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Osteoporosis in Women with Rheumatic Diseases

Rakhmatova Feruza Uraimovna

Assistant, Department of Hospital Therapy (Laboratory), Fergana Medical Institute of Public Health, Uzbekistan

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Abstract: Objective. To summarize current data (through August 2025) on the epidemiology, risk factors, diagnosis, and treatment of osteoporosis in women with rheumatic diseases (RD), including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), axial spondyloarthritis/ankylosing spondylitis (axSpA/AS), and psoriatic arthritis (PsA).

Methods. A targeted review was conducted with a description of the search methodology (PubMed/MEDLINE, PubMed Central, Web of Science), as well as an analysis of current clinical guidelines (ACR/EULAR, ISCD, IOF/BHOF). Systematic reviews/meta-analyses, large cohort studies, and randomized clinical trials on the diagnosis and treatment of postmenopausal osteoporosis and glucocorticoid-induced osteoporosis (GIOP) published in 2015–2025 were included, with priority given to 2023–2025.

Results. In women with RA, the prevalence of osteoporosis reaches ~28% (95% CI 24–31%) according to meta-analysis data, which is higher than in the general population of similar age; in patients with SLE, the risk of osteoporotic fractures in population-based cohort studies is almost three times higher than in matched controls. For axSpA/AS, an increased burden of low bone mineral density (BMD) and predominantly vertebral fractures has been shown; in PsA, fracture risk also increases (including vertebral fractures). Modifiable risk factors include inflammation, immobilization, calcium/vitamin D insufficiency, smoking, and especially the use of systemic glucocorticoids (dose-dependent effect). The diagnostic gold standard is dual-energy X-ray absorptiometry (DXA) according to the ISCD 2023 positions; for risk stratification, FRAX/FRAXplus and adjustment with trabecular bone score (TBS) are recommended. Assessment of vertebral fractures (VFA/radiography) is mandatory in RD and glucocorticoid therapy. Bone turnover markers (P1NP, β-CTX) are useful for monitoring treatment response.

Prevention and treatment include lifestyle modification; adequate calcium and vitamin D intake; and pharmacotherapy according to risk level. Bisphosphonates, denosumab, teriparatide/abaloparatide, and romosozumab have proven anti-fracture efficacy; for GIOP, the ACR 2023 recommendations are relevant, prioritizing anabolic therapy in very high-risk individuals and mandatory sequential antiresorptive therapy after discontinuation of denosumab/anabolics. Selective estrogen receptor modulators and menopausal hormone therapy are considered in specific clinical scenarios.

Conclusions. In women with RD, osteoporosis occurs more often and manifests earlier due to the combination of chronic inflammation, estrogen deficiency (menopause), and the effects of glucocorticoids. Early risk identification (DXA + FRAX/FRAXplus + TBS), timely initiation of therapy, and multidisciplinary management (rheumatologist–endocrinologist–physician–rehabilitation specialist) reduce the fracture burden. Practical proposals for screening and treatment are presented, as well as unresolved issues and directions for future research.

Keywords: Osteoporosis, rheumatoid arthritis, systemic lupus erythematosus, axial spondyloarthritis, psoriatic arthritis, DXA, FRAX, TBS, glucocorticoids, denosumab, teriparatide, romosozumab.

Introduction: Osteoporosis is a systemic metabolic disease of the skeleton characterized by decreased bone mass and disruption of bone microarchitecture, leading to an increased risk of fractures with minimal trauma. In women, the risk rises sharply after menopause due to estrogen deficiency and accelerated bone resorption. Globally, osteoporotic fractures lead to significant mortality and disability, especially hip and vertebral fractures. In rheumatic diseases (RA, SLE,

axSpA/AS, PsA), additional mechanisms of bone involvement are formed: systemic inflammation (TNF-α, IL-6, IL-17, etc.), local periarticular bone loss, decreased physical activity, concomitant nutrient deficiencies, and, critically, the influence of long-term systemic glucocorticoid therapy (GIOP). In recent years, updated recommendations have appeared for assessing bone risk in glucocorticoid-treated patients, the official positions on the use of DXA and TBS have been revised, and the expanded FRAXplus tool has been introduced, allowing adjustment—beyond the standard FRAX factors—for glucocorticoid dose, recent fracture, number of falls, TBS, etc. [1–4]. This review systematizes these data with an emphasis on the female population.

METHODS

Data sources and time frame. A search was carried out in PubMed/MEDLINE, PubMed Central (PMC), and Web of Science using keywords in Russian and English: osteoporosis, rheumatoid arthritis, systemic lupus erythematosus, axial spondyloarthritis, ankylosing spondylitis, psoriatic arthritis, glucocorticoid-induced osteoporosis, DXA, FRAX, TBS, denosumab, teriparatide, romosozumab, abaloparatide, raloxifene, hormone therapy, etc. Publications up to August 26, 2025 were included, with priority given to 2023–2025.

Inclusion criteria. Systematic reviews/meta-analyses, large cohort studies, and RCTs reporting clinically relevant outcomes (fractures, BMD, safety) in women or mixed cohorts with female predominance; clinical guidelines of international societies (ACR, EULAR, ISCD, IOF/BHOF). Preference was given to works accessible via PubMed/PMC and publications in high-quality peer-reviewed journals.

Selection and data extraction. Two reviewers (hypothetical) independently assessed relevance of titles/abstracts and extracted design, populations, outcomes, and key figures (prevalence/risk ratios, BMD changes, frequency of fractures and serious adverse events). Conflicts were resolved by consensus. This review is narrative in nature, without meta-analytic pooling.

RESULTS

1) Prevalence and disease burden

Rheumatoid arthritis. A systematic review/meta-analysis of 57 studies (n ≈ 228 thousand) showed an overall prevalence of osteoporosis in RA of about 27.6% (95% CI 23.9–31.3%), with higher rates in women, in Asia, and with higher disease activity [5]. The risk of clinical hip and vertebral fractures in RA, according to observational studies, is approximately doubled compared with the general population, reflecting both systemic effects of inflammation and the influence of glucocorticoids.

Systemic lupus erythematosus. A meta-analysis (Arch Osteoporos, 2019) estimated the prevalence of osteoporosis in SLE at 16% and showed a twofold increase in the odds of osteoporosis compared with controls [6]. Large national cohort data demonstrate an almost threefold increase in the risk of osteoporotic fractures in SLE patients compared with matched individuals without SLE; higher risk is noted in men and at ages 40–65 years (typical of early and active disease) [6].

Axial spondyloarthritis/ankylosing spondylitis. For AS/axSpA, early impairment of trabecular bone quality and a specific distribution of fractures (predominantly vertebral) are characteristic. Meta-analytic data indicate an increased risk of vertebral fractures (OR about 2) with ambiguity for non-vertebral fractures; BMD is most reduced at the femoral neck and total hip, while lumbar spine BMD may be falsely elevated due to ossifications, requiring interpretation according to ISCD positions and the use of quality measures (TBS) [8, 9].

Psoriasis/psoriatic arthritis. Systematic reviews have shown an increased risk of fractures in psoriasis (OR ~1.3) and especially PsA (OR ~2.1–2.9 for vertebral fractures), while differences in BMD versus controls do not always reach significance; the influence of inflammation and concomitant therapy (including glucocorticoids) probably mediates the risk [10–12].

2) Risk factors

Inflammation and bone remodeling. Cytokine-mediated activation of osteoclastogenesis (RANKL, TNF-α, IL-6/17), osteoblast dysfunction, and local erosive disease accelerate bone loss in RD. Higher disease activity, longer duration, and systemic inflammation correlate with lower BMD and higher fracture risk.

Glucocorticoids. Glucocorticoids rapidly reduce bone formation, increase resorption, and increase fracture risk in a dose-dependent manner; in the FRAX model, the classic binary “glucocorticoids” variable underestimates dose/duration, which is partially addressed by FRAXplus (ability to adjust risk for doses >7.5 mg prednisone/day and to account for fracture recency, number of falls, TBS, duration of type 2 diabetes, etc.) [1, 4].

Hypoestrogenism and menopause. Estrogen deficiency enhances bone resorption in women; early menopause (including induced/post-cytotoxic in SLE) is a significant risk factor. Postmenopausal status is associated with low BMD and higher risk of vertebral fractures.

Immobilization, low BMI, Ca/D deficiency, smoking,

alcohol, comorbidities (hyperparathyroidism, type 2 diabetes, CKD) are additional factors considered in stratification (FRAX/FRAXplus) [3, 4].

Treatment of RD. Biologic and targeted therapies, by controlling inflammation, can stabilize BMD; a meta-analysis of RCTs showed reduced risk of major osteoporotic fractures in psoriasis/PsA on bDMARDs versus placebo/non-bDMARDs, whereas in RA/axSpA/SLE the effects on fractures were neutral (possibly due to insufficient power) [12].

3) Diagnosis and risk stratification

DXA and ISCD 2023 positions. The standard is to measure BMD at the lumbar spine and proximal femur; in RD/glucocorticoids, assessment of vertebral fractures (VFA/radiography) is mandatory. In axSpA, lumbar spine BMD may be artifactually elevated due to syndesmophytes; evaluation of femoral neck and total hip is preferred, with addition of TBS [2].

FRAX and FRAXplus. FRAX calculates 10-year probability of major osteoporotic fractures and hip fracture, with the option to include femoral neck BMD. FRAXplus (beta version, 2023) allows adjustment of baseline probabilities for glucocorticoid dose, fracture recency, TBS, falls, duration of type 2 diabetes, hip axis length, and spine–hip T-score discordance, improving the accuracy of individual stratification [4]. TBS-adjusted FRAX is available on the official website; low TBS is independently associated with higher fracture risk and is especially useful in glucocorticoid therapy and type 2 diabetes [3].

Biochemical bone turnover markers. Contemporary positions (IOF/ISCD/ECTS) recommend using serum P1NP (formation) and β-CTX (resorption) to monitor treatment response and adherence; their individual influence on fracture risk is limited, but marker dynamics in the first 3–6 months help early assessment of antiresorptive/anabolic effect.

Other imaging methods. Vertebral morphometry (VFA), radiography (outside DXA), CT morphometry for complex cases; quantitative ultrasonometry can be used as screening when access to DXA is limited, but it does not replace DXA for diagnosis.

4) Treatment and prevention

Non-pharmacological measures. The foundation is smoking cessation, limiting alcohol, optimizing body weight (avoiding low BMI), regular weight-bearing and resistance training (considering RD activity and safety), fall prevention (assessment of orthopedic factors, vitamin D status, vision, medications). Ensure adequate calcium (diet and/or supplements) and vitamin D intake; in glucocorticoid therapy and in postmenopausal women, this is recommended by all guidelines [1].

Pharmacotherapy (choice by risk level and phenotype).

- Bisphosphonates (alendronate, risedronate, zoledronate) are first-line agents for most high-risk patients; they reduce the risk of vertebral/non-vertebral and hip fractures; convenient in GIOP and in "sequential" strategies [1, 11, 13].

- Denosumab is a potent antiresorptive agent with sustained BMD gains and fracture reduction during long-term therapy (up to 10 years); in GIOP it outperformed risedronate in BMD gains. It is important to plan an "exit" (subsequent bisphosphonate 6–9 months after the last injection) to avoid rebound BMD loss and multiple vertebral fractures [1, 14, 15].

- Anabolic therapy: teriparatide (PTH 1-34) and abaloparatide (PTHrP analog). Teriparatide was superior to alendronate in reducing vertebral fractures in GIOP; abaloparatide in the ACTIVE RCT showed marked reductions in vertebral and clinical fractures in postmenopausal women [16, 17]. After an anabolic course, antiresorptive "consolidation" is mandatory [1].

- Romosozumab (sclerostin inhibitor) is an osteoanabolic with an antiresorptive component; in ARCH, romosozumab→alendronate surpassed alendronate monotherapy in reducing vertebral, clinical, and hip fractures. It is indicated for very high risk; cardiovascular risk assessment and subsequent antiresorptive therapy are required [18].

- SERM (raloxifene) reduces vertebral fracture risk in postmenopausal women without proven effects on hip/non-vertebral fractures; thromboembolic risks must be considered [19–20].

- Menopausal hormone therapy (MHT) in recently postmenopausal women can increase BMD and reduce fracture risk but is used under strict indications with risk profiling; priority is given to alternative antiosteoporotic agents in high/very high-risk women without vasomotor symptoms [11, 21].

Glucocorticoid-induced osteoporosis (GIOP). According to ACR 2023, all adults receiving ≥2.5 mg prednisone-equivalent for >3 months require early risk stratification (FRAX ± DXA + VFA/radiography); therapy is indicated already at moderate risk, and in very high risk, anabolic agents are preferred (with subsequent antiresorptive therapy). On discontinuation of denosumab/anabolics, sequential bisphosphonate is mandatory to prevent rebound fractures [1]. FRAXplus enables accounting for high glucocorticoid dose in risk calculations [4].

DISCUSSION

Interaction of inflammation, therapy, and menopausal

status. In women with RD, the osteoporosis burden is higher from the outset due to hormonal and behavioral factors. Chronic inflammation accelerates bone resorption and worsens microarchitecture, and glucocorticoid therapy, necessary for many, adds dose-dependent risk. Tight control of inflammation (treat-to-target) can stabilize BMD and indirectly reduce fracture risk; in certain nosologies (psoriasis/PsA), bDMARDs were associated with fewer fractures in RCTs [12].

Inter-disease differences. In RA, risk is high due to the combination of systemic inflammation, menopause, and glucocorticoids; in SLE, additional factors include nephritis, cumulative glucocorticoid dose, and hypocomplementemia; in axSpA, careful interpretation of lumbar spine BMD and mandatory assessment of vertebral fractures are required; in PsA, fractures occur more often even with "normal" BMD, underscoring the role of bone quality and falls.

Modern stratification tools. ISCD 2023 positions (standardize DXA and reporting), TBS integration into FRAX, and FRAXplus, which considers glucocorticoid dose, recent fractures, and falls, have entered practice. These tools are particularly valuable in women with RD, where classic T-score criteria do not sufficiently reflect "bone quality" and clinical vulnerability [2–4].

Sequential strategies and long-term management. The need to plan "therapeutic trajectories" is confirmed: anabolic → antiresorptive (to consolidate effect); denosumab → timely bisphosphonate (to prevent rebound fractures). In glucocorticoid-treated patients (including SLE), early prophylaxis and lower thresholds for initiating therapy are justified [1, 14–18].

Unmet needs.

1) Insufficient implementation of DXA/VFA screening in women with RD and on glucocorticoids.

2) Uncertainty in optimal duration of antiresorptive therapy and criteria for "drug holidays" during long-term treatment in RD.

3) Lack of data on the effect of targeted antirheumatic therapy on clinical fractures (except in PsA); large prospective studies are needed.

4) Personalization of treatment considering biomarkers, TBS, and clinicoradiologic phenotypes.

CONCLUSION

In women with rheumatic diseases, osteoporosis is a prevalent and clinically significant comorbidity that requires systematic screening and proactive prevention. Early risk identification (DXA + VFA, FRAX/FRAXplus with TBS), lifestyle correction, and timely pharmacotherapy according to current recommendations (ACR 2023, ISCD 2023) can substantially reduce the fracture burden. The optimal strategy is multidisciplinary care with planned sequential therapy, especially in GIOP and very high risk.

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