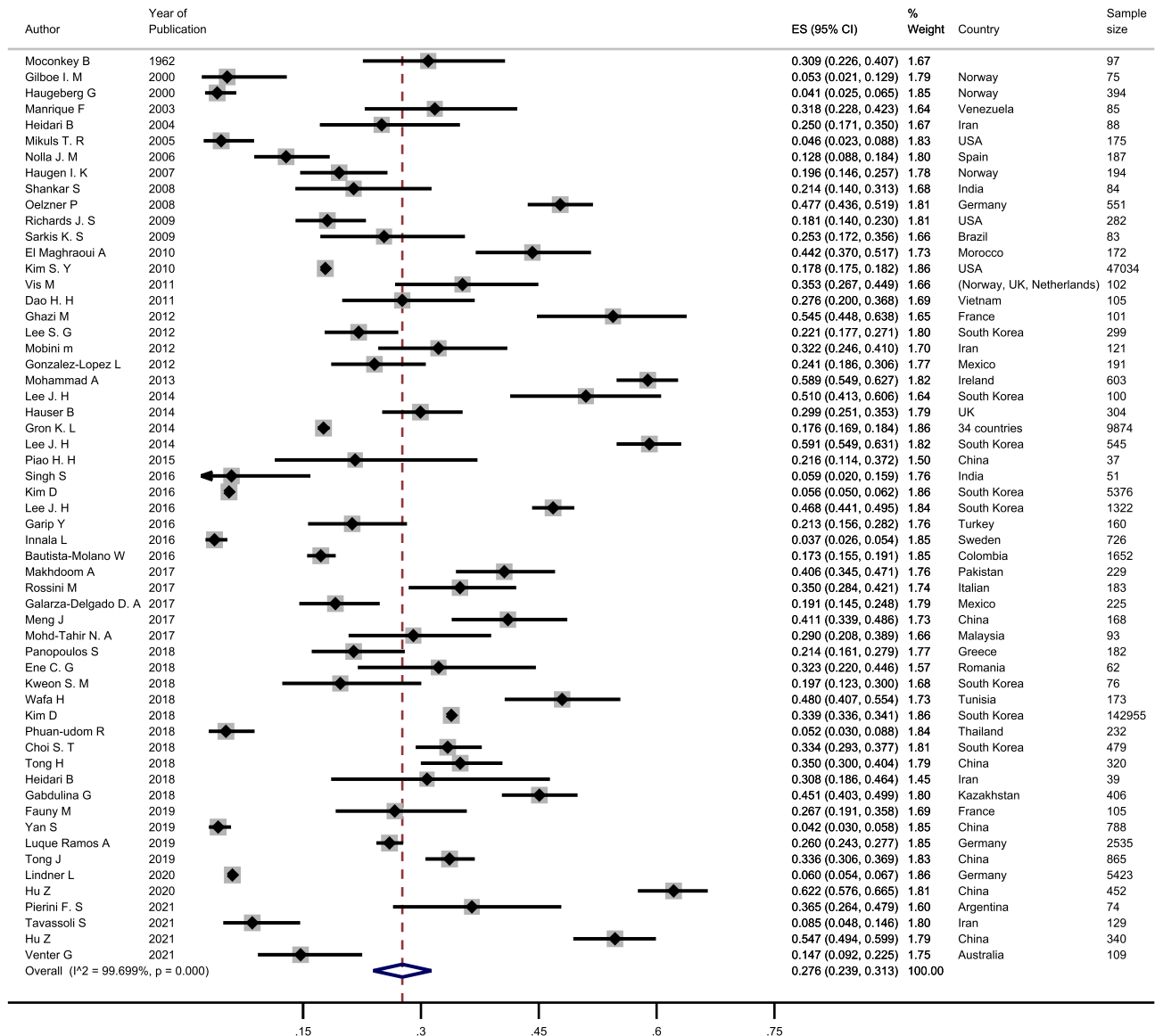
Author	Year of Publication	ES (95% CI)	% Weight	Country	Sample size
Moconkey B	1962	0.309 (0.226, 0.407)	1.67		97
Gilboe I. M	2000	0.053 (0.021, 0.129)	1.79	Norway	75
Haugeberg G	2000	0.041 (0.025, 0.065)	1.85	Norway	394
Manrique F	2003	0.318 (0.228, 0.423)	1.64	Venezuela	85
Heidari B	2004	0.250 (0.171, 0.350)	1.67	Iran	88
Mikuls T. R	2005	0.046 (0.023, 0.088)	1.83	USA	175
Nolla J. M	2006	0.128 (0.088, 0.184)	1.80	Spain	187
Haugen I. K	2007	0.196 (0.146, 0.257)	1.78	Norway	194
Shankar S	2008	0.214 (0.140, 0.313)	1.68	India	84
Oelzner P	2008	0.477 (0.436, 0.519)	1.81	Germany	551
Richards J. S	2009	0.181 (0.140, 0.230)	1.81	USA	282
Sarkis K. S	2009	0.253 (0.172, 0.356)	1.66	Brazil	83
El Maghraoui A	2010	0.442 (0.370, 0.517)	1.73	Morocco	172
Kim S. Y	2010	0.178 (0.175, 0.182)	1.86	USA	47034
Vis M	2011	0.353 (0.267, 0.449)	1.66	(Norway, UK, Netherlands)	102
Dao H. H	2011	0.276 (0.200, 0.368)	1.69	Vietnam	105
Ghazi M	2012	0.545 (0.448, 0.638)	1.65	France	101
Lee S. G	2012	0.221 (0.177, 0.271)	1.80	South Korea	299
Mobini m	2012	0.322 (0.246, 0.410)	1.70	Iran	121
Gonzalez-Lopez L	2012	0.241 (0.186, 0.306)	1.77	Mexico	191
Mohammad A	2013	0.589 (0.549, 0.627)	1.82	Ireland	603
Lee J. H	2014	0.510 (0.413, 0.606)	1.64	South Korea	100
Hauser B	2014	0.299 (0.251, 0.353)	1.79	UK	304
Gron K. L	2014	0.176 (0.169, 0.184)	1.86	34 countries	9874
Lee J. H	2014	0.591 (0.549, 0.631)	1.82	South Korea	545
Piao H. H	2015	0.216 (0.114, 0.372)	1.50	China	37
Singh S	2016	0.059 (0.020, 0.159)	1.76	India	51
Kim D	2016	0.056 (0.050, 0.062)	1.86	South Korea	5376
Lee J. H	2016	0.468 (0.441, 0.495)	1.84	South Korea	1322
Garip Y	2016	0.213 (0.156, 0.282)	1.76	Turkey	160
Innala L	2016	0.037 (0.026, 0.054)	1.85	Sweden	726
Bautista-Molano W	2016	0.173 (0.155, 0.191)	1.85	Colombia	1652
Makhdoom A	2017	0.406 (0.345, 0.471)	1.76	Pakistan	229
Rossini M	2017	0.350 (0.284, 0.421)	1.74	Italian	183
Galarza-Delgado D. A	2017	0.191 (0.145, 0.248)	1.79	Mexico	225
Meng J	2017	0.411 (0.339, 0.486)	1.73	China	168
Mohd-Tahir N. A	2017	0.290 (0.208, 0.389)	1.66	Malaysia	93
Panopoulos S	2018	0.214 (0.161, 0.279)	1.77	Greece	182
Ene C. G	2018	0.323 (0.220, 0.446)	1.57	Romania	62
Kweon S. M	2018	0.197 (0.123, 0.300)	1.68	South Korea	76
Wafa H	2018	0.480 (0.407, 0.554)	1.73	Tunisia	173
Kim D	2018	0.339 (0.336, 0.341)	1.86	South Korea	142955
Phuan-udom R	2018	0.052 (0.030, 0.088)	1.84	Thailand	232
Choi S. T	2018	0.334 (0.293, 0.377)	1.81	South Korea	479
Tong H	2018	0.350 (0.300, 0.404)	1.79	China	320
Heidari B	2018	0.308 (0.186, 0.464)	1.45	Iran	39
Gabdulina G	2018	0.451 (0.403, 0.499)	1.80	Kazakhstan	406
Fauny M	2019	0.267 (0.191, 0.358)	1.69	France	105
Yan S	2019	0.042 (0.030, 0.058)	1.85	China	788
Luque Ramos A	2019	0.260 (0.243, 0.277)	1.85	Germany	2535
Tong J	2019	0.336 (0.306, 0.369)	1.83	China	865
Lindner L	2020	0.060 (0.054, 0.067)	1.86	Germany	5423
Hu Z	2020	0.622 (0.576, 0.665)	1.81	China	452
Pierini F. S	2021	0.365 (0.264, 0.479)	1.60	Argentina	74
Tavassoli S	2021	0.085 (0.048, 0.146)	1.80	Iran	129
Hu Z	2021	0.547 (0.494, 0.599)	1.79	China	340
Venter G	2021	0.147 (0.092, 0.225)	1.75	Australia	109
Overall (I^2 = 99.699%, p = 0.000)		0.276 (0.239, 0.313)	100.00		

Figure 2. Forest plot showing the prevalence of osteoporosis among rheumatoid arthritis patient.
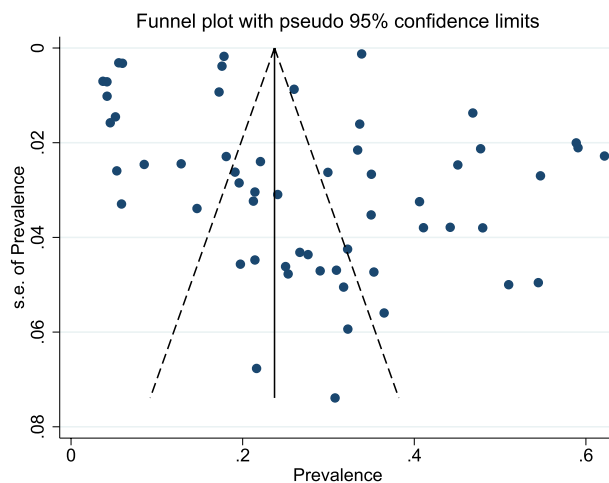

Figure 3. Funnel plot to check the publication bias.

reduction, which is an important risk factor to increase prevalence of OP. It should be noted that because most studies used the DEXA method to evaluate OP, there is lower error in the diagnostic method. Although in some countries, limited studies have been conducted, but it can be said that the prevalence of OP in RA is high and it is necessary to have a decent platform for screening and timely use of medications and patients' education to reduce modifiable risk factors to reduce the incidence of OP to minimize the complications.

One of the main limitations of the study is the lack of sufficient number of studies conducted in each area (for example only two studies from the African continent were included in this meta-analysis), which makes it difficult to generalize the results. Also, in other WHO regions, studies have been conducted in limited countries, which makes it impossible to show the true prevalence in each region. On the other hand, in a number of studies in which people were treated with corticosteroids and DMARDs, the rate of bone mass reduction was not examined separately, so it was not possible to compare between drug users and other people. Finally, due to the disparity of results in different continents and countries, more comprehensive studies are recommended to make a better conclusion.

Conclusion

Despite significant advances in prevention, treatment and diagnostic methods in RA patients, it still seems that the prevalence of OP in these patients is high and requires better and timelier interventions.

Data availability

All data for the analyses is available from the corresponding author on request.

References

1. Singh, S., Lihite, R. J., Baruah, C., Lahkar, M. & Singh, P. K. A pilot study of comorbidities in patients with rheumatoid arthritis at a tertiary care hospital in Northeast India. *Biomed. Res. Ther.* **3**, 454–459. https://doi.org/10.7603/s40730-016-0001-0 (2016).
2. Ziegelasch, M. *et al.* Decrease in bone mineral density during three months after diagnosis of early rheumatoid arthritis measured by digital X-ray radiogrammetry predicts radiographic joint damage after one year. *Arthritis Res. Ther.* **19**, 195. https://doi.org/10.1186/s13075-017-1403-0 (2017).
3. Innala, L. *et al.* Co-morbidity in patients with early rheumatoid arthritis—Inflammation matters. *Arthritis Res. Ther.* **18**, 33. https://doi.org/10.1186/s13075-016-0928-y (2016).
4. Hu, Z. *et al.* Prevalence and risk factors for bone loss in rheumatoid arthritis patients from South China: Modeled by three methods. *BMC Musculoskelet. Disord.* **22**, 534. https://doi.org/10.1186/s12891-021-04403-5 (2021).
5. Fardellone, P., Salawati, E., Le Monnier, L. & Goëb, V. Bone loss, osteoporosis, and fractures in patients with rheumatoid arthritis: A review. *J. Clin. Med.* **9**, 3361 (2020).
6. Jin, S. *et al.* Bone mineral density and microarchitecture among Chinese patients with rheumatoid arthritis: A cross-sectional study with HRpQCT. *Arthritis Res. Ther.* **23**, 127. https://doi.org/10.1186/s13075-021-02503-0 (2021).
7. Tavassoli, S., Rajaei, A., Emam, M. M. & Farsad, F. Evaluating the value-added of the trabecular bone score in patients with rheumatoid arthritis. *Arch. Iran. Med.* **24**, 193–198. https://doi.org/10.34172/aim.2021.30 (2021).
8. Sarkis, K. S. *et al.* Association between osteoporosis and rheumatoid arthritis in women: A cross-sectional study. *Sao Paulo Med. J.* **127**, 216–222. https://doi.org/10.1590/s1516-31802009000400007 (2009).
9. Raterman, H. G. & Lems, W. F. Pharmacological management of osteoporosis in rheumatoid arthritis patients: A review of the literature and practical guide. *Drugs Aging* **36**, 1061–1072 (2019).
10. Herrera, A. *et al.* Prevalence of osteoporotic vertebral fracture in Spanish women over age 45. *Maturitas* **80**, 288–295. https://doi.org/10.1016/j.maturitas.2014.12.004 (2015).
11. Phuan-Udom, R., Lektrakul, N. & Katchamart, W. The association between 10-year fracture risk by FRAX and osteoporotic fractures with disease activity in patients with rheumatoid arthritis. *Clin. Rheumatol.* **37**, 2603–2610. https://doi.org/10.1007/s10067-018-4218-8 (2018).
12. Mazzucchelli, R. *et al.* Trends in hip fracture in patients with rheumatoid arthritis: results from the Spanish National Inpatient Registry over a 17-year period (1999–2015). TREND-AR study. *Rmd Open.* https://doi.org/10.1136/rmdopen-2018-000671 (2018).
13. Pierini, F. S. *et al.* Osteoporotic fractures in rheumatoid arthritis patients in Argentina: A matched retrospective cohort study. *Adv. Rheumatol.* https://doi.org/10.1186/s42358-021-00179-3 (2021).
14. Adami, G. & Saag, K. G. Osteoporosis pathophysiology, epidemiology, and screening in rheumatoid arthritis. *Curr. Rheumatol. Rep.* **21**, 1–10 (2019).
15. Lin, Y. C. *et al.* Rheumatoid arthritis patients with hip fracture: A nationwide study. *Osteoporos. Int. J. Establ. Result Coop. Between Eur. Found. Osteoporos. Natl. Osteoporos. Found. USA* **26**, 811–817. https://doi.org/10.1007/s00198-014-2968-y (2015).
16. Lee, S. G. *et al.* Increased frequency of osteoporosis and BMD below the expected range for age among South Korean women with rheumatoid arthritis. *Int. J. Rheum. Dis.* **15**, 289–296. https://doi.org/10.1111/j.1756-185X.2012.01729.x (2012).
17. Nyhäll-Wåhlin, B. M., Ajeganova, S., Petersson, I. F. & Andersson, M. Increased risk of osteoporotic fractures in Swedish patients with rheumatoid arthritis despite early treatment with potent disease-modifying anti-rheumatic drugs: a prospective general population-matched cohort study. *Scand. J. Rheumatol.* **48**, 431–438. https://doi.org/10.1080/03009742.2019.1611918 (2019).
18. El Maghraoui, A. *et al.* Prevalence and risk factors of vertebral fractures in women with rheumatoid arthritis using vertebral fracture assessment. *Rheumatology (Oxford)* **49**, 1303–1310. https://doi.org/10.1093/rheumatology/keq084 (2010).
19. Chen, B., Cheng, G. Q., Wang, H. T. & Feng, Y. Increased risk of vertebral fracture in patients with rheumatoid arthritis A meta-analysis. *Medicine.* https://doi.org/10.1097/md.0000000000005262 (2016).
20. 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 (Baltimore)* **96**, e6677. https://doi.org/10.1097/md.0000000000006677 (2017).
21. Moher, D., Liberati, A., Tetzlaff, J. & Altman, D. G. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Ann. Intern. Med.* **151**, 264–269 (2009).
22. Higgins, J. P. & Green, S. *Cochrane Handbook for Systematic Reviews of Interventions* (2008).
23. Hoy, D. *et al.* Assessing risk of bias in prevalence studies: Modification of an existing tool and evidence of interrater agreement. *J. Clin. Epidemiol.* **65**, 934–939. https://doi.org/10.1016/j.jclinepi.2011.11.014 (2012).
24. Nyaga, V. N., Arbyn, M. & Aerts, M. Metaprop: A Stata command to perform meta-analysis of binomial data. *Arch. Public Health* **72**, 39. https://doi.org/10.1186/2049-3258-72-39 (2014).

25. Page, M. J. *et al.* The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* **372**, n71. https://doi.org/10.1136/bmj.n71 (2021).
26. Bautista-Molano, W. *et al.* Epidemiological profile of colombian patients with rheumatoid arthritis in a specialized care clinic. *Reumatologia Clinica* **12**, 313–318. https://doi.org/10.1016/j.reuma.2015.11.009 (2016).
27. Choi, S. T. *et al.* Prevalence and fracture risk of osteoporosis in patients with rheumatoid arthritis: A multicenter comparative study of the FRAX and WHO criteria. *J. Clin. Med.* https://doi.org/10.3390/jcm7120507 (2018).
28. Dao, H. H., Do, Q. T. & Sakamoto, J. Bone mineral density and frequency of osteoporosis among Vietnamese women with early rheumatoid arthritis. *Clin. Rheumatol.* **30**, 1353–1361. https://doi.org/10.1007/s10067-011-1762-x (2011).
29. Ene, C. G. *et al.* Incidence of osteoporosis and the risk of fracture in patients with rheumatoid arthritis undergoing corticosteroid treatment. *Rev. Chim.* **69**, 1851–1854 (2018).
30. Fauny, M. *et al.* Study of vertebral fracture and Scanographic bone attenuation coefficient in rheumatoid arthritis and ankylosing spondylitis vs controls. *Sci. Rep.* **9**, 13323. https://doi.org/10.1038/s41598-019-49712-x (2019).
31. Gabdulina, G. *et al.* An epidemiological analysis of osteoporotic characteristics in patients affected with rheumatoid arthritis in Kazakhstan. *Arch. Osteoporos.* **13**, 99. https://doi.org/10.1007/s11657-018-0514-9 (2018).
32. Galarza-Delgado, D. A. *et al.* Prevalence of comorbidities in Mexican mestizo patients with rheumatoid arthritis. *Rheumatol. Int.* **37**, 1507–1511. https://doi.org/10.1007/s00296-017-3769-3 (2017).
33. Garip, Y., Eser, F. & Bodur, H. Comorbidities in Turkish patients with rheumatoid arthritis: Association with the health-related quality of life in terms of disease activity, functional and radiological status, severity of pain, and social and emotional functioning. *Acta Reumatologica Portuguesa* **41**, 344–349 (2016).
34. Ghazi, M. *et al.* Prevalence of vertebral fractures in patients with rheumatoid arthritis: Revisiting the role of glucocorticoids. *Osteoporos. Int.* **23**, 581–587. https://doi.org/10.1007/s00198-011-1584-3 (2012).
35. Gilboe, I. M., Kvien, T. K., Haugeberg, G. & Husby, G. Bone mineral density in systemic lupus erythematosus: Comparison with rheumatoid arthritis and healthy controls. *Ann. Rheum. Dis.* **59**, 110–115. https://doi.org/10.1136/ard.59.2.110 (2000).
36. Gonzalez-Lopez, L. *et al.* Performance of risk indices for identifying low bone mineral density and osteoporosis in Mexican Mestizo women with rheumatoid arthritis. *J. Rheumatol.* **39**, 247–253. https://doi.org/10.3899/jrheum.110467 (2012).
37. Gron, K. L. *et al.* The association of fatigue, comorbidity burden, disease activity, disability and gross domestic product in patients with rheumatoid arthritis—Results from 34 countries participating in the Quest-RA programme. *Clin. Exp. Rheumatol.* **32**, 869–877 (2014).
38. Haugeberg, G., Uhlig, T., Falch, J. A., Halse, J. I. & Kvien, T. K. Reduced bone mineral density in male rheumatoid arthritis patients: frequencies and associations with demographic and disease variables in ninety-four patients in the Oslo County Rheumatoid Arthritis Register. *Arthritis Rheum.* **43**, 2776–2784. https://doi.org/10.1002/1529-0131(200012)43:12%3c2776::aid-anr18%3e3.0.co;2-n (2000).
39. Haugen, I. K., Slatkowsky-Christensen, B., Orstavik, R. & Kvien, T. K. Bone mineral density in patients with hand osteoarthritis compared to population controls and patients with rheumatoid arthritis. *Ann. Rheum. Dis.* **66**, 1594–1598. https://doi.org/10.1136/ard.2006.068940 (2007).
40. Hauser, B., Riches, P. L., Wilson, J. F., Horne, A. E. & Ralston, S. H. Prevalence and clinical prediction of osteoporosis in a contemporary cohort of patients with rheumatoid arthritis. *Rheumatology (Oxford)* **53**, 1759–1766. https://doi.org/10.1093/rheumatology/keu162 (2014).
41. Heidari, B., Heidari, P., Hajian-Tilaki, K., Bayani, M. A. & Babaei, M. Effect of long-term low dose prednisolone administration on bone mineral density: Relating to non-compliant women with rheumatoid arthritis. *Caspian J. Intern. Med.* **9**, 171–177. https://doi.org/10.22088/cjim.9.2.171 (2018).
42. Heidari, B. & Jalali, F. Bone densitometry in patients with rheumatoid arthritis. *Acta Med. Iran.* **43**, 99–104 (2005).
43. Hu, Z. *et al.* Prevalence and risk factors for bone loss in Southern Chinese with rheumatic diseases. *BMC Musculoskelet. Disord.* **21**, 416. https://doi.org/10.1186/s12891-020-03403-1 (2020).
44. Kim, D. *et al.* Incidence and risk factors of fractures in patients with rheumatoid arthritis: an Asian prospective cohort study. *Rheumatol. Int.* **36**, 1205–1214. https://doi.org/10.1007/s00296-016-3453-z (2016).
45. Kim, D. *et al.* Glucocorticoids are associated with an increased risk for vertebral fracture in patients with rheumatoid arthritis. *J. Rheumatol.* **45**, 612–620. https://doi.org/10.3899/jrheum.170054 (2018).
46. Kim, S. Y. *et al.* Risk of osteoporotic fracture in a large population-based cohort of patients with rheumatoid arthritis. *Arthritis Res. Ther.* **12**, R154. https://doi.org/10.1186/ar3107 (2010).
47. Kweon, S. M. *et al.* Male patients with rheumatoid arthritis have an increased risk of osteoporosis: Frequency and risk factors. *Medicine (Baltimore)* **97**, e11122. https://doi.org/10.1097/md.0000000000011122 (2018).
48. Lee, J. H. *et al.* Validity and role of vertebral fracture assessment in detecting prevalent vertebral fracture in patients with rheumatoid arthritis. *Joint Bone Spine* **81**, 149–153. https://doi.org/10.1016/j.jbspin.2013.07.003 (2014).
49. Lee, J. H. *et al.* The risk of osteoporotic fractures according to the FRAX model in Korean patients the rheumatoid arthritis. *J. Korean Med. Sci.* **29**, 1082–1089. https://doi.org/10.3346/jkms.2014.29.8.1082 (2014).
50. Lee, J. H. *et al.* The frequency of and risk factors for osteoporosis in Korean patients with rheumatoid arthritis. *BMC Musculoskelet. Disord.* **17**, 98. https://doi.org/10.1186/s12891-016-0952-8 (2016).
51. Lindner, L. *et al.* Osteoporosis in patients with rheumatoid arthritis: Trends in the German National Database 2007–2017. *Rheumatol. Int.* **40**, 2005–2012. https://doi.org/10.1007/s00296-020-04593-6 (2020).
52. Ramos, L. *et al.* Comorbidities in patients with rheumatoid arthritis and their association with patient-reported outcomes. *J. Rheumatol.* **46**, 564–571. https://doi.org/10.3899/jrheum.180668 (2019).
53. Makhdoom, A. *et al.* Bone mineral density level by dual energy X-ray absorptiometry in rheumatoid arthritis. *JPMA J. Pak. Med. Assoc.* **67**, 15–19 (2017).
54. Manrique, F. *et al.* Abnormalities of bone mineral density and bone metabolism in Venezuelan patients with rheumatoid arthritis. *J. Clin. Rheumatol. Pract. Rep. Rheum. Musculoskelet. Dis.* **9**, 219–227. https://doi.org/10.1097/01.rhu.0000081262.36127.53 (2003).
55. McConkey, B., Fraser, G. M. & Bligh, A. S. Osteoporosis and purpura in rheumatoid disease: Prevalence and relation to treatment with corticosteroids. *QJM* **31**, 419–427. https://doi.org/10.1093/oxfordjournals.qjmed.a066977 (1962).
56. Mikuls, T. R. *et al.* Prevalence of osteoporosis and osteopenia among African Americans with early rheumatoid arthritis: the impact of ethnic-specific normative data. *J. Natl. Med. Assoc.* **97**, 1155–1160 (2005).
57. Mobini, M., Kashi, Z. & Ghobadifar, A. Prevalence and associated factors of osteoporosis in female patients with rheumatoid arthritis. *Casp. J. Intern. Med.* **3**, 447–450 (2012).
58. Mohammad, A. *et al.* The prevalence of vertebral fracture on vertebral fracture assessment imaging in a large cohort of patients with rheumatoid arthritis. *Rheumatology (Oxford)* **53**, 821–827. https://doi.org/10.1093/rheumatology/ket353 (2014).
59. Mohd-Tahir, N. A., Thomas, P., Mohamed-Said, M. S., Makmor-Bakry, M. & Li, S. C. Cost-effectiveness of bisphosphonates for prevention of fracture related to glucocorticoid-induced osteoporosis in Malaysia. *Int. J. Rheum. Dis.* **21**, 647–655. https://doi.org/10.1111/1756-185x.13206 (2018).
60. Nolla, J. M. *et al.* Frequency of osteoporosis in 187 men with rheumatoid arthritis followed in a university hospital. *J. Rheumatol.* **33**, 1472–1475 (2006).
61. Oelzner, P. *et al.* Significance of risk factors for osteoporosis is dependent on gender and menopause in rheumatoid arthritis. *Rheumatol. Int.* **28**, 1143–1150. https://doi.org/10.1007/s00296-008-0576-x (2008).

62. Panopoulos, S. *et al.* Prevalence of comorbidities in systemic sclerosis versus rheumatoid arthritis: A comparative, multicenter, matched-cohort study. *Arthritis Res. Ther.* **20**, 267. https://doi.org/10.1186/s13075-018-1771-0 (2018).
63. Piao, H. H., Zhang, K. Q. & Tang, Z. H. Association between rheumatoid arthritics and osteoporosis among Chinese men, a community based study. *Int. J. Clin. Exp. Med.* **8**, 16592–16598 (2015).
64. Richards, J. S. *et al.* Dual-energy X-ray absorptiometry and evaluation of the osteoporosis self-assessment tool in men with rheumatoid arthritis. *J. Clin. Densitom. Off. J. Int. Soc. Clin. Densitom.* **12**, 434–440. https://doi.org/10.1016/j.jocd.2009.06.003 (2009).
65. Rossini, M. *et al.* Prevalence and incidence of osteoporotic fractures in patients on long-term glucocorticoid treatment for rheumatic diseases: the Glucocorticoid Induced OsTeoporosis TOol (GIOTTO) study. *Reumatismo* **69**, 30–39. https://doi.org/10.4081/reumatismo.2017.922 (2017).
66. Shankar, S. *et al.* Bone mineral density in Indian women with rheumatoid arthritis. *Rheumatol. Int.* **29**, 377–381. https://doi.org/10.1007/s00296-008-0706-5 (2009).
67. Tong, H. *et al.* Osteoporosis self-assessment tool as a screening tool for predicting osteoporosis in elderly chinese patients with established rheumatoid arthritis. *J. Clin. Densitom. Off. J. Int. Soc. Clin. Densitom.* **22**, 321–328. https://doi.org/10.1016/j.jocd.2018.08.002 (2019).
68. Tong, J. J. *et al.* Prevalence and risk factors associated with vertebral osteoporotic fractures in patients with rheumatoid arthritis. *Clin. Rheumatol.* **39**, 357–364. https://doi.org/10.1007/s10067-019-04787-9 (2020).
69. Venter, G. *et al.* Perspectives of glucocorticoid use in patients with rheumatoid arthritis. *ACR Open Rheumatol.* **3**, 231–238. https://doi.org/10.1002/acr2.11234 (2021).
70. Vis, M. *et al.* High incidence of vertebral and non-vertebral fractures in the OSTRA cohort study: A 5-year follow-up study in postmenopausal women with rheumatoid arthritis. *Osteoporos. Int. J. Establ. Result Coop. Between Eur. Found. Osteoporos. Natl. Osteoporos. Found. USA* **22**, 2413–2419. https://doi.org/10.1007/s00198-010-1517-6 (2011).
71. Wafa, H. *et al.* Risk factors associated with bone loss and occurrence of fragility fractures in rheumatoid arthritis patients. *Egyp. Rheumatol.* **41**, 1–5. https://doi.org/10.1016/j.ejr.2018.01.004 (2019).
72. Yan, S. *et al.* The incidence of extra-articular manifestations in southern Chinese patients with inflammatory joint diseases. *Int. J. Rheum. Dis.* **22**, 1686–1694. https://doi.org/10.1111/1756-185x.13657 (2019).
73. Sun, T., Wang, J., Zhang, R. & Li, Y. A systematic review and meta-analysis: Effects of glucocorticoids on rheumatoid arthritis and systemic lupus erythematosus. *Ann. Palliat. Med.* **10**, 7977 (2021).
74. Jin, S. *et al.* Incidence of fractures among patients with rheumatoid arthritis: A systematic review and meta-analysis. *Osteoporos. Int.* **29**, 1263–1275 (2018).
75. Salari, N. *et al.* The global prevalence of osteoporosis in the world: A comprehensive systematic review and meta-analysis. *J. Orthop. Surg. Res.* **16**, 1–20 (2021).
76. Ramírez, J., Nieto-González, J. C., Curbelo Rodríguez, R., Castañeda, S. & Carmona, L. Prevalence and risk factors for osteoporosis and fractures in axial spondyloarthritis: A systematic review and meta-analysis. *Semin. Arthritis Rheum.* **48**, 44–52. https://doi.org/10.1016/j.semarthrit.2017.12.001 (2018).
77. Chen, P., Li, Z. & Hu, Y. Prevalence of osteoporosis in China: A meta-analysis and systematic review. *BMC Public Health* **16**, 1039. https://doi.org/10.1186/s12889-016-3712-7 (2016).
78. Llorente, I., García-Castañeda, N., Valero, C., González-Álvaro, I. & Castañeda, S. Osteoporosis in rheumatoid arthritis: Dangerous liaisons. *Front Med (Lausanne)* **7**, 601618–601618. https://doi.org/10.3389/fmed.2020.601618 (2020).
79. Rotta, D. *et al.* Osteoporosis in inflammatory arthritides: New perspective on pathogenesis and treatment. *Front. Med.* **7**, 896 (2020).
80. Corrado, A. *et al.* Influence of glucocorticoid treatment on trabecular bone score and bone remodeling regulators in early rheumatoid arthritis. *Arthritis Res. Ther.* **23**, 1–9 (2021).
81. Tanaka, Y. Managing osteoporosis and joint damage in patients with rheumatoid arthritis: An overview. *J. Clin. Med.* **10**, 1241 (2021).
82. Kostoglou-Athanassiou, I., Athanassiou, P., Lyraki, A., Raftakis, I. & Antoniadis, C. Vitamin D and rheumatoid arthritis. *Ther. Adv. Endocrinol. Metab.* **3**, 181–187. https://doi.org/10.1177/2042018812471070 (2012).
83. Lee, Y. H. & Bae, S. C. Vitamin D level in rheumatoid arthritis and its correlation with the disease activity: A meta-analysis. *Clin. Exp. Rheumatol.* **34**, 827–833 (2016).

Acknowledgements

Author contributions

S.M., B.T. and A.A.H. conceived the study. S.M. and A.A.H. contributed to the title and full-text screening. A.A.H. and S.M. extracted the data. All authors contributed equally to the initial draft of the manuscript. A.A.H. analyzed the data and all authors have read, revised and approved the final version of the manuscript.

Funding

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-022-20016-x.

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