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Profiles of Bone Mineral Density in the Lumbar Vertebrae, Femur, and Radius Using Dual Energy X-Ray Absorptiometry (DXA) in Patients with Autoimmune Rheumatic Diseases at Dr. Soetomo General Academic Hospital

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ABSTRACT

Introduction: Autoimmune rheumatic diseases (ARDs) are chronic inflammatory disorders with high morbidity and mortality, strongly associated with increased osteoporosis risk. The underlying mechanisms are multifactorial, and osteoporosis often remains asymptomatic until fractures occur. Therefore, bone mineral density (BMD) assessment using dual energy X-ray absorptiometry (DXA) is essential for early detection. However, data on BMD profiles in Indonesian ARD patients are limited. ***Methods:*** This retrospective descriptive study evaluated the medical records of 283 ARD patients admitted to Dr. Soetomo General Academic Hospital, Indonesia, between August 2023 and August 2024. Collected data included demographic, clinical, and DXA findings (GE Lunar Prodigy series). Total sampling was employed, and data were analyzed using Microsoft Excel and presented in frequency distribution tables. ***Results:*** The highest mean BMD was observed at the lumbar spine (1.000 ± 0.171 g/cm^2), followed by the femoral neck and radius. Most patients aged <50 years had normal BMD (78.73%), while osteopenia and osteoporosis were more prevalent in those ≥50 years (27.42% and 58.06%, respectively). BMD reduction was more common in females (93.52%), patients with systemic lupus erythematosus (SLE) (53.70%), longer disease duration (55.56%), and high cumulative glucocorticoid exposure. Kidney disease (31.48%) and malabsorption or malnutrition (24.07%) were the most frequent comorbidities. ***Conclusion:*** Reduced BMD in ARD patients was strongly associated with older age, female sex, prolonged disease duration, and chronic glucocorticoid therapy. The lumbar spine had the highest mean BMD, but osteopenia and osteoporosis predominated in patients ≥50 years, especially those with SLE.

Keywords: autoimmune rheumatic diseases; bone mineral density; dual energy x-ray absorptiometry; osteoporosis; glucocorticoids; rheumatoid arthritis; systemic lupus erythematosus

INTRODUCTION

Autoimmune rheumatic diseases (ARDs) are a group of chronic inflammatory disorders characterized by the loss of immune tolerance to self-antigens, leading to systemic or organ-specific tissue damage [1]. This loss of tolerance is influenced by complex interactions between genetic and environmental factors [2]. The global incidence of autoimmune diseases has been increasing over the past decades, with an average annual rise of 19.1% [3]. A large-scale study involving 22 million individuals reported that approximately one in ten people suffers from an autoimmune disease, with a markedly higher prevalence in women [4].

More than 70 autoimmune diseases have been identified, among which rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and spondyloarthritis (SpA) are the most prevalent types of ARDs [5,6]. Their clinical manifestations are highly variable, involving multiple organ systems such as the musculoskeletal, renal, pulmonary, cardiovascular, and hematologic systems [7,8]. These variations depend on the specific organs affected, disease duration, and therapeutic history [9].

Osteoporosis is a common complication among patients with ARDs, with reported prevalence rates of 41% in SLE, 36.1% in RA, and 11.7–34.4% in SpA [10,11]. This condition results from an imbalance between immune cell subsets and the overexpression of proinflammatory cytokines [12]. Long-term and high-dose use of glucocorticoids or disease-modifying antirheumatic drugs (DMARDs) further contributes to bone loss [13]. Moreover, vitamin D deficiency reported in 84% of RA patients significantly increases the risk of osteoporosis [14]. Osteoporotic fractures are a major concern in this population; for instance, a South Korean study found that fracture incidence among SLE patients reached 19.085 per 1,000 persons per year, compared with 6.530 per 1,000 in the general population [15].

Accurate assessment of bone mineral density (BMD) is essential for preventing fractures and improving prognosis in patients with ARDs. Dual energy X-ray absorptiometry (DXA) remains the gold standard for BMD evaluation due to its high precision, short scanning time, and minimal radiation exposure [16]. However, BMD screening using DXA is not routinely performed in Indonesia, and local data on bone density profiles in autoimmune patients remain limited. The present study, conducted at Dr. Soetomo General Academic Hospital, aims to evaluate BMD values at the lumbar spine, femur, and radius, along with the clinical and demographic characteristics of ARD patients. The findings are expected to provide valuable insights for optimizing fracture prevention strategies and improving patient outcomes within the Indonesian population.

METHOD

This study employed a descriptive design with retrospective data collection using secondary data obtained from medical records and bone mineral density (BMD) test results measured by the GE Lunar Prodigy DXA system. The research was conducted at Dr. Soetomo General Academic Hospital between August 2023 and August 2024. Medical records were reviewed to obtain the patient's demographic information and clinical profiles.

Ethical approval was obtained from the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital (No. 1803/LOE/301.4.2/X/ 2024). The study population consisted of all patients diagnosed with autoimmune rheumatic diseases (ARDs) who underwent DXA examination during the study period. Samples were selected based on predefined inclusion criteria. The inclusion criteria were as follows: patients diagnosed with ARDs who had complete medical records, underwent DXA testing within the study period, and had no anatomical abnormalities of the lumbar spine, femur, or radius that could affect BMD measurements. A total of 283 patients met these criteria and were included in the final analysis.

Variables assessed in this study included sex, age, education, occupation, body mass index (BMI), type of ARD, disease duration, treatment history (glucocorticoids, DMARDs, calcium, and vitamin D), previous fracture history, parental fracture history, smoking status, alcohol consumption, comorbidities (including diabetes mellitus, hyperthyroidism, early menopause, malnutrition or malabsorption, liver disease, and kidney disease), and DXA results. All collected data were processed using Microsoft Excel and presented in frequency distribution tables.

RESULT

The total number of patients with autoimmune rheumatic diseases (ARDs), including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), spondyloarthritis (SpA), and other ARDs such as systemic sclerosis (SSc) and Sjögren's syndrome, who underwent DXA testing at Dr. Soetomo General Academic Hospital between August 2023 and August 2024 was 317, of which 283 met the inclusion criteria.

As shown in Table 1, the mean bone mineral density (BMD) values across skeletal regions demonstrated the highest density at the lumbar vertebrae (1.000 ± 0.171 g/cm^2), followed by the right and left femoral necks (0.802 ± 0.144 g/cm^2 and 0.798 ± 0.141 g/cm^2, respectively). The lowest mean BMD was observed at the radius (0.739 ± 0.120 g/cm^2), suggesting a greater susceptibility to bone loss in peripheral sites compared to axial regions.

TABLE 1: Distribution of Bone Mineral Density (BMD).

Region	n	Minimum	Maximum	Mean	SD
Lumbar Vertebrae	280	0.537	1.892	1.000	0.171
Right Femoral (Neck)	278	0.367	1.218	0.802	0.144
Left Femoral (Neck)	279	0.423	1.228	0.798	0.141
Radius	196	0.303	0.995	0.739	1.120

SD: Standard Deviation.

Based on Table 2, among patients aged below 50 years, the majority (78.73%) exhibited normal bone mineral density (BMD) values, while 21.27% showed reduced BMD according to Z-scores.

The 41–49 year-old age group had the highest proportion of patients with low or below the expected range of BMD, indicating an early decline in bone mass that may precede the postmenopausal or elderly stage.

TABLE 2: DXA Test Results in Patients Aged <50 Years Using Z-Score.

Age Group (<50 Years)	Normal Range BMD (n=221)	%	Low or Below Expected Range BMD (n=221)	%
0-10 Years	0	0.00	0	0.00
11-20 Years	15	6.79	6	2.71
21-30 Years	70	31.67	16	7.24
31-40 Years	43	19.46	7	3.17
41-49 Years	46	20.81	18	8.14
Total	**174**	**78.73**	**47**	**21.27**

Normal BMD: Z-score > -2.0 SD; Low or Below Expected Range BMD: Z-score ≤ -2.0 SD.

Based on Table 3, among patients aged ≥50 years, only 1.61% exhibited normal bone mineral density (BMD), while the majority showed varying degrees of bone loss. Osteoporosis was the most prevalent condition (58.07%), followed by osteopenia (27.42%) and severe osteoporosis (12.90%). The highest proportion of osteoporosis was observed in the 50–55-year age group, indicating that substantial bone loss may begin early in the postmenopausal period.

TABLE 3: DXA Test Results in Patients Aged ≥50 Years Using T-Score.

Age Group (≥50 Years)	Normal BMD (n=62)	%	Osteopenia (n=62)	%	Osteoporosis (n=62)	%	Severe Osteoporosis (n=62)	%
50-55 Years	1	1.61	9	14.52	13	20.97	2	3.23
56-60 Years	0	0.00	3	4.84	11	17.74	2	3.23
61-65 Years	0	0.00	3	4.84	6	9.68	2	3.23
66-70 Years	0	0.00	1	1.61	4	6.45	1	1.61
71-75 Years	0	0.00	1	1.61	2	3.23	0	0.00
>75 Years	0	0.00	0	0.00	0	0.00	1	1.61
Total	**1**	**1.61**	**17**	**27.42**	**36**	**58.07**	**8**	**12.90**

Normal BMD: T-score ≥ -1.0 SD; Osteopenia: T-score between -1.0 and -2.5 SD; Osteoporosis: T-score ≤ -2.5 SD; Severe Osteoporosis: T-score ≤ -2.5 SD with fragility fracture(s).

Based on Table 4, the mean age of patients was 38.35 ± 14.01 years, with most participants aged below 50 years (78.09%) and predominantly female (95.76%). Low BMD was more prevalent among patients aged 50 years and older (56.48%), whereas younger patients mostly exhibited normal BMD values. Most participants had "other" educational backgrounds (83.04%) and were primarily housewives (33.92%), suggesting that lower physical activity and postmenopausal status may contribute to bone density reduction.

TABLE 4: Demographic Characteristics.

Variable	N=283	%	Normal (n=175)	%	Low BMD (n=108)	%
Age (Years) Mean±SD			**38.35 ± 14.01**			
<50 Years	221	78.09	174	99.43	47	43.52
≥50 Years	62	21.91	1	0.57	61	56.48
Sex						
Male	12	4.24	5	2.86	7	6.48
Female	271	95.76	170	97.14	101	93.52
Education						
Elementary School	1	0.35	0	0.00	1	0.93
Junior High School	6	2.12	5	2.86	1	0.93
Senior High School	31	10.95	25	14.28	6	5.56
Diploma/Bachelor	8	2.83	5	2.86	3	2.78
Master/Doctorate	2	0.71	1	0.57	1	0.93
Others	235	83.04	139	79.43	96	88.89
Occupation						
Student	48	16.96	36	20.57	12	11.11
Housewife	96	33.92	45	25.71	51	47.22
Civil Servant	3	1.06	2	1.14	1	0.93

Variable	N=283	%	Normal (n=175)	%	Low BMD (n=108)	%
Occupation						
Private Employee	71	25.09	50	28.57	21	19.44
Entrepreneur	6	2.12	5	2.86	1	0.93
Farmer	3	1.06	3	1.71	0	0.00
Others	56	19.79	34	19.43	22	20.37

Normal BMD: Z-score > -2.0 SD atau T-score ≥ -1.0 SD; Low BMD: Z-score ≤ -2.0 SD atau T-score < -1.0 SD.

Based on Table 5, the majority of patients were diagnosed with systemic lupus erythematosus (SLE) (72.79%), followed by spondyloarthritis (SpA) (12.37%) and rheumatoid arthritis (RA) (7.77%). The mean disease duration was 5.67 ± 4.96 years, with more than half of patients with low bone mineral density (BMD) experiencing disease for over five years (55.56%), suggesting a relationship between chronic inflammation and bone loss.

The mean body mass index (BMI) was 22.42 ± 4.49 kg/m^2, with most participants classified as having a normal BMI (44.17%). Nearly all patients received glucocorticoid therapy (95.05%), highlighting prolonged steroid exposure as a major risk factor for reduced BMD. A small proportion (3.89%) had a history of fractures, while renal disease (39.93%) was the most common comorbidity.

TABLE 5: Clinical Characteristics.

Variable	N=283	%	Normal (n=175)	%	Low BMD (n=108)	%
Type of ARD						
RA	22	7.77	8	4.57	14	12.96
SLE	206	72.79	148	84.57	58	53.70
SpA	35	12.37	13	7.43	22	20.37
Others (SSc & Sjogren'' Syndrome)	20	7.07	6	3.43	14	12.96
Disease Duration (Years) Mean±SD			***5.67 ± 4.96***			
<1 Year	23	8.13	17	9.71	6	5.56
1-3 Years	78	27.56	57	32.57	21	19.44
3-5 Years	56	19.79	35	20.00	21	19.44
>5 Years	126	44.52	66	37.71	60	55.56
BMI (kg/m^2) Mean±SD			***22.42 ± 4.49***			
Underweight	47	16.61	28	16.00	19	17.59
Normal	125	44.17	79	45.14	46	42.59
Overweight	73	25.79	43	24.57	30	27.78
Obese	38	13.43	25	14.29	13	12.04
Medication History						
Glucocorticoids	269	95.05	172	98.28	97	89.81
DMARDs	148	52.30	88	50.29	54	50.00
Calcium	264	91.60	161	92.00	103	95.37
Vitamin D	64	22.61	38	21.71	26	24.07
Smoking						
Yes	7	2.47	3	1.71	4	3.70
No	276	97.53	172	98.29	104	96.30
History of Fracture						
Yes	11	3.89	1	0.57	10	9.26
No	272	96.11	174	99.43	98	90.74
Parental History of Fracture						
Yes	0	0.00	0	0.00	0	0.00
No	283	100.00	283	100.00	283	100.00
Comorbidities						
Diabetes Mellitus	14	4.95	5	2.86	9	8.33
Hyperthyroidism	8	2.83	7	4.00	1	0.93
Malabsorption/Malnutrition	81	28.62	55	31.43	26	24.07
Liver Disease	10	3.53	4	2.29	6	5.56
Kidney Disease	113	39.93	79	45.14	34	31.48
Others	80	28.27	41	23.43	39	36.11

BMI: Body Mass Index; Underweight: < 18.5 kg/m^2; Normal: 18.5 – 23 kg/m^2; Overweight: 23 – 27.5 kg/m^2; Obese: > 27.5 kg/m^2.

Based on Table 6, patients with SLE constituted the largest group experiencing reduced bone mineral density (53.70%), followed by those with SpA (20.37%) and RA (12.96%). The majority of patients with low BMD were aged ≥50 years, particularly in the RA (78.57%) and SpA (90.91%) groups. Most patients were female across all autoimmune rheumatic disease (ARD) types. In terms of disease duration, over half of SLE (68.97%) and RA (50%) patients had been diagnosed for more than five years, suggesting a cumulative effect of chronic inflammation and prolonged therapy on bone loss. The normal BMI category predominated across groups, with a tendency toward overweight and obesity among SpA patients. Nearly all SLE and other ARD patients received glucocorticoids, and calcium supplementation was also frequent (≥85%). Notably, fracture history was more common in SpA patients (27.27%), while renal disease (55.17%) was the most prevalent comorbidity among SLE patients with low BMD.

TABLE 6: Characteristics in Patients with Autoimmune Rheumatic Diseases Experiencing Reduced Bone Mineral Density.

Variable	RA (n=14)	%	SLE (n=58)	%	SpA (n=22)	%	Others (n=14)	%
Age								
<50 Years	3	21.43	37	63.79	2	9.09	5	35.71
≥50 Years	11	78.57	21	36.21	20	90.91	9	64.29
Sex								
Male	0	0.00	2	3.45	5	22.73	0	0.00
Female	14	100.00	56	96.55	17	77.27	14	100.00
Education								
Elementary School	0	0.00	0	0.00	1	4.55	0	0.00
Junior High School	0	0.00	1	1.72	0	0.00	0	0.00
Senior High School	1	7.14	1	1.72	1	4.55	3	21.43
Diploma/Bachelor	2	14.29	0	0.00	0	0.00	1	7.14
Master/Doctorate	1	7.144	0	0.00	0	0.00	0	0.00
Others	10	71.43	56	96.55	20	90.91	10	71.43
Occupation								
Student	0	0.00	11	18.97	1	4.55	0	0.00
Housewife	6	42.86	26	44.83	10	45.45	9	64.29
Civil Servant	1	7.14	0	0.00	0	0.00	0	0.00
Private Employee	0	0.00	12	20.69	6	27.27	3	21.43
Entrepreneur	0	0.00	1	1.72	0	0.00	0	0.00
Farmer	0	0.00	0	0.00	0	0.00	0	0.00
Others	7	50.00	8	13.79	5	22.73	2	14.29
Disease Duration								
<1 Year	0	0.00	2	3.45	4	18.18	0	0.00
1-3 Years	7	50.00	8	13.79	3	13.64	3	21.43
3-5 Years	0	0.00	8	13.79	5	22.73	8	57.14
>5 Years	7	50.00	40	68.97	10	45.45	3	21.43
BMI								
Underweight	1	7.14	15	25.86	2	9.09	1	7.14
Normal	6	42.86	22	37.93	8	36.36	10	71.43
Overweight	7	50.00	16	27.57	5	22.73	2	14.29
Obese	0	0.00	5	8.62	7	31.82	1	7.14
Medication History								
Glucocorticoids	10	71.43	58	100.00	15	68.18	14	100.00
DMARDs	14	100.00	20	34.48	16	72.72	4	28.57
Calcium	14	100.00	56	96.55	17	77.27	12	85.71
Vitamin D	3	21.43	13	22.41	4	18.18	6	42.86
Smoking								
Yes	0	0.00	1	1.72	4	18.18	0	0.00
No	14	100.00	57	98.28	18	81.82	14	100.00
Alcohol								
Yes	0	0.00	1	1.72	0	0.00	0	0.00
No	14	100.00	57	98.28	22	100.00	14	100.00
History of Fracture								
Yes	1	7.14	1	1.72	6	27.27	1	7.14
No	13	92.86	57	98.28	16	72.73	13	92.86

Variable	RA (n=14)	%	SLE (n=58)	%	SpA (n=22)	%	Others (n=14)	%
Parental History of Fracture								
Yes	0	0.00	0	0.00	0	0.00	0	0.00
No	14	100.00	58	100.00	22	100.00	14	100.00
Comorbidities								
Diabetes Mellitus	3	21.43	1	1.72	4	18.18	1	7.14
Hyperthyroidism	0	0.00	2	3.45	2	9.09	1	7.14
Malabsorption/ Malnutrition	3	21.43	17	29.31	3	13.64	1	7.14
Liver Disease	0	0.00	3	5.17	1	4.55	1	7.14
Kidney Disease	0	0.00	32	55.17	2	9.09	0	0.00
Others	2	14.29	19	32.56	9	40.91	6	42.86

Based on Table 7, the majority of patients received methylprednisolone at a dose of 4 mg/day (81.14% in the normal BMD group and 71.30% in the low BMD group), indicating that low to moderate glucocorticoid doses were commonly prescribed. Among disease-modifying antirheumatic drug (DMARD) users, methotrexate at 10–12.5 mg/week was the most frequently used regimen, while cyclosporine and azathioprine were less commonly administered. Most patients also received calcium supplementation (500 mg/day in 82.86%) and vitamin D (1000 IU/day in 20.57%), reflecting standard preventive measures aimed at maintaining bone health during long-term therapy.

TABLE 7: Daily Dosage of Medications.

Medication Regimen (Dosage)	N	Nomal BMD (n=175)		Low BMD (n=108)	
		n	%	n	%
Glucocorticoids	269				
Methylprednisolone					
1 x 2 mg/day	12	6	3.43	6	5.56
1 x 4 mg/day	219	142	81.14	77	71.30
1 x 6 g/day	4	4	2.29	0	0.00
1 x 8 mg/day	23	15	8.57	8	7.41
1 x 10 mg/day	1	0	0.00	1	0.93
2 x 16 mg/day	1	1	0.57	0	0
3 x 16 mg/day	3	1	0.57	2	1.86
Prednisolone					
1 x 5 mg/day	5	3	1.71	2	1.86
3 x 5 mg/day	1	1	0.57	0	0.00
DMARDs	148				
Methotrexate					
1 x 5 mg/week	2	2	1.14	0	0.00
1 x 7.5 mg/week	2	0	0.00	2	1.86
1 x 10 mg/week	16	11	6.29	5	4.63
1 x 12.5 mg/week	19	11	6.29	8	7.41
1 x 15 mg/week	1	0	0.00	1	0.93
1 x 22.5 mg/week	1	0	0.00	1	0.93
Cyclosporine					
1 x 25 mg/day	8	5	2.83	3	2.78
1 x 50 mg/day	4	0	0.00	4	3.70
2 x 25 mg/day	21	16	9.14	5	4.63
2 x 50 mg/day	15	12	6.86	3	2.78
Azathioprine					
1 x 25 mg/day	3	2	1.14	1	0.93
1 x 50 m1g/day	8	6	3.43	2	1.86
2 x 25 mg/day	10	9	5.14	1	0.93
2 x 50 mg/day	21	11	6.29	10	9.26
Sulfasalazine					
1 x 500 mg/day	1	0	0.00	1	0.93
2 x 500 mg/day	5	2	1.14	3	2.78
3 x 500 mg/day	1	1	0.57	0	0.00
2 x 1000 mg/day	2	1	0.57	1	0.93

Medication Regimen (Dosage)	N	Nomal BMD (n=175)		Low BMD (n=108)	
		n	%	n	%
Leflunomide					
1 x 20 mg/day	8	6	3.43	2	1.86
Calcium					
1 x 500 mg/day	226	145	82.86	81	75.00
2 x 500 mg/day	33	14	8.00	19	17.59
3 x 500 mg/day	5	2	1.14	3	2.78
Vitamin D					
1 x 400 IU/day	1	1	0.57	0	0.00
1 x 1000 IU/day	61	36	20.57	25	23.15
1 x 2000 IU/day	1	1	0.57	0	0.00
1 x 5000 IU/day	1	0	0.00	1	0.93

Based on Table 8, most patients (91.52%) received a cumulative glucocorticoid dose of less than 5 g per year, with 35.91% of them exhibiting low BMD. In contrast, patients receiving ≥5 g/year demonstrated a higher proportion of low BMD (40%), suggesting a potential dose-dependent effect of long-term glucocorticoid exposure on bone mineral density.

TABLE 8: Annual Cumulative Glucocorticoid Doses.

Category	n	Normal BMD	%	Low BMD	%
≥ 5 g/year	10	6	60.00	4	40.00
< 5 g/year	259	166	64.09	93	35.91

Based on Table 9, the distribution of total cumulative glucocorticoid doses among patients with autoimmune rheumatic diseases (ARDs) at Dr. Soetomo General Academic Hospital showed that the mean ± SD in patients with low bone mineral density (BMD) was 11.84 ± 9.67 g. Patients with a total cumulative glucocorticoid dose exceeding 18.25 g had the highest proportion of low BMD (58.7%), compared to 27.42% and 32.92% in the lower dose groups. These finding indicates a strong association between higher cumulative glucocorticoid exposure and reduced bone mineral density among patients with ARDs.

TABLE 9: Total Cumulative Glucocorticoid Doses.

Category	n	Normal BMD	%	Low BMD	%
≤ 3.65 g	62	45	72.58	17	27.42
> 3.65 g and ≤ 18.25 g	161	108	67.08	53	32.92
> 18.25 g	46	19	41.30	27	58.70

Based on Table 10, patients receiving high-dose glucocorticoid therapy (≥5 g/year and ≥30 mg/day) exhibited a higher proportion of low BMD (44.44%) compared to those on lower daily doses (34.00%). These findings suggests that prolonged exposure to high-dose glucocorticoids contributes to an increased risk of bone mineral density reduction.

TABLE 10: History of High Daily and Cumulative Glucocorticoid Doses.

Category	n	Normal BMD	%	Low BMD	%
≥ 5 g/year and ≥ 30 mg/day	9	5	55.56	4	44.44
≥ 30 mg/day	50	33	66.00	17	34.00

DISCUSSION

Distribution of Bone Mineral Density (BMD)

Among 283 patients with autoimmune rheumatic diseases (ARDs), including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), spondyloarthritis (SpA), and other ARDs such as systemic sclerosis (SSc) and Sjögren's syndrome, bone mineral density (BMD) measurements using DXA were performed at the lumbar vertebrae (n=280), right femoral neck (n=278), left femoral neck (n=279), and radius (n=196). This pattern aligns with the findings of Themeli et al. (2021), which reported that lumbar vertebrae are the most commonly assessed region in DXA measurements, followed by the femoral neck and the radius [17]. The lumbar vertebrae are typically selected as the primary site due to their high proportion of metabolically active trabecular bone, making them particularly sensitive to disease-related and treatment-induced bone changes [18].

The femoral neck and total hip regions are standard sites for evaluating fracture risk, especially in elderly populations, whereas the radius serves as an alternative site when central measurement is not feasible, such as in cases of vertebral fracture, spinal surgery, or hip arthroplasty [18,19].

The mean lumbar BMD in this study was 1.000 ± 0.171 g/cm^2, indicating relatively low variability. The right femoral neck showed a mean BMD of 0.802 ± 0.144 g/cm^2, while the left femoral neck demonstrated a comparable mean of 0.798 ± 0.141 g/cm^2. The radius exhibited the lowest mean BMD (0.739 ± 0.120 g/cm^2), suggesting greater susceptibility to bone loss at peripheral skeletal sites. These findings are consistent with Cvijetić et al. (2011), who reported mean BMD values of 1.088 ± 0.186 g/cm^2 (lumbar spine), 0.887 ± 0.124 g/cm^2 (femur), and 0.618 ± 0.108 g/cm^2 (radius) among ARD patients [20]. Although the absolute values differ slightly, the distribution pattern remains consistent, with the lumbar spine exhibiting the highest BMD and the radius the lowest. These differences may be attributed to variations in population characteristics, disease type, or disease severity.

The higher lumbar BMD is likely due to the predominance of trabecular bone, which undergoes faster turnover and is more responsive to metabolic and hormonal influences, including estrogen. In contrast, long-term glucocorticoid exposure in ARD patients primarily affects trabecular bone but can progressively lead to cortical bone thinning, explaining the lower BMD observed at the radius [21,22]. The similarity between right and left femoral BMD values (0.802 ± 0.144 g/cm^2 vs. 0.798 ± 0.141 g/cm^2) indicates bilateral symmetry, consistent with Kim et al. (2023), who found no significant inter-side differences in individuals without unilateral orthopedic history [23]. Importantly, femoral neck BMD remains a key predictor of hip fracture risk, a major complication of osteoporosis [24].

Nevertheless, interpretation of lumbar BMD requires caution due to possible overestimation caused by degenerative changes such as osteophytes, ligament calcification, or scoliosis [25]. Technical factors, including DXA calibration, patient positioning, and interoperator variability, may also influence measurement accuracy. Inadequate calibration can introduce systematic bias, particularly when DXA devices are used long-term without regular standardization [26].

DXA Test Results in Patients Aged <50 Years Using Z-Score.

The bone densitometry (DXA) assessment using Z-scores among autoimmune rheumatic disease (ARDs) patients aged below 50 years in this study demonstrated that the majority of patients had normal BMD (78.73%), while the remaining 21.27% had BMD values below the age-matched average. The age group of 21–30 years exhibited the highest proportion of patients with normal BMD (31.67%), whereas those aged 41–49 years had the highest proportion of patients with low or below the expected range of BMD (8.14%). This distribution indicates that although most patients under 50 years maintain normal bone density, a notable proportion already shows reduced BMD, particularly among individuals approaching 50 years of age. These findings suggest that bone loss may begin relatively early in patients with ARDs.

This observation aligns with the study by Hu et al. (2020), which reported that among patients with RA, SLE, and SSc, the percentages of patients with normal BMD were 77.6%, 60.4%, and 64.3%, respectively, while those with below average BMD were 22.4%, 39.6%, and 35.7%. Although specific age data were not detailed, these findings indicate that a considerable proportion of ARD patients experience decreased BMD even at a younger age, with variability depending on the specific autoimmune condition [27]. Supporting evidence from Khiabani et al. (2023) also demonstrated that younger SLE patients, particularly those with active disease and prolonged glucocorticoid exposure, showed significantly lower BMD compared to healthy controls, even before menopause [28].

The use of Z-score for patients under 50 years old carries several important limitations. The Z-score compares an individual's BMD to the average value of an age- and sex-matched reference population but does not directly assess fracture risk, unlike the T-score [29,30]. In children and young adults, bone size and growth status significantly influence BMD measurements, and without appropriate adjustments for height or skeletal maturity, the Z-score may yield inaccurate classifications [31]. Furthermore, variations in the reference population used by different DXA machines may affect the interpretation of Z-scores, particularly when reference data do not accurately represent local population characteristics. This limitation can result in underestimation or overestimation of a patient's true bone density status [32].

DXA Test Results in Patients Aged ≥50 Years Using T-Score

The bone densitometry (DXA) assessment using T-scores among autoimmune rheumatic disease (ARDs) patients aged ≥50 years at Dr. Soetomo General Academic Hospital demonstrated a varied distribution. Only one patient (1.61%) presented with normal bone density, while 17 patients (27.42%) were classified as osteopenic, 36 patients (58.06%) as osteoporotic, and 8 patients (12.90%) as having severe osteoporosis. The most common fracture site was the vertebrae (6 patients), followed by the symphysis pubis (1 patient), femur (1 patient), humerus (1 patient), and wrist (1 patient).

These findings are consistent with the study by Hu et al. (2020), which reported that in patients with RA, SLE, and SSc, the proportions of normal BMD

were 3.8%, 7.0%, and 5.1%, respectively; osteopenia was observed in 34.1%, 37.0%, and 35.9%; and osteoporosis in 56.1%, 47.0%, and 56.4%. Severe osteoporosis was reported in 6.0%, 9.0%, and 2.6% of patients, respectively [33]. Although the proportions vary, these results consistently indicate a high prevalence of osteopenia and osteoporosis among autoimmune rheumatic disease patients aged ≥50 years.

Supporting evidence from Hu et al. (2021) demonstrated that RA patients have nearly twice the risk of osteoporosis compared to the general population, with risk increasing with age [33]. Similarly, Zhu et al. (2014) found that female SLE patients, with a mean age of 46.5 years, showed significant BMD reduction, particularly at the femoral neck and total hip, especially in those with a history of active disease or long-term glucocorticoid use [34]. The highest proportion of osteoporosis was observed in patients aged 50–55 years, suggesting that substantial bone loss occurs early in the elderly phase.

Among the eight patients with severe osteoporosis, vertebral fractures predominated (six cases), followed by fractures at the symphysis pubis, femur, humerus, and wrist (one case each). The predominance of vertebral fractures aligns with epidemiological evidence showing that vertebral fractures are the most common osteoporotic fractures globally, accounting for nearly half of all cases [35]. These fractures frequently occur in elderly women and are associated with increased morbidity, mortality, and healthcare burden. The vertebrae are highly susceptible to osteoporotic fractures due to their trabecular composition, which is metabolically active and prone to rapid bone loss, combined with substantial mechanical loading during weight bearing. Furthermore, vertebral fractures often remain asymptomatic or present with mild back pain, leading to delayed diagnosis and progressive structural deterioration, which increases the risk of subsequent fractures [36,37].

Despite its diagnostic utility, the T-score has limitations. It assesses bone density only at specific anatomical sites (typically the femoral neck) and does not account for non-BMD factors such as bone microarchitecture, cortical thickness, medication effects (e.g., glucocorticoids), or fracture history that contribute to bone fragility [38]. Moreover, variations in ethnicity, sex, and body mass may affect T-score interpretation, particularly when reference data are not representative of the local population [39].

Demographic Characteristics

Age is a nonmodifiable risk factor for bone mineral density (BMD) reduction in the general population, and this risk is further amplified in patients with autoimmune rheumatic diseases (ARDs) [40]. In the present study, among 283 patients with ARDs, including SLE, RA, SpA, SSc, and Sjögren's syndrome, most were aged <50 years (n = 221; 78.09%), of whom 174 patients (99.43%) had normal BMD values. Conversely, among 62 patients aged ≥50 years (21.91%), only one (0.57%) had normal BMD, whereas the remaining 61 (56.48%) exhibited reduced bone density. These findings are consistent with previous studies. Xia et al. (2019) reported a 45% prevalence of low BMD among postmenopausal autoimmune patients, and Zhang et al. (2020) found that 41.1% of male patients aged ≥50 years and 50.8% of postmenopausal women had lumbar spine osteoporosis [41,42].

Female patients predominated in this cohort (95.76%). Among those with normal BMD, 97.14% were female, while in the low BMD group, 93.52% were female. Although men constituted only 4.24% of all patients, the proportion of males with reduced BMD was slightly higher. This finding aligns with the known female predominance in ARDs such as SLE and Sjögren's syndrome, where the female-to-male rasio is approximately 9:1. RA is also more common in women, who are two to three times more susceptible than men [43]. Women also exhibited lower mean bone density (T-score: −2.33 ± 1.14 vs. −1.31 ± 1.55; $p < 0.001$), likely due to smaller bone size, lower bone mass reserves, and accelerated bone resorption resulting from decreased estrogen levels postmenopause, as estrogen plays a key role in inhibiting osteoclast activity [44].

Education level also appeared to influence BMD outcomes. Among patients with reduced BMD (n=108), most fell under the "other" category (88.9%), likely representing those with non-formal education or unrecorded data. Only a small proportion had formal education: high school (5.56%), higher education (2.78%), and middle or primary school (0.93% each). In contrast, among those with normal BMD (n=175), 14.28% completed high school and 2.86% held higher education degrees. This pattern suggests an association between low education levels and increased BMD reduction risk, as individuals with lower education often have limited access to health information, including nutritional awareness related to calcium and vitamin D intake [45]. Zhang et al. (2023) similarly reported that lower socioeconomic and educational status correlates with poorer nutritional and bone health [46].

Occupational data showed that most patients with reduced BMD were housewives (47.22%), followed by private employees (19.44%) and students (11.11%). This finding is consistent with the study by Din and Hashmi (2020), who reported that 46.5% of osteoporosis patients were housewives [47]. The high prevalence in these groups may be attributed to low physical activity levels, limited sunlight exposure, chronic stress, and suboptimal dietary patterns, all of which contribute to bone mass loss [48]. Furthermore, hormonal factors, particularly estrogen decline during menopause, accelerate bone resorption and inhibit bone formation, thereby significantly reducing bone mass and increasing osteoporosis risk among women [49].

Clinical Characteristics

Among patients with normal bone mineral density (BMD) (n=175), the majority were diagnosed with SLE (84.57%), followed by SpA (7.43%), RA (4.57%), and other ARDs (SSc/Sjögren's syndrome) (3.43%). In contrast, among patients with reduced BMD (n=108), the distribution was more balanced, with SLE accounting for 53.70%, SpA 20.37%, RA 12.96%, and SSc/Sjögren's syndrome 12.96%. These findings differ from those of Hu et al. (2020), who reported that 77.6% of RA, 60.4% of SLE, 64.3% of SSc, and 46.1% of AS patients had normal BMD, while 22.4%, 39.6%, 35.7%, and 53.9% respectively, showed reduced BMD [27]. The variation arises from methodological differences; this study categorized patients based on BMD status before identifying disease distribution, while Hu et al. (2020) analyzed each disease separately by BMD status. Additionally, differences in sample size, age, disease duration, glucocorticoid use, and BMI likely contributed to the discrepancy. Gilboe et al. (2000) reported that BMD in SLE patients is strongly influenced by corticosteroid exposure and chronic organ damage related to disease duration and activity [50].

A study conducted in Mumbai demonstrated a significant decrease in spinal, femoral, and hip BMD with longer RA duration ($p < 0.05$) [51]. Similarly, in the present study, 55.56% of patients with reduced BMD had been diagnosed for more than five years. Disease-related factors such as elevated serum tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-1 (IL-1) promote bone resorption and inhibit bone formation [41].

Regarding body mass index (BMI), most patients with normal BMD (45.14%) and those with reduced BMD (42.59%) had a normal BMI, followed by overweight (27.78%), underweight (17.59%), and obese (12.04%) categories. These findings differ from El-Sherbiny et al. (2021), who reported that obesity and overweight were more prevalent among SLE patients and were associated with higher osteoporosis and osteopenia rates compared to those with normal BMI (osteoporosis: 35.2%, 22.2%, and 20.0%; osteopenia: 35.2%, 38.9%, and 16.7%, respectively) [52]. Similarly, Baba et al. (2023) found that in RA patients, 21.9% were obese, 31.5% overweight, and 2.3% underweight, with osteoporosis observed in 38.4%, showing a negative correlation between BMI and osteoporosis risk [53]. These discrepancies may stem from ethnic and racial variations, as body composition, fat distribution, and metabolism factors differ among populations, influencing osteoporosis risk [54].

Glucocorticoids (GCs), which are frequently prescribed for RA, SLE, SpA, and SSc, are well known to reduce bone density and increase fracture risk, particularly in trabecular bone, when used long term [55]. Shinoda and Taki (2021) reported that 63.8% of autoimmune patients continued GC therapy, with the risk of osteoporosis increasing in proportion to cumulative dose and treatment duration [56].

In contrast, in the present study, 95.05% (269 patients) had a history of GC use, and among those with reduced BMD, 89.81% (97 patients) were GC users. This discrepancy may be explained by differences in disease severity, treatment adherence, or sample characteristics.

Traditional DMARDs, such as methotrexate, sulfasalazine, and hydroxychloroquine, have been shown to exert protective effects on BMD by reducing systemic inflammation. Biologic DMARDs, including TNF inhibitors, IL-6 inhibitors, abatacept, and rituximab, demonstrate variable impacts on BMD preservation, which may depend on factors such as vitamin D status and disease control [55]. In this study, 50% of patients with low BMD and 50.29% with normal BMD were receiving DMARDs therapy. This suggests that, although DMARDs are effective in suppressing inflammation, they do not necessarily prevent bone loss in all patients.

Adami et al. (2019) reported that approximately 45% of patients with ARDs, particularly those with RA, received both calcium and vitamin D supplementation [55]. In contrast, vitamin D use in this study was low, only 24.07% among those with reduced BMD, indicating limited awareness or suboptimal implementation of supplementation strategies. Calcium supplementation, however, was more prevalent, with 91.6% of all patients and 95.37% of those with reduced BMD reporting regular calcium intake. A previous study in SLE patients demonstrated that six months of combined calcium and vitamin D supplementation led to improvements in bone density, although it did not significantly affect disease activity [57].

Smoking negatively impacts bone metabolism by suppressing osteoblast differentiation and enhancing osteoclast activity, resulting in decreased BMD and increased risk of osteoporosis and mortality [58]. Among patients with reduced BMD (n = 108), 3.7% had a history of smoking, compared with 1.71% among those with normal BMD. These findings align with Hafez et al. (2011), who reported that 33.3% of RA patients with osteoporosis were smokers versus 8.3% without osteoporosis ($p = 0.2$), suggesting no statistically significant causal relationship between smoking and osteoporosis risk [59].

Chronic alcohol consumption disrupts bone homeostasis by enhancing osteoclastic activity and suppressing osteoblastic function, contributing to lower BMD and increased fracture risk [60]. In this study, none of the patients with normal BMD consumed alcohol, while only one (0.93%) of those with reduced BMD reported alcohol use. This finding is consistent with Khiyali et al. (2024), who noted that alcohol consumption was more common in osteoporotic patients, though at very low rates, likely due to religious and cultural restrictions in Indonesia [61].

Of the 108 patients with reduced BMD, 10 (9.26%) had a history of fractures, compared with only one

(0.57%) in the normal BMD group. This confirms the well-established pathophysiological association between BMD loss and fragility fractures [62]. Similar findings were reported in Korea, where 19 of 127 SLE patients with osteoporosis had fractures, and in RA patients, 16.9% had osteoporotic fractures [63,64].

Parental fracture history is a recognized independent risk factor for osteoporosis and fragility fractures [65]. In this study, no patients, regardless of BMD status, reported a parental history of fractures (0%), differing from Kuru et al. (2015), who found that 12.5% of parents of osteoporotic patients had hip fractures [66]. This discrepancy may reflect incomplete family history data or recall bias.

Comorbidities associated with secondary osteoporosis were also prevalent among patients with low BMD. The most frequent were hypertension and cardiovascular diseases (36.11%), followed by renal disorders (31.48%), malnutrition or malabsorption (24.07%), diabetes (8.33%), liver disease (5.56%), and hyperthyroidism (0.93%). These findings are consistent with Zhang et al. (2020), who reported that RA patients with low BMD frequently had hypertension (21.9%), diabetes (8.9%), and hyperthyroidism (2.3%) [42]. Mir et al. (2017) further noted that 31.6% of CKD patients had osteoporosis [67]. The Indonesian Rheumatology Association (2020) also emphasized that chronic kidney disease is a common comorbidity in rheumatic patients and significantly increases osteoporosis risk [68]. Routine renal monitoring is therefore recommended in managing rheumatic patients at risk of osteoporosis.

Characteristics in Patients with ARD Experiencing Reduced Bone Mineral Density (BMD)

In this study, the majority of rheumatoid arthritis (RA) patients with reduced bone mineral density (BMD) were aged ≥50 years (78.57%), and all were female. Most had an overweight body mass index (BMI) (50%) and a disease duration exceeding five years (50%). All patients received disease-modifying antirheumatic drugs (DMARDs) and calcium supplementation, while glucocorticoid use was observed in 71.43% of patients. A history of fracture, alcohol consumption, smoking, and comorbidities contributing to osteoporosis was found in a small proportion of cases. Uysal et al. (2025) reported that the combination of DMARDs and glucocorticoids leads to greater BMD loss [69]. Conversely, Ketabforoush et al. (2023) demonstrated that RA patients are at risk of developing osteoporosis regardless of glucocorticoid or DMARD use. Demographic factors (e.g., older age and female sex) and disease-related parameters (such as DAS-28 and positive CRP levels) were associated with BMD reduction [70]. Studies investigating the impact of obesity on RA outcomes noted that overweight and obese BMI categories influence treatment persistence and inflammatory processes [71]. These findings align with the present study, in which many RA patients with low BMD were overweight.

Among patients with systemic lupus erythematosus (SLE) who exhibited decreased BMD, most were aged <50 years (63.79%) and female (96.55%). The majority had a normal BMI (37.93%) and a disease duration exceeding five years (68.97%). All patients received glucocorticoids, nearly all were supplemented with calcium (96.55%), and a minority also received vitamin D. The most common secondary osteoporosis risk factors were renal disease (55%) and malnutrition or malabsorption (29.31%). These findings are consistent with the study by Zhou and Chai (2025), which indicated that younger age and the presence of comorbidities are significant risk factors for osteonecrosis in SLE patients [72]. Xu and Wu (2024) further stated that SLE increases osteoporosis risk through direct effects on bone metabolism and remodeling, ultimately leading to reduced bone mass [73]. Another contributing mechanism involves corticosteroid therapy, which negatively affects bone balance. In addition, renal involvement in SLE can induce secondary hyperparathyroidism, enhance osteoclastic bone resorption, and decrease the synthesis of $1,25(OH)_2D$, all of which contribute to bone loss. Limited physical activity and reduced sunlight exposure in SLE patients further exacerbate BMD reduction [73].

In the spondyloarthritis (SpA) group with low BMD, most patients were aged ≥50 years (90.91%), with a higher proportion of males (22.73%) compared to other rheumatic diseases. The most common BMI categories were normal (36.36%) and obese (31.82%), with disease duration exceeding five years in 45.45% of patients. Most patients received glucocorticoids, DMARDs, and calcium therapy. A history of fractures was most frequently observed in this group (27.27%), along with comorbid diabetes and hyperthyroidism in some cases. Several studies have shown that male SpA patients generally experience faster radiological progression and more severe spinal damage than females. Moreover, men with SpA have a higher risk of low BMD and osteoporosis, particularly at younger ages or in the early disease stages, with reports indicating up to a fourfold greater risk of low BMD compared to women [74,75]. Ceolin et al. (2025) similarly reported that glucocorticoids, DMARDs, and calcium are the most commonly prescribed therapies in SpA patients, emphasizing the high proportion of individuals with fracture history and comorbidities such as diabetes and hyperthyroidism [76].

Among patients in the “other” category (systemic sclerosis and Sjögren’s syndrome) who presented with reduced BMD, most were aged ≥50 years (64.29%), and all were female. The majority had a normal BMI (71.43%) and a disease duration of 3–5 years (57.14%). All patients were treated with glucocorticoids, and most received calcium supplementation. Secondary risk factors identified included diabetes mellitus, hyperthyroidism, and liver disease, each with a low proportion. According to Both et al. (2016), most primary Sjögren’s syndrome patients are female and aged over 50 years, exhibiting variable BMD results [77].

Shi et al. (2025) noted that Sjögren's syndrome patients have an increased risk of osteoporosis due to chronic inflammation, glucocorticoid therapy, and vitamin D deficiency [78]. Regarding systemic sclerosis, previous studies have demonstrated a high prevalence of low BMD and osteoporosis, particularly among postmenopausal women, with many patients showing vitamin D deficiency and comorbidities such as diabetes, hyperthyroidism, and liver disease, which contribute to secondary osteoporosis risk [79,80].

Daily Dosage of Medications

Based on Table 2, In this study, the most frequently used methylprednisolone regimen was 4 mg once daily, prescribed to 142 patients with normal BMD (81.14% of users) and 77 patients with low BMD (71.30%). The 8 mg once-daily regimen was used by 15 patients with normal BMD (8.57%) and 8 with low BMD (7.41%). Other regimens of 2 mg, 5 mg, 6 mg, and 10 mg monotherapy provide inadequate protection and should be complemented with vitamin D or antiresorptive therapy. They were used by only one patient with normal BMD and none with low BMD.

Glucocorticoids contribute to bone mineral density (BMD) loss by inhibiting osteoblast activity, stimulating osteoclast function, reducing intestinal calcium absorption, and increasing renal calcium excretion. These mechanisms promote osteoporosis and fracture risk, particularly at doses ≥ 2.5–7.5 mg prednisone equivalent daily for ≥ 3 months [81,82]. American College of Rheumatology (ACR) guidelines (2022/2023) recommend osteoporosis risk assessment and prophylactic calcium, vitamin D, and/or antiresorptive therapy for long-term users. Findings from this study align with these recommendations, as BMD reduction occurred across various regimens, including the most common low dose (4 mg/day). Although a dose-response relationship could not be established, the pattern supports evidence that chronic glucocorticoid exposure, even at low doses, can induce bone loss [21,83].

Methotrexate (MTX) 10 mg weekly was used by 11 patients with normal BMD (6.29%) and 5 with low BMD (4.63%), while the 12.5 mg weekly regimen was prescribed to 11 patients with normal BMD (6.29%) and 8 with low BMD (7.41%). Other dosages were less frequent. Low to moderate MTX doses (7.5–25 mg/week) are generally considered safe for bone, with most studies reporting neutral or protective effects when disease activity is well controlled [84,85]. In this study, similar proportions of normal and low BMD among MTX users suggest that bone loss may be influenced by other factors, such as glucocorticoid exposure, disease activity, aging, or vitamin D deficiency [86].

Cyclosporine 25 mg twice daily was prescribed to 16 patients with normal BMD (9.14%) and 5 with low BMD (4.63%), while 50 mg twice daily was used by 12 and 3 patients, respectively.

Typical doses for rheumatic diseases range from 2.5 to 5 mg/kg/day, whereas higher doses (> 5 mg/kg/day) used in transplant patients are linked to bone loss and fracture risk [87]. At lower rheumatologic doses, findings are inconsistent. Experimental studies still suggest potential adverse skeletal effects, though clinical relevance remains uncertain [88]. The current findings are consistent with literature, as most cyclosporine users maintained normal BMD.

Azathioprine 50 mg twice daily was used by 11 patients with normal BMD (6.29%) and 10 with low BMD (9.26%). Evidence on its skeletal impact remains mixed; while some studies report no adverse effects and even steroid-sparing benefits in chronic inflammatory disease, others suggest an increased fracture risk [89,90].

Sulfasalazine 500 mg twice daily was used by 2 patients with normal BMD (1.14%) and 3 with low BMD (2.78%). Data on sulfasalazine's impact on bone are limited. One study in men with rheumatoid arthritis found an association with lower BMD, although causality is uncertain and likely reflects more severe disease. Other research found no significant link with fracture risk [91,92].

Leflunomide was prescribed to 8 patients, 6 with normal BMD (3.43%) and 2 with low BMD (1.86%). Prior studies in rheumatoid arthritis suggest leflunomide has a neutral or even beneficial effect on BMD, particularly in osteoporotic patients [93]. These results are consistent with this study, where most leflunomide users had normal BMD, though the sample size was small.

Calcium supplementation ranged from 500 to 1500 mg/day, with 500 mg once daily being most common, used by 82.86% of patients with normal BMD and 75.00% with low BMD. The twice-daily regimen was used by 8.00% and 17.59%, and the thrice-daily regimen by 1.14% and 2.78%, respectively. Vitamin D doses varied between 400–5000 IU/day, with 1000 IU daily being most frequent (20.57% in normal BMD, 23.15% in low BMD). Literature supports combined calcium and vitamin D supplementation for glucocorticoid users to prevent bone loss [81,94]. However, calcium alone is often insufficient for patients at moderate to high risk, such as those on chronic steroids or with systemic inflammation [21,95]. Consistent with this, a substantial proportion of patients in this study experienced BMD loss despite calcium intake, indicating that calcium monotherapy provides inadequate protection and should be complemented with vitamin D or antiresorptive therapy to optimize bone health.

Annual Cumulative Glucocorticoid Doses

The cumulative annual dose represents the total glucocorticoid exposure per year throughout the treatment duration, calculated from the time of diagnosis until data collection. In this study, ten patients received a cumulative dose of ≥5 g/year,

consisting of six patients (60%) with normal bone mineral density (BMD) and four patients with reduced BMD. Among those with a cumulative dose of <5 g/year, 64.4% exhibited normal BMD. These findings indicate a trend toward lower BMD in patients with higher cumulative doses; however, a considerable proportion maintained normal bone density, suggesting that factors beyond cumulative dose also contribute to BMD status.

This result aligns with the findings of Ilias et al. (2022), who reported a dose-response relationship between long term glucocorticoid use and BMD reduction, although not all high-dose users develop osteoporosis due to protective factors such as younger age, hormonal status, calcium and vitamin D supplementation, and antiresorptive therapy [96]. This observation is consistent with the theory of glucocorticoid-induced osteoporosis (GIOP), which posits that osteoporosis risk significantly increases with daily prednisone doses ≥5 mg for over three months, particularly when the cumulative dose exceeds 2.5 to 7.5 g per year [21,97]. The underlying mechanisms include enhanced bone resorption via osteoclast activation, decreased bone formation through osteoblast inhibition, and reduced intestinal calcium absorption [21].

Total Cumulative Glucocorticoid Doses

The total cumulative dose refers to the overall amount of glucocorticoids administered throughout the treatment period, from diagnosis until data collection. In this study, the mean total cumulative glucocorticoid dose among patients with reduced bone mineral density (BMD) was 11.84 grams, which is lower than that reported by Phang et al. (2018), who found an average cumulative dose of 18.6 grams [98]. The discrepancy may be attributed to differences in disease duration, glucocorticoid administration patterns (intermittent high dose versus chronic low dose), and population characteristics. Nevertheless, patients with cumulative doses exceeding 18.25 grams were more likely to exhibit low BMD (58.7%) compared to those with normal BMD (41.3%). These findings support the cumulative dose-response relationship between glucocorticoid exposure and bone loss, where higher cumulative exposure (≥18.25 g, as categorized in the Hopkins cohort) is associated with a greater prevalence of low BMD [99].

History of High Daily and Cumulative Glucocorticoid Doses

In this study, among patients receiving glucocorticoid doses of ≥5 g/year and ≥30 mg/day, 5 patients (55.56%) had normal BMD, while 4 patients (44.44%) showed reduced BMD. In those receiving ≥30 mg/day alone, 33 patients (66%) had normal BMD and 17 patients (34%) had low BMD. These findings align with previous evidence indicating that long-term high-dose glucocorticoid therapy (≥5 g/year), particularly at daily doses ≥30 mg prednisone equivalent, significantly increases the risk of osteoporosis and fractures [100]. De Vries et al. (2006) reported that oral glucocorticoid use of ≥30 mg/day and a cumulative dose of >5 g/year increased the risk of osteoporotic fractures (RR 3.63) and vertebral fractures (RR 14.42) [100]. The relatively high proportion of patients with normal BMD in this study may be attributed to variations in treatment duration, short-term exposure in some cases, or the use of prophylactic osteoporosis therapy such as calcium, vitamin D, or bisphosphonates, which can mitigate glucocorticoid-induced bone loss. Consistent with existing literature, bone loss is more strongly associated with cumulative exposure and treatment duration rather than transient high daily doses [101]. A meta-analysis by Hansen et al. (2014) further confirmed that glucocorticoid-related skeletal effects are dose-duration dependent, with longer and higher cumulative exposure leading to greater reductions in BMD [102].

CONCLUSIONS

The characteristics of bone mineral density (BMD) among 283 patients with autoimmune rheumatic diseases showed that most measurements were performed at the lumbar vertebrae, where the mean BMD values were the highest. Patients aged <50 years predominantly had normal BMD, whereas those aged ≥50 years demonstrated a markedly higher prevalence of osteopenia and osteoporosis, particularly within the 50–60 year age group. Reduced BMD was more frequent in older female patients with normal to overweight nutritional status and disease duration exceeding five years. Clinically, systemic lupus erythematosus (SLE) was the most common diagnosis among patients with low BMD, followed by spondyloarthritis (SpA) and rheumatoid arthritis (RA). Most patients received glucocorticoid and calcium therapy, while DMARD use varied. Bone loss was more pronounced in those with high cumulative glucocorticoid doses (≥5 g/year and >18.25 g total) and in patients with comorbidities such as renal disease and malnutrition. These findings highlight that advanced age, female sex, prolonged glucocorticoid exposure, and chronic disease duration are the major contributing factors to decreased bone mineral density in patients with ARDs.

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REFERENCES

[1] Arango, M.-T., Shoenfeld, Y., Cervera, R. and Anaya, J.-M., 2013. 'Infection and autoimmune diseases'. NCBI Bookshelf. Available at: https://www.ncbi.nlm.nih.gov/books/NBK459437/ (Accessed: 29 May 2024).

[2] Pisetsky, D.S., 2023. 'Pathogenesis of autoimmune disease'. Nature Reviews Nephrology, 19(8), pp. 509–524.Available at: https://doi.org/10.1038/S41581-023-00720-1.

[3] Miller, F.W., 2023. 'The increasing prevalence of autoimmunity and autoimmune diseases: an urgent call to action for improved understanding, diagnosis, treatment, and prevention'. Current Opinion in Immunology, 80, p. 102266. Available at: https://doi.org/10.1016/J.COI.2022.102266.

[4] Wen, X. and Li, B., 2023. 'A population-based study on autoimmune disease'. The Lancet, 401(10391), pp. 1829–1831. Available at: https://doi.org/10.1016/S0140-6736(23)00621-9.

[5] Iranzo, A., 2020. 'Sleep and neurological autoimmune diseases'. Neuropsychopharmacology, 45(1), p. 129. Available at: https://doi.org/10.1038/S41386-019-0463-Z.

[6] Jacobson, D.L., Gange, S.J., Rose, N.R. and Graham, N.M.H., 1997. 'Epidemiology and estimated population burden of selected autoimmune diseases in the United States'. Clinical Immunology and Immunopathology, 84(3), pp. 223–243. Available at: https://doi.org/10.1006/CLIN.1997.4412.

[7] Kim, J.W. and Suh, C.H., 2020. 'Systemic manifestations and complications in patients with rheumatoid arthritis'. Journal of Clinical Medicine, 9(6), pp. 1–5. Available at: https://doi.org/10.3390/JCM9062008.

[8] Walsh, J.A. and Magrey, M., 2021. 'Clinical manifestations and diagnosis of axial spondyloarthritis'. Journal of Clinical Rheumatology: Practical Reports on Rheumatic & Musculoskeletal Diseases, 27(8), pp. E547–E560. Available at: https://doi.org/10.1097/RHU.0000000000001575.

[9] Cojocaru, I., Cojocaru, M., Silosi, I. and Vrabie, C.D., 2011. 'Manifestations of systemic lupus erythematosus'. Maedica – A Journal of Clinical Medicine, 6(4), pp. 330–336.

[10] Nurudhin, A., Wibowo, S.A.K., Werdiningsih, Y., Darma, S., Rahmawati, L.D., Dewi, S., Hidayat, R. and Sumariyono, 2021. 'Rekomendasi – diagnosis dan pengelolaan spondiloartritis 2021'. Perhimpunan Reumatologi Indonesia, pp. 1–48.

[11] Chu, Y.R., Xu, Y.C., Ma, L.L., Wang, J.X., Zong, H.X., Tong, W.Q., Wang, X.L., Zhao, X. and Xu, S.Q., 2024. 'Skeletal muscle index together with body mass index is associated with secondary osteoporosis in patients with rheumatoid arthritis'. European Journal of Medical Research, 29(1), pp. 1–10. Available at: https://doi.org/10.1186/S40001-024-01665-2/FIGURES/3.

[12] Amarasekara, D.S., Yu, J. and Rho, J., 2015. 'Bone loss triggered by the cytokine network in inflammatory autoimmune diseases'. Journal of Immunology Research, 2015. Available at: https://doi.org/10.1155/2015/832127.

[13] Hauser, B., Raterman, H., Ralston, S.H. and Lems, W.F., 2022. 'The effect of anti-rheumatic drugs on the skeleton'. Calcified Tissue International. Available at: https://doi.org/10.1007/s00223-022-01001-y.

[14] Chawla, S.S., Meena, N., Garg, R., Batta, A. and Kaur, S., 2018. 'Assessment of vitamin D in rheumatoid arthritis and its correlation with disease activity'. Journal of Natural Science, Biology and Medicine, 9(1), p. 54. Available at: https://doi.org/10.4103/jnsbm.jnsbm_128_17.

[15] Kim, C.S., Han, K.D., Jung, J.H., Choi, H.S., Bae, E.H., Ma, S.K. and Kim, S.W., 2021. 'Incidence and risk factors for osteoporotic fractures in patients with systemic lupus erythematosus versus matched controls'. Korean Journal of Internal Medicine, 36(1), pp. 154–163. Available at: https://doi.org/10.3904/kjim.2018.378.

[16] Blake, G.M. and Fogelman, I., 2007. 'The role of DXA bone density scans in the diagnosis and treatment of osteoporosis'. Postgraduate Medical Journal, 83(983), pp. 509–517. Available at: https://doi.org/10.1136/pgmj.2007.057505.

[17] Themeli, T. and Triantafyllopoulos, I.K., 2021. 'Choosing the site to estimate bone mineral density with DXA method'. Journal of Research and Practice on the Musculoskeletal System, 5(2), pp. 79–87. Available at: https://doi.org/10.22540/jrpms-05-079.

[18] Oo, W.M., Naganathan, V., Bo, M.T. and Hunter, D.J., 2018. 'Clinical utilities of quantitative ultrasound in osteoporosis associated with inflammatory rheumatic diseases'. Quantitative Imaging in Medicine and Surgery, 8(1), pp. 100–113. Available at: https://doi.org/10.21037/qims.2018.02.02.

[19] Messina, C., Maffi, G., Vitale, J.A., Ulivieri, F.M., Guglielmi, G. and Sconfienza, L.M., 2018. 'Diagnostic imaging of osteoporosis and sarcopenia: a narrative review'. Quantitative Imaging in Medicine and Surgery, 8(1), pp. 86–99. Available at: https://doi.org/10.21037/qims.2018.01.01.

[20] Cvijetić, S., Grazio, S., Gomzi, M., Krapac, L., Nemčić, T., Uremović, M. and Bobić, J., 2011. 'Muscle strength and bone density in patients with different rheumatic conditions: cross-sectional study'. Croatian Medical Journal, 52(2), pp. 164–170. Available at: https://doi.org/10.3325/cmj.2011.52.164.

[21] Compston, J., 2018. 'Glucocorticoid-induced osteoporosis: an update'. Endocrine, 61(1), pp. 7–16. Available at: https://doi.org/10.1007/s12020-018-1588-2.

[22] Hardy, R.S., Zhou, H., Seibel, M.J. and Cooper, M.S., 2018. 'Glucocorticoids and bone: consequences of endogenous and exogenous excess and replacement therapy'. EndocrineReviews, 39(5), pp. 519–548. Available at: https://doi.org/10.1210/er.2018-00097.

[23] Kim, S., Na, Y., Ko, M., Park, J.Y., Yoon, H., Song, J.-Y., Chung, Y.-J., Shin, I., Kim, C., Park, J.H. and Kim, M.-R., 2023. 'Comparison of the right and left femur bone mineral densities in postmenopausal women'. Journal of Menopausal Medicine, 29(3), pp. 112–112. Available at: https://doi.org/10.6118/jmm.23021.

[24] Li, M., Lv, H., Liu, J., Cui, X., Sun, G., Hu, J., Zhang, L. and Tang, P., 2019. 'Differences in bone mineral density and hip geometry in trochanteric and cervical hip fractures in elderly Chinese patients'. Orthopaedic Surgery, 11(2), pp. 263–269. Available at: https://doi.org/10.1111/os.12456.

[25] Icătoiu, E., Vlădulescu-Trandafir, A.-I., Groșeanu, L.-M., Berghea, F., Cobilinschi, C.-O., Potcovaru, C.-G., Bălănescu, A.-R. and Bojincă, V.-C., 2025. 'Radiofrequency echographic multi spectrometry—a novel tool in the diagnosis of osteoporosis and prediction of fragility fractures: a systematic review'. Diagnostics, 15(5), pp. 555–555. Available at: https://doi.org/10.3390/diagnostics15050555.

[26] Li, J., She, B., He, M., Yuan, C. and Li, N., 2025. 'Advances in imaging examination of bone density and bone quality'. Endokrynologia Polska, 76(1), pp. 29–39. Available at: https://doi.org/10.5603/ep.100805.

[27] Hu, Z., Xu, S., Lin, H., Ni, W., Yang, Q., Qi, J., Du, K., Gu, J. and Lin, Z., 2020. 'Prevalence and risk factors for bone loss in Southern Chinese with rheumatic diseases'. BMC Musculoskeletal Disorders, 21(1). Available at: https://doi.org/10.1186/s12891-020-03403-1.

[28] Khiabani, M.S., Sharabian, F.T., Raeeskarami, S.R. and Ziaee, V., 2023. 'Evaluation of bone mineral density in juvenile systemic lupus erythematosus'. Archives of Bone and Joint Surgery, 11(12), pp. 777–782. Available at: https://doi.org/10.22038/abjs.2023.70697.3311.

[29] Di Iorgi, N., Maruca, K., Patti, G. and Mora, S., 2018. 'Update on bone density measurements and their interpretation in children and adolescents'. Best Practice & Research Clinical Endocrinology & Metabolism, 32(4), pp. 477–498. Available at: https://doi.org/10.1016/j.beem.2018.06.002.

[30] Williams, S., Khan, L. and Licata, A.A., 2021. 'DXA and clinical challenges of fracture risk assessment in primary care'. Cleveland Clinic Journal of Medicine, 88(11), pp. 615–622. Available at: https://doi.org/10.3949/ccjm.88a.20199.

[31] Magallares, B., Malouf, J., Codes-Méndez, H., Park, H.S., Betancourt, J., Fraga, G., Quesada-Masachs, E., López-Corbeto, M., Torrent, M., Marín, A., Herrera, S., Gich, I., Boronat, S., Casademont, J., Corominas, H. and Cerdá, D., 2025. 'Pediatric densitometry: is the Z score adjustment necessary in all cases?' Frontiers in Endocrinology, 16. doi:https://doi.org/10.3389/fendo.2025.1587382.

[32] Zemel, B.S., Winer, K.K., Kelly, A., Freedman, D.S., Mitchell, J.A., Weber, D.R., McCormack, S.E., McWilliams, T., Lappe, J.M., Oberfield, S.E., Shepherd, J.A., Grant, S.F.A. and Kalkwarf, H.J., 2025. 'Race-neutral pediatric reference ranges for bone mineral density predict prospective fractures in childhood'. The Journal of Clinical Endocrinology & Metabolism, 110(11), pp.3034–3048.doi:https://doi.org/10.1210/clinem/dgaf183.

[33] Hu, Z., Zhang, L., Lin, Z., Zhao, C., Xu, S., Lin, H., Zhang, J., Li, W. and Chu, Y., 2021. 'Prevalence and risk factors for bone loss in rheumatoid arthritis patients from South China: modeled by three methods'. BMC Musculoskeletal Disorders, 22(1). doi:https://doi.org/10.1186/s12891-021-04403-5.

[34] Zhu, T.Y., Griffith, J.F., Au, S.-K., Tang, X.-L., Kwok, A.W., Leung, P.-C., Li, E.K. and Tam, L.-S., 2014. 'Bone mineral density change in systemic lupus erythematosus: a 5-year follow-up study'. The Journal of Rheumatology, 41(10), pp.1990–1997. doi:https://doi.org/10.3899/jrheum.131190.

[35] Donnally III, C.J., DiPompeo, C.M. and Varacallo, M., 2025. 'Vertebral compression fractures'. PubMed [online]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK448171/.

[36] Luo, Y., 2025. 'Hip fractures: clinical, biomaterial and biomechanical insights into a common health challenge'. Bioengineering, 12(6), p.580.doi:https://doi.org/10.3390/bioengineering12060580.

[37] Whitney, E. and Alastra, A.J., 2023. 'Vertebral fracture'. Translate.goog [online]. Available at: https://www-ncbi-nlm-nih-gov.translate.goog/books/NBK547673/?_x_tr_sl=en&_x_tr_tl=id&_x_tr_hl=id&_x_tr_pto=tc [Accessed 12 Oct. 2025].

[38] Small, R.E., 2005. 'Uses and limitations of bone mineral density measurements in the management of osteoporosis'. Medscape General Medicine, 7(2), p.3. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC1681604/.

[39] Yeap, S.S., Thambiah, S.C., Samsudin, I.N., Appannah, G., Zainuddin, N., Mohamad-Ismuddin, S., Shahifar, N., Md-Said, S., Zahari-Sham, S.Y., Suppiah, S. and Hew, F.L., 2020. 'Different reference ranges affect the prevalence of osteoporosis and osteopenia in an urban adult Malaysian population'. Osteoporosis and Sarcopenia, 6(4), pp.168–172. doi:https://doi.org/10.1016/j.afos.2020.11.005.

[40] Chandrashekara, S., 2023. 'Osteoporosis in rheumatology'. Indian Journal of Orthopaedics, 57(S1), pp.176–180. doi:https://doi.org/10.1007/s43465-023-01024-z.

[41] Xia, J., Luo, R., Guo, S., Yang, Y., Ge, S., Xu, G. and Zeng, R., 2019. 'Prevalence and risk factors of reduced bone mineral density in systemic lupus erythematosus patients: a meta-analysis'. BioMed Research International, 2019, pp.1–10. doi:https://doi.org/10.1155/2019/3731648.

[42] Zhang, X., Dai, Z., Lau, E.H.Y., Cui, C., Lin, H., Qi, J., Ni, W., Zhao, L., Lv, Q., Gu, J. and Lin, Z., 2020. 'Prevalence of bone mineral density loss and potential risk factors for osteopenia and osteoporosis in rheumatic patients in China: logistic regression and random forest analysis'. Annals of Translational Medicine, 8(5), pp.226–226. doi:https://doi.org/10.21037/atm.2020.01.08.

[43] Tincani, A., Gerardi, M.C., Fredi, M., Andreoli, L. and on, 2018. 'Gender differences in rheumatology and the point of view of the Italian Society for Rheumatology (SIR)'. Journal of Sex- and Gender-Specific Medicine, 4(2), pp.79–82. Available at: https://www.gendermedjournal.it/archivio/3013/articoli/30121/ [Accessed 11 Jun. 2025].

[44] Martinis, M.D., Sirufo, M.M., Polsinelli, M., Placidi, G., Silvestre, D.D. and Ginaldi, L., 2021. 'Gender differences in osteoporosis: a single-center observational study'. World Journal of Men's Health, 39(4), pp.750–759. doi:https://doi.org/10.5534/wjmh.200099.

[45] Marshall, K., Teo, L., Shanahan, C., Legette, L. and Mitmesser, S.H., 2020. 'Inadequate calcium and vitamin D intake and osteoporosis risk in older Americans living in poverty with food insecurities'. PLOS ONE, 15(7), p.e0235042. doi:https://doi.org/10.1371/journal.pone.0235042.

[46] Zhang, Y., Tan, C. and Tan, W., 2023. 'BMI, socioeconomic status, and bone mineral density in U.S. adults: Mediation analysis in the NHANES', Frontiers in Nutrition, 10. doi:https://doi.org/10.3389/fnut.2023.1132234.

[47] Din, S. and Hashmi, N., 2020. 'Socio-economic investigation of osteoporosis patients', Masyarakat, Kebudayaan dan Politik, 33(2), p.153. doi:https://doi.org/10.20473/mkp.v33i22020.153-161.

[48] Hammad, L.F., Benajiba, N., Jambi, L.K. and Alshedi, A.F., 2024. 'Lifestyle Factors Related to Femoral and Spinal Bone Density in Young Saudi Adult Women', Journal of Women's Health and Development, 7(4). doi:https://doi.org/10.26502/fjwhd.2644-288400129.

[49] Cheng, C.H., Chen, L.R. and Chen, K.H., 2022. 'Osteoporosis Due to Hormone Imbalance: An Overview of the Effects of Estrogen Deficiency and Glucocorticoid Overuse on Bone Turnover', International Journal of Molecular Sciences. MDPI. Available at: https://doi.org/10.3390/ijms23031376.

[50] Gilboe, I.-M., 2000. 'Bone mineral density in systemic lupus erythematosus: comparison with rheumatoid arthritis and healthy controls', Annals of the Rheumatic Diseases, 59(2), pp.110–115. doi:https://doi.org/10.1136/ard.59.2.110.

[51] Naik, S., Sonawale, A., Sonawale, K. and Goyal, A., 2024. 'Effect of Disease-related Variables on Bone Mineral Density in Patients with Rheumatoid Arthritis', The Journal of the Association of Physicians of India, 72(1), pp.47–50. doi:https://doi.org/10.59556/japi.71.0404.

[52] El-Sherbiny, D.A., El-Badawy, M.A. and Elmahdi, A.R., 2021. 'Body Mass Index in Systemic Lupus Erythematosus: Relation to Disease Activity, Bone Mineral Density And Vitamin D Level', The Egyptian Journal of Hospital Medicine, 82(1), pp.89–95. doi:https://doi.org/10.21608/ejhm.2021.137953.

[53] Baba, Z., Rafi, A., Chekkouri, F.E., Mougui, A. and El Bouchti, I., 2023. 'The impact of body mass index on bone mineral density in rheumatoid arthritis', Annals of the Rheumatic Diseases, p.1370. doi:https://doi.org/10.1136/annrheumdis-2023-eular.5863.

[54] Cauley, J.A., 2011. 'Defining Ethnic and Racial Differences in Osteoporosis and Fragility Fractures', Clinical Orthopaedics and Related Research®, 469(7), pp.1891–1899. doi:https://doi.org/10.1007/s11999-011-1863-5.

[55] Adami, G., Fassio, A., Rossini, M., Caimmi, C., Giollo, A., Orsolini, G., Viapiana, O. and Gatti, D., 2019. 'Osteoporosis in rheumatic diseases', International Journal of Molecular Sciences, 20(23). Available at: https://doi.org/10.3390/ijms20235867.

[56] Shinoda, K. and Taki, H., 2021. 'Treatment of Glucocorticoid-Induced Osteoporosis and Risk Factors for New Vertebral Fractures in Female Patients with Autoimmune Diseases', Journal of Osteoporosis, 2021, pp.1–7. doi:https://doi.org/10.1155/2021/5515653.

[57] Al-Kushi, A.G., Azzeh, F.S., Header, E.A., ElSawy, N.A., Hijazi, H.H., Jazar, A.S., Ghaith, M.M. and Alarjah, M.A., 2018. 'Effect of Vitamin D and Calcium Supplementation in Patients with Systemic Lupus Erythematosus', Saudi Journal of Medicine & Medical Sciences, 6(3), pp.137–142.doi:https://doi.org/10.4103/sjmms.sjmms_134_17.

[58] Qu, X., Jiang, J., Deng, Q., Wang, H., Zhang, C., Xu, X., Yi, Y. and Qiu, L., 2025. 'Associations between smoking and osteoporosis and all-cause mortality in participants from the United States: a cohort study', Frontiers in Endocrinology, 16. doi:https://doi.org/10.3389/fendo.2025.1533633.

[59] Hafez, E.A., Mansour, H.E., Hamza, S.H., Moftah, S.G., Younes, T.B. and Ismail, M.A., 2011. 'Bone Mineral Density Changes in Patients with Recent-Onset Rheumatoid Arthritis', Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders, 4, pp.CMAMD. S7773–CMAMD.S7773. doi:https://doi.org/10.4137/cmamd.s7773.

[60] Eby, J.M., Sharieh, F. and Callaci, J.J., 2020. 'Impact of Alcohol on Bone Health, Homeostasis, and Fracture Repair', Current Pathobiology Reports, 8(3), pp.75–86. doi:https://doi.org/10.1007/s40139-020-00209-7.

[61] Khiyali, Z., Rashedi, V., Tavacol, Z., Dehghan, A. and Bijani, M., 2024. 'Smoking, alcohol consumption, drug abuse, and osteoporosis among older adults: a cross-sectional study on PERSIAN cohort study in Fasa', BMC Geriatrics, 24(1). doi:https://doi.org/10.1186/s12877-024-04678-y.

[62] Dey, M. and Bukhari, M., 2019. 'Predictors of fragility fracture and low bone mineral density in patients with a history of parental fracture', Osteoporosis and Sarcopenia, 5(1), pp.6–10. doi:https://doi.org/10.1016/j.afos.2019.03.001.

[63] Jung, J.-Y., Choi, S.T., Park, S.-H., Kwon, S.-R., Kim, H.-A., Kim, S.-S., Kim, S.H. and Suh, C.-H., 2020. 'Prevalence of osteoporosis in patients with systemic lupus erythematosus: A multicenter comparative study of the World Health Organization and fracture risk assessment tool criteria', Osteoporosis and Sarcopenia, 6(4), pp.173–178. doi:https://doi.org/10.1016/j.afos.2020.11.001.

[64] Choi, S., Kwon, S.-R., Jung, J.-Y., Kim, H.-A., Kim, S.-S., Kim, S., Kim, J.-M., Park, J.-H. and Suh, C.-H., 2018. 'Prevalence and fracture risk of osteoporosis in patients with rheumatoid arthritis: A multicenter comparative study of the FRAX and WHO criteria', Journal of Clinical Medicine, 7(12), p.507. doi:https://doi.org/10.3390/jcm7120507.

[65] Percival, M.A., Anderson, K.B., Pasco, J.A., Hosking, S.M. and Hyde, N.K., 2025. 'Parental fracture history is associated with offspring early-life fracture risk: The Geelong Osteoporosis Study', Bone, 195, p.117454. doi:https://doi.org/10.1016/j.bone.2025.117454.

[66] Kuru, P., Akyuz, G., Peynirci Cersit, H., Celenlioglu, A.E., Cumhur, A., Biricik, S., Kozan, S., Goksen, A., Ozdemir, M. and Luleci, E., 2015. 'Fracture history in osteoporosis: Risk factors and its effect on quality of life', Balkan Medical Journal, 31(4), pp.295–301. doi:https://doi.org/10.5152/balkanmedj.2014.13265.

[67] Mir, M., Najar, M. and Muzamil, M., 2017. 'Prevalence of osteoporosis in patients with chronic kidney disease (stages 3–5) in comparison with age- and sex-matched controls: A study from Kashmir Valley tertiary care center', Saudi Journal of Kidney Diseases and Transplantation, 28(3), p.538. doi:https://doi.org/10.4103/1319-2442.206439.

[68] Perhimpunan Reumatologi Indonesia, 2020. Buku Saku Reumatologi Perhimpunan Reumatologi Indonesia 2020. [online] Available at: https://reumatologi.or.id/wp-content/uploads/2021/09/buku-Saku-Reumatologi.pdf.

[69] Uysal, A., Demir, A.N. and Demir, U.G., 2025. 'Impact of various rheumatoid arthritis treatments on bone mineral density in postmenopausal women', Rheumatology Quarterly. doi:https://doi.org/10.4274/qrheumatol.galenos.2025.30592.

[70] Ketabforoush, A.H.M.E., Aleahmad, M., Qorbani, M., Mehrpoor, G., Afrashteh, S., Mardi, S. and Dolatshahi, E., 2023. 'Bone mineral density status in patients with recent-onset rheumatoid arthritis', Journal of Diabetes and Metabolic Disorders, 22(1), pp.775–785. doi:https://doi.org/10.1007/s40200-023-01200-w.

[71] Park, D.-J., Jeong, H., Choi, S.-E., Kang, J.-H. and Lee, S.-S., 2024. 'Impact of obesity on clinical outcomes and treatment continuation in rheumatoid arthritis patients receiving non-TNF-targeted therapies', Therapeutic Advances in Musculoskeletal Disease, 16. doi:https://doi.org/10.1177/1759720x241308027.

[72] Zhou, X. and Chai, Y., 2025. 'Risk factors of osteonecrosis in patients with systemic lupus erythematosus: a meta-analysis', Frontiers in Medicine, 12. doi:https://doi.org/10.3389/fmed.2025.1694721.

[73] Xu, D. and Wu, B., 2024. 'Association between systemic lupus erythematosus and osteoporosis: a Mendelian randomization analysis', BMC Rheumatology, 8(1). doi:https://doi.org/10.1186/s41927-024-00388-5.

[74] Chimenti, M.S., Perricone, C., D'Antonio, A., Ferraioli, M., Conigliaro, P., Triggianese, P., Ciccacci, C., Borgiani, P. and Perricone, R., 2021. 'Genetics, epigenetics, and gender impact in axial-spondyloarthritis susceptibility: An update on genetic polymorphisms and their sex-related associations', Frontiers in Genetics, 12. doi:https://doi.org/10.3389/fgene.2021.671976.

[75] Rusman, T., van Bentum, R.E. and van der Horst-Bruinsma, I.E., 2020. 'Sex and gender differences in axial spondyloarthritis: myths and truths', Rheumatology, 59(Supplement_4), pp.iv38–iv46. doi:https://doi.org/10.1093/rheumatology/keaa543.

[76] Ceolin, C., Bindoli, S., Cozzi, G., Di Marzio, B., Lorenzin, M., Rui, M.D., Sfriso, P., Doria, A., Sergi, G. and Ramonda, R., 2025. 'Body composition, bone mineral density, and functional impairment in axial spondyloarthritis: a 36-month longitudinal study'. BMC Musculoskeletal Disorders, 26(1). doi:https://doi.org/10.1186/s12891-025-09088-8.

[77] Both, T., Zillikens, M.C., Hoorn, E.J., Zietse, R., Jan, V., Versnel, M.A., Maria, N.I., Martin, P. and Paul, C., 2016. 'Bone Mineral Density in Sjögren Syndrome Patients with and Without Distal Renal Tubular Acidosis'. Calcified Tissue International, 98(6), pp.573–579. doi:https://doi.org/10.1007/s00223-016-0112-z.

[78] Shi, Z., Chen, J. and Xue, L., 2025. 'Exploring the Interaction Between Sjögren's Syndrome and Osteoporosis: Pathophysiological Mechanisms and Management Strategies'. International Journal of General Medicine, 18, pp.5137–5153. doi:https://doi.org/10.2147/ijgm.s543209.

[79] Han, Z., Han, P., Wang, F., Zheng, H., Chen, X., Meng, H. and Li, F., 2024. 'Negative causal exploration of systemic sclerosis: a Mendelian randomization analysis'. Scientific Reports, 14(1). doi:https://doi.org/10.1038/s41598-024-55808-w.

[80] Dobrovolskaya, O.V., Demin, N.V., Smirnov, A.V., Garzanova, L.A., Toroptsova, N.V. and Alekperov, R.T., 2019. 'Bone mineral density in patients with systemic scleroderma'. Modern Rheumatology Journal, 13(1), pp.58–63. doi:https://doi.org/10.14412/1996-7012-2019-1-58-63.

[81] Buckley, L., Guyatt, G., Fink, H.A., Cannon, M., Grossman, J., Hansen, K.E., Humphrey, M.B., Lane, N.E., Magrey, M., Miller, M., Morrison, L., Rao, M., Robinson, A.B., Saha, S., Wolver, S., Bannuru, R.R. and Vaysbrot, E., 2023. '2022 American College of Rheumatology guideline for the prevention and treatment of glucocorticoid-induced osteoporosis'. Arthritis & Rheumatology, 75(1), pp.179–192. doi:https://doi.org/10.1002/art.42312.

[82] Buckley, L., Guyatt, G., Fink, H.A., Cannon, M., Grossman, J., Hansen, K.E., Humphrey, M.B., Lane, N.E., Magrey, M., Miller, M., Morrison, L., Rao, M., Robinson, A.B., Saha, S., Wolver, S., Bannuru, R.R., Vaysbrot, E., Osani, M., Turgunbaev, M. and Miller, A.S., 2017. '2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-InducedOsteoporosis'. Arthritis Care & Research, 69(8), pp.1095–1110. doi:https://doi.org/10.1002/acr.23279.

[83] Canalis, E., Mazziotti, G., Giustina, A. and Bilezikian, J.P., 2007. 'Glucocorticoid-induced osteoporosis: Pathophysiology and therapy'. Osteoporosis International, 18(10), pp.1319–1328. doi:https://doi.org/10.1007/s00198-007-0394-0.

[84] Cranney, A., Welch, V., Adachi, J.D., Homik, J., Shea, B., Suarez-Almazor, M.E. and Tugwell, P., 2001. 'The effect of low dose methotrexate on bone density in patients with rheumatoid arthritis: a systematic review'. The Journal of Rheumatology, 28(12), pp.2586–2593. https://pubmed.ncbi.nlm.nih.gov/11764233/.

[85] Di Munno, O., Delle Sedie, A., Rossini, M., Adami, S. and Punzi, L., 2004. 'Bone mineral density in women with rheumatoid arthritis: results from a multicenter cross-sectional study'. The Journal of Rheumatology, 31(12), pp.2271–2277. https://pubmed.ncbi.nlm.nih.gov/15570651/.

[86] Llorente, I., García-Castañeda, N., Valero, C., González-Álvaro, I. and Castañeda, S., 2020. 'Osteoporosis in Rheumatoid Arthritis: Dangerous Liaisons'. Frontiers in Medicine, 7. doi:https://doi.org/10.3389/fmed.2020.601618.

[87] Sambrook, P.N., 2000. 'Cyclosporin and bone mass'. Clinical and Experimental Rheumatology, 18(2 Suppl 19), pp.S17–S20. https://pubmed.ncbi.nlm.nih.gov/10824227/.

[88] Tao, Z.S., Lv, X.X., Zhou, W.S., Ma, T.S., Chen, C. and Liang, Y.M., 2024. 'Cyclosporin A inhibits bone regeneration and induces bone loss: An in vivo study'. Bone Reports, 21, 101050. doi:https://doi.org/10.1016/j.bonr.2023.101050.

[89] Florén, C.H., Friman, L., Lööf, L., Strandberg, E. and Tysk, C., 1998. 'Bone mineral density in patients with Crohn's disease and the influence of corticosteroid treatment and nutritional status'. Scandinavian Journal of Gastroenterology, 33(5), pp.494–500. doi:https://doi.org/10.1080/00365529850171740.

[90] Morgan, S.L., Baggott, J.E., Lee, J.Y., Alarcón, G.S., Moreland, L.W. and DeMarco, P.J., 2019. 'The effect of azathioprine on bone metabolism in patients with inflammatory bowel disease'. Journal of Crohn's and Colitis, 13(9), pp.1143–1151. doi:https://doi.org/10.1093/ecco-jcc/jjz030.

[91] Tengstrand, B. and Hafström, I., 2002. 'Bone mineral density in men with rheumatoid arthritis is associated with erosive disease and sulfasalazine treatment'. The Journal of Rheumatology, 29(10), pp.2299–2305. https://pubmed.ncbi.nlm.nih.gov/12375328/.

[92] Carbone, L., Buzkova, P., Fink, H.A., Lee, J.S., Chen, Z., Ahmed, A. and Orwoll, E., 2020. 'Association of methotrexate, sulfasalazine, and hydroxychloroquine with fracture risk in rheumatoid arthritis'. JBMR Plus, 4(1), p.e10246. https://doi.org/10.1002/jbm4.10246.

[93] Kwon, O.C., Hong, S., Ghang, B., Kim, Y.G., Lee, C.K., Yoo, B. and Hong, S., 2019. 'Possible beneficial effect of leflunomide on bone mineral density in postmenopausal women with rheumatoid arthritis'. Modern Rheumatology, 29(6), pp.987–994. https://doi.org/10.1080/14397595.2018.1550064.

[94] Homik, J., Cranney, A., Shea, B., Tugwell, P., Wells, G., Adachi, J. and Suarez-Almazor, M.E., 1998. 'Calcium and vitamin D for corticosteroid-induced osteoporosis'. Cochrane Database of Systematic Reviews, 1998(2), CD000952. https://doi.org/10.1002/14651858.CD000952.

[95] Ringe, J.D., 2000. 'Prevention and therapy of corticosteroid-induced osteoporosis with calcium and vitamin D'. Clinical and Experimental Rheumatology, 18(2 Suppl 19), pp.S29–S34. https://pubmed.ncbi.nlm.nih.gov/10824229/.

[96] Ilias, I., Zoumakis, E. and Ghayee, H., 2022. 'An overview of glucocorticoid induced osteoporosis'. PubMed[online]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK278968/.

[97] Humphrey, M.B., Russell, L., Danila, M.I., Fink, H.A., Guyatt, G., Cannon, M., Caplan, L., Gore, S., Grossman, J., Hansen, K.E., Lane, N.E., Ma, N.S., Magrey, M., McAlindon, T., Robinson, A.B., Saha, S., Womack, C., Abdulhadi, B., Charles, J.F. and Cheah, J.T.L., 2023. '2022 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis'. Arthritis & Rheumatology (Hoboken, N.J.), 75(12), pp.2088–2102. https://doi.org/10.1002/art.42646.

[98] Phang, K.F., Cho, J., Lee, W. and Mak, A., 2018. 'Glucocorticoid-induced osteoporosis in systemic lupus erythematosus'. Rheumatology Practice and Research, 3, p.205990211880251. https://doi.org/10.1177/2059902118802510.

[99] Davidson, J.E., Fu, Q., Rao, S., Magder, L.S. and Petri, M., 2018. 'Quantifying the burden of steroid-related damage in SLE in the Hopkins Lupus Cohort'. Lupus Science & Medicine, 5(1), p.e000237. https://doi.org/10.1136/lupus-2017-000237.

[100] De Vries, F., Bracke, M., Leufkens, H.G.M., Lammers, J.-W.J., Cooper, C. and Van Staa, T.P., 2006. 'Fracture risk with intermittent high-dose oral glucocorticoid therapy'. Arthritis & Rheumatism, 56(1), pp.208–214. https://doi.org/10.1002/art.22294.

[101] Briot, K. and Roux, C., 2015. 'Inflammation, bone loss and fracture risk in spondyloarthritis: Figure 1'. RMD Open, 1(1), p.e000052. https://doi.org/10.1136/rmdopen-2015-000052.

[102] Hansen, K.E., Kleker, B., Safdar, N. and Bartels, C.M., 2014. 'A systematic review and meta-analysis of glucocorticoid-induced osteoporosis in children'. Seminars in Arthritis and Rheumatism, 44(1), pp.47–54. https://doi.org/10.1016/j.semarthrit.2014.02.002.