http://www.jhpr.ir
Hosp Pract Res. 2022 Dec;7(4):123-130
doi 10.34172/hpr.2022.25
HPR
Hospital Practices and Research
Original Article

# Prevalence of Vertebral Compression Fracture Among Rheumatoid Arthritis Patients in Sulaymaniyah

**Hemn Hassan Mohammed**[1*], **Raouf Rahim Merza**[2]

[1]Ministry of Health, Sulaimani, Kurdistan Region, Iraq
[2]Sulaimani Medical school, University of Sulaimani, Kurdistan Region, Iraq

***Corresponding Author:** Hemn Hassan Mohammed, Ph.D., Rheumatologist, Ministry of Health, Sulaimani, Kurdistan Region, Iraq. Tel: +964-7501941402, Email: hemnhasan110@gmail.com

**Received** October 21, 2020; **Accepted** November 10, 2022; **Online Published** November 15, 2022

**Abstract**

**Background:** The risk of fractured vertebral increases in patients with rheumatoid arthritis as they are more likely to suffer from osteopenia, and osteoporosis.

**Objectives:** This study aimed to investigating the rate and risk factors of vertebral fractures in patients with rheumatoid arthritis.

**Methods:** We recruited 201 patients aged between 30 and 70 who attended the rheumatology department at Shahid Hemn Teaching Hospital in Sulaymaniyah, between January and September 2022. Medical records were reviewed for disease and treatment characteristics while also clinically evaluated by a rheumatologist. Spinal radiographs were assessed by two experienced radiologists blinded to patients' clinical diagnosis and status. Compression fractures were classified by using the Genant semiquantitative method, and the type of fracture was classified as wedged fracture, biconcave fracture, or crushed fracture.

**Results:** Of the 201 included participants, 151 were female, and 50 were male. The BMI of women was higher than men by nearly four points ($P<0.001$). Most women were also illiterate (68/151, 45.0%) and unemployed (139/151, 92.1%). Hypertension (28.4%) and diabetes mellitus (14.4%) were the most reported comorbidities. Women were more likely to have higher DAS28 scores while men had more vertebral fractures ($P=0.003$). The probability of fractures increased with age, male sex, and illiteracy compared to primary school, osteopenia, and osteoporosis through simple and multiple logistic regression models.

**Conclusion:** With at least one fracture affects females and males at a rate of 27.8% and 52.0%, respectively. Also reported that age, male sex, illiteracy, osteopenia, and osteoporosis significantly increase the risk of fractures.

**Keywords:** Rheumatoid Arthritis, Risk Factors, Osteoporosis

## 1. Background

Rheumatoid arthritis is an autoimmune disease that affects synovial joints and has variable extraarticular manifestations.[1] The joint involvement is typically bilaterally symmetrical with metacarpophalangeal, metatarsophalangeal, and proximal interphalangeal joints most commonly involved.[2] Atypical joints involved include the cervical spine, cricoarytenoid, distal interphalangeal, sacroiliac, and lumbar spine joints.[2,3]

Coupled with senile osteopenia and osteoporosis, rheumatoid arthritis increases the risk of fractures and subsequent mortality due to multifactorial bone demineralization.[1,4-6] There have been some factors associated with the development of fractures in rheumatoid arthritis patients. These factors include disease severity, duration, autoantibody status, and treatment regimen.[6-9] Other general factors that increase the risk of fractures in osteoporotic patients (and patients with rheumatoid arthritis and osteoporosis) are age, female sex, low body mass index (BMI), family history of osteoporosis, previous fractures, and others.[10-15]

Although there have been previous studies that discuss the risk factors of rheumatoid arthritis-associated fractures,[6,9-18] we still require more research to assess the risk of fractures in underrepresented patients. Therefore, in this study, we aimed at estimating the prevalence of vertebral compression fractures in patients with rheumatoid arthritis in Sulaymaniyah. We also analyzed confounding factors and effect modifiers that can contribute to those fractures.

## 2. Objectives

This study designs to determine the prevalence of vertebral compression fracture among rheumatoid arthritis patients through lateral thoracolumbar spine X-ray. Also to reveal the relation of confounding factors (duration of rheumatoid arthritis, medications, age, sex, smoking, comorbidities, back pain, bone mineral density, etc.) with the presence of vertebral compression fracture. And obtaining information regarding the fracture grade, and type of vertebral compression fracture on X-ray film.

## 3. Methods

### *3.1. Study Design and Participants*

In this cross-sectional study, 201 patients who registered in the rheumatology department at Shahid Hemn Teaching Hospital in Sulaymaniyah, Kurdistan/Iraq, between

January and September 2022, were recruited for this study. The inclusion criteria were patients between 30 and 70 years of age diagnosed by a rheumatologist with rheumatoid arthritis using the 2010 ACR/EULAR classification criteria.[19] Patients younger than 30 years, older than 70 years with a history of traumatic vertebral compression fracture, and who refused to provide informed consent were excluded from the study.

### *3.2. Data Collection*

Convenient sampling was used to collect the enrolled data. Medical records were reviewed for disease and treatment characteristics while also clinically evaluated by a rheumatologist. The data recorded included basic data like (e.g., age, height, weight, body mass index, educational level, employment, comorbidities, personal medical history, family medical history) and disease characteristics (e.g., duration of disease, ACR classification, DEXA scan findings, medications, and disease activity score using a 28-joint count (DAS28).[20] In addition, female patients provided their age at menarche.

### *3.3. Sample Size Calculation*

Since the design of the study is cross sectional study and one group. The below equation was used; n = (Zα)2 * P (1 - P)/ d2. The total sample size was = 201 cases. n = the sample size, P = prevalence of the variable under the study, d = the difference the investigator wishes to detect, Zα = 1.96.

### *3.4. Imaging Studies*

Spinal radiographs (sagittal projections) were obtained. All radiographs were assessed by two experienced radiologists who were blinded to patients' clinical diagnosis and status. The radiologists first independently analyzed the visibility and morphology of each vertebra. The conclusions were reached by consensus. Compression fractures were classified by using the Genant semiquantitative method[21] based on the height of T4-L4 vertebrae that was shown on lateral views. The grading was done by visual inspection and without direct vertebral measurement as follows: normal (grade 0), mild (grade 1, where there is approximately 20-25% reduction in anterior, middle, and/or posterior height), moderate (grade 2, where there is approximately 25%-40% in any height), and severe (grade 3, where there is approximately 40% reduction in any height). The type of fracture was classified as wedged fracture, biconcave fracture, or compressed/crushed fracture (predominantly anterior, midportion, posterior, or anterior and posterior portions) respectively.

### *3.5. Statistical Analysis*

The characteristics of the participants enrolled in the study according to their sex were compared. The *P* values for continuous variables were obtained using a *t* test, while the *P* values for categorical variables were obtained using a chi-squared test. Simple and multiple logistic regression models were performed using R programming (version 4.1.3) language to assess which factors can affect the occurrence of any vertebral fracture. The selection of variables included in the multiple regression model was done using stepwise backward elimination, which guaranteed no change in coefficients more than 5% when compared to the previous model. In all analyses, the statistical significance was evaluated at $P < 0.05$.

## 4. Results

Of the 201 included participants, 151 were female, and 50 were male. All their basic characteristics are summarized in Table 1. Their ages ranged between 30 and 70, with a mean of 54.17 (SD = 9.75). The BMI of women was higher than men by nearly four points ($P < 0.001$). Most women were also illustrated (68/151, 45.0%) and unemployed (139/151, 92.1%). Mostly 70% of the included females were menopausal. In both sexes, the most reported comorbidities were hypertension (28.4%) and diabetes mellitus (14.4%). Hypertension was more common in women ($P = 0.040$) while more men identified as current smokers ($P < 0.001$).

As for disease characteristics, women were diagnosed earlier than men by around 4 years ($P = 0.008$) and had a longer disease duration ($P = 0.084$). Women were more likely to have higher DAS28 scores, especially in tenderness ($P = 0.004$), general health ($P < 0.001$), and erythrocyte sedimentation rate (ESR) ($P < 0.001$). And while more women had high disease activity, more men had moderate activity. The medications received by all participants were disease-modifying antirheumatic drugs (DMARDs) that included methotrexate, leflunomide, and hydroxychloroquine. Other medications included biological drugs, prednisolone, vitamin $D_3$, anti-resorptive drugs, and folic acid supplementation.

In addition to the data presented in Table 1, we also report that all patients were Kurds and lived in urban areas. Nine female patients had received oophorectomy. Six patients (two male and four female) had joint replacement surgeries. None had neuromuscular disorders, cancer, or a history of traumatic accidents; however, six patients had a history of at least one fall.

In Table 2, all reported fractures along with the grades and types are reported. On average, men had more chances of having vertebral fractures ($P = 0.003$). In the whole sample, we report a total of 92 wedged, 15 biconcave, and 13 compression fractures. No patients had T4 or T5 fractures. But some patients had more than one fracture.

Through univariable logistic regression, we identified age (OR = 1.08, 95% CI: 1.04-1.12, $P < 0.001$), male sex (OR = 2.81, 95% CI: 1.46-5.47, $P < 0.002$), primary school compared to illiteracy (OR = 0.48, 95% CI: 0.24-0.93, P = 0.033), osteopenia (OR = 3.18, 95% CI: 1.50-7.18, $P = 0.004$), and osteoporosis (OR = 6.70, 95% CI: 2.87-16.59, $P < 0.001$) to affect the probability of fractures. The same factors were also identified to be statistically significant in the multiple logistic regression after adjusting for BMI, comorbidities, disease duration, socioeconomic status, and the ACR classification,

**Table 1.** Baseline Characteristics of the Whole Sample and by Sex Group

| Characteristics | Total (N = 201) | Female (n = 151) | Male (n = 50) | *P* Value |
|---|---|---|---|---|
| **Demographics** | | | | |
| Age (y) | | | | |
| Mean (SD) | 54.17 (9.75) | 53.50 (9.51) | 56.18 (10.29) | |
| Median (IQR) | 55.00 (13.00) | 53.00 (13.5) | 56.50 (13.5) | 0.108 |
| Range | 30 to 70 | 30 to 70 | 32 to 70 | |
| BMI | | | | |
| Mean (SD) | 29.24 (5.71) | 30.15 (5.86) | 26.51 (4.23) | |
| Median (IQR) | 28.52 (6.59) | 29.09 (9.74) | 26.11 (4.99) | <0.001* |
| Range | 15.19 to 57.81 | 17.58 to 57.81 | 15.19 to 36.36 | |
| Education | | | | |
| Illiterate | 76 (37.8%) | 68 (45.0%) | 8 (16.0%) | |
| Primary school | 81 (40.3%) | 55 (36.4%) | 26 (52.0%) | 0.002* |
| Secondary school | 25 (12.4%) | 17 (11.3%) | 8 (16.0%) | |
| University | 19 (9.5%) | 11 (7.3%) | 8 (16.0%) | |
| Employment | | | | |
| Unemployed | 159 (79.1%) | 139 (92.1%) | 20 (40.0%) | |
| Employed | 25 (12.4%) | 11 (7.3%) | 14 (28.0%) | <0.001* |
| Retired | 17 (8.5%) | 1 (0.7%) | 16 (32.0%) | |
| Socioeconomic status | | | | |
| Low income | 76 (37.8%) | 58 (38.4%) | 18 (36.0%) | 0.892 |
| Middle income | 125 (62.2%) | 93 (61.6%) | 32 (64.0%) | |
| Comorbidities | | | | |
| At least one | 86 (42.8%) | 70 (46.4%) | 16 (32.0%) | 0.107 |
| Hypertension | 57 (28.4%) | 49 (32.5%) | 8 (16.0%) | 0.040* |
| Diabetes mellitus | 29 (14.4%) | 21 (13.9%) | 8 (16.0%) | 0.894 |
| Hypercholesterolemia | 12 (6.0%) | 11 (7.3%) | 1 (2.0%) | 0.307 |
| Hyperthyroidism | 4 (2.0%) | 4 (2.6%) | 0 (0.0%) | 0.563 |
| CKD | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | 1.000 |
| CLD | 2 (1.0%) | 2 (1.3%) | 0 (0.0%) | 1.000 |
| Asthma | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | 1.000 |
| COPD | 10 (5.0%) | 8 (5.3%) | 2 (4.0%) | 1.000 |
| IHD | 15 (7.5%) | 11 (7.3%) | 4 (8.0%) | 1.000 |
| Personal history | | | | |
| Smoking | | | | |
| *Current* | 16 (8.0%) | 1 (0.7%) | 15 (30.0%) | |
| *Ex-smoker* | 18 (9.0%) | 1 (0.7%) | 17 (34.0%) | <0.001* |
| *Never smoked* | 167 (83.0) | 149 (98.6%) | 18 (36.0%) | |
| Immobilization | 2 (1.0%) | 2 (1.3%) | 0 (0.0%) | 1.000 |
| Regular exercise | 8 (4.0%) | 7 (4.6%) | 1 (2.0%) | 0.683 |
| Non-vertebral fracture | 15 (7.5%) | 10 (6.6%) | 5 (10.0%) | 0.633 |
| Back pain | 71 (35.3%) | 60 (39.7%) | 11 (22.0%) | 0.035* |
| Family history | | | | |
| Osteoporosis | 21 (10.4%) | 19 (12.6%) | 2 (4.0%) | 0.146 |
| Fragility fracture | 13 (6.5%) | 9 (6.0%) | 4 (8.0%) | 0.860 |
| **Disease Characteristics** | | | | |
| Age at diagnosis | | | | |
| Mean (SD) | 45.21 (10.46) | 44.01 (9.99) | 48.86 (11.11) | |
| Median (IQR) | 45.00 (14.00) | 45.00 (13.00) | 48.50 (8.25) | 0.008* |
| Range | 15 to 68 | 16 to 65 | 22 to 68 | |

**Table 1.** Continued.

| Characteristics | Total (N = 201) | Female (n = 151) | Male (n = 50) | *P* Value |
|---|---|---|---|---|
| Duration of disease (m) | | | | |
| Mean (SD) | 107.29 (73.60) | 111.93 (76.86) | 93.28 (61.31) | |
| Median (IQR) | 96.00 (94.00) | 96.00 (120.00) | 84.00 (69.00) | 0.084 |
| Range | 12 to 360 | 12 to 360 | 24 to 240 | |
| Positive RF | 160 (79.6%) | 121 (80.1%) | 39 (78.0%) | 0.903 |
| Positive ACPA | 114 (56.7%) | 82 (54.3%) | 32 (64.0%) | 0.301 |
| **DAS28** | | | | |
| Tenderness | | | | |
| Mean (SD) | 7.19 (5.46) | 7.81 (5.40) | 5.30 (5.24) | |
| Median (IQR) | 6.00 (10.00) | 8.00 (10.00) | 3.00 (5.75) | 0.004* |
| Range | 0 to 20 | 0 to 20 | 0 to 18 | |
| Swelling | | | | |
| Mean (SD) | 5.99 (3.37) | 6.12 (3.10) | 5.60 (4.09) | |
| Median (IQR) | 5.00 (4.00) | 6.00 (4.00) | 5.00 (5.50) | 0.414 |
| Range | 1 to 16 | 1 to 16 | 1 to 16 | |
| General health | | | | |
| Mean (SD) | 5.83 (2.20) | 6.27 (1.95) | 4.48 (2.36) | |
| Median (IQR) | 6.00 (4.00) | 7.00 (3.00) | 5.00 (4.75) | <0.001* |
| Range | 0 to 10 | 2 to 10 | 0 to 9 | |
| ESR | | | | |
| Mean (SD) | 29.67 (17.55) | 32.05 (17.27) | 22.48 (16.55) | |
| Median (IQR) | 27.00 (26.00) | 30.00 (25.00) | 20.00 (19.00) | <0.001* |
| Range | 2 to 98 | 2 to 98 | 3 to 90 | |
| Disease activity | | | | |
| Remission | 7 (3.5%) | 4 (2.6%) | 3 (6.0%) | |
| Low | 6 (3.0%) | 2 (1.3%) | 4 (8.0%) | 0.002* |
| Moderate | 90 (44.8%) | 61 (40.4%) | 29 (58.0%) | |
| High | 98 (48.8%) | 84 (55.6%) | 14 (28.0%) | |
| ACR classification | | | | |
| Class I | 27 (13.4%) | 15 (9.9%) | 12 (24.0%) | |
| Class II | 66 (32.8%) | 48 (31.8%) | 18 (36.0%) | 0.014* |
| Class III | 94 (46.8%) | 79 (52.3%) | 15 (30.0%) | |
| Class IV | 14 (7.0%) | 9 (6.0%) | 5 (10.0%) | |
| DEXA scan | | | | |
| Normal | 70 (34.8%) | 57 (37.7%) | 13 (26.0%) | |
| Osteopenia | 86 (42.8%) | 62 (41.1%) | 24 (48.0%) | 0.317 |
| Osteoporosis | 45 (22.4%) | 32 (21.2%) | 13 (26.0%) | |
| **Medications** | | | | |
| DMARDs | | | | |
| Methotrexate | 147 (73.1%) | 109 (72.2%) | 38 (76.0%) | |
| Leflunomide | 12 (6.0%) | 8 (5.3%) | 4 (8.0%) | 0.523 |
| Hydroxychloroquine | 42 (20.9%) | 34 (22.5%) | 8 (16.0%) | |
| Biological drugs | 45 (22.4%) | 32 (21.2%) | 13 (26.0%) | 0.609 |
| Prednisolone | 200 (99.5%) | 150 (99.3%) | 50 (100%) | 1.000 |
| Vitamin $D_3$ | 198 (98.5%) | 148 (98.0%) | 50 (100%) | 0.740 |
| Anti-resorptive drugs | 23 (11.4%) | 21 (13.9%) | 2 (4.0%) | 0.099 |

*Indicates statistically significant *P* value of < 0.05. The *P* values are for *t* test (continuous data) and chi-square test (categorical data).
Abbreviations: BMI, body mass index; CKD, chronic kidney disease; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disease; IHD, ischemic heart disease; RF, rheumatoid factor; DMARDs, disease-modifying anti-rheumatic drugs; ACR, American College of Rheumatology; ACPA, anti-citrullinated protein antibody.

**Table 2.** The Grades of Sustained Fractures of the Whole Sample and by Sex Group

| Fractures | Total (N = 201) | Female (n = 151) | Male (n = 50) | *P* Value |
|---|---|---|---|---|
| At least one fracture | 68 (33.8%) | 42 (27.8%) | 26 (52.0%) | 0.003* |
| T6 | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | 1.000 |
| *Grade 1* | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | NA |
| *Wedged* | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | NA |
| T7 | 2 (1.0%) | 2 (1.3%) | 0 (0.0%) | 1.000 |
| *Grade 1* | 2 (1.0%) | 2 (1.3%) | 0 (0.0%) | NA |
| *Biconcave* | 2 (1.0%) | 2 (1.3%) | 0 (0.0%) | NA |
| T8 | 6 (3.0%) | 4 (2.6%) | 2 (4.0%) | 0.994 |
| *Grade 1* | 4 (2.0%) | 4 (2.6%) | 0 (0.0%) | NA |
| *Grade 3* | 2 (1.0%) | 0 (0.0%) | 2 (4.0%) | NA |
| *Wedged* | 3 (1.5%) | 2 (1.3%) | 1 (2.0%) | NA |
| *Biconcave* | 2 (1.0%) | 1 (0.7%) | 1 (2.0%) | NA |
| *Compression* | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | NA |
| T9 | 8 (4.0%) | 4 (2.6%) | 4 (8.0%) | 0.208 |
| *Grade 1* | 7 (3.5%) | 4 (2.6%) | 3 (6.0%) | NA |
| *Grade 2* | 1 (0.5%) | 0 (0.0%) | 1 (2.0%) | NA |
| *Wedged* | 5 (2.5%) | 2 (1.3%) | 3 (6.0%) | NA |
| *Compression* | 3 (1.5%) | 2 (1.3%) | 1 (2.0%) | NA |
| T10 | 11 (5.5%) | 6 (4.0%) | 5 (10.0%) | 0.206 |
| *Grade 1* | 8 (4.0%) | 5 (3.3%) | 3 (6.0%) | NA |
| *Grade 2* | 3 (1.5%) | 1 (0.7%) | 2 (4.0%) | NA |
| *Wedged* | 6 (3.0%) | 3 (2.0%) | 3 (6.0%) | NA |
| *Compression* | 5 (2.5%) | 3 (2.0%) | 2 (4.0%) | NA |
| T11 | 11 (5.5%) | 4 (2.6%) | 7 (14.0%) | 0.007* |
| *Grade 1* | 8 (4.0%) | 4 (2.6%) | 4 (8.0%) | NA |
| *Grade 2* | 2 (1.0%) | 0 (0.0%) | 2 (4.0%) | NA |
| *Grade 3* | 1 (0.5%) | 0 (0.0%) | 1 (2.0%) | NA |
| *Wedged* | 11 (5.5%) | 4 (2.6%) | 7 (14.0%) | NA |
| T12 | 29 (14.4%) | 14 (9.3%) | 15 (30.0%) | 0.001* |
| *Grade 1* | 24 (11.9%) | 12 (7.9%) | 12 (24.0%) | NA |
| *Grade 2* | 4 (2.0%) | 1 (0.7%) | 3 (6.0%) | NA |
| *Grade 3* | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | NA |
| *Wedged* | 25 (12.4%) | 12 (7.9%) | 13 (26.0%) | NA |
| *Biconcave* | 2 (1.0%) | 2 (1.3%) | 0 (0.0%) | NA |
| *Compression* | 2 (1.0%) | 0 (0.0%) | 2 (4.0%) | NA |
| L1 | 27 (13.4%) | 12 (8.0%) | 15 (30.0%) | <0.001* |
| *Grade 1* | 18 (9.0%) | 7 (4.6%) | 11 (22.0%) | NA |
| *Grade 2* | 8 (4.0%) | 4 (2.6%) | 4 (8.0%) | NA |
| *Grade 3* | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | NA |
| *Wedged* | 22 (10.9%) | 8 (5.3%) | 14 (28.0%) | NA |
| *Biconcave* | 5 (2.5%) | 4 (2.6%) | 1 (2.0%) | NA |
| L2 | 10 (5.0%) | 4 (2.6%) | 6 (12.0%) | 0.024* |
| *Grade 1* | 7 (3.5%) | 3 (2.0%) | 4 (8.0%) | NA |
| *Grade 2* | 1 (0.5%) | 0 (0.0%) | 1 (2.0%) | NA |
| *Grade 3* | 2 (1.0%) | 1 (0.7%) | 1 (2.0%) | NA |
| *Wedged* | 8 (4.0%) | 3 (2.0%) | 5 (10.0%) | NA |
| *Biconcave* | 2 (1.0%) | 1 (0.7%) | 1 (2.0%) | NA |
| L3 | 10 (5.0%) | 7 (4.6%) | 3 (6.0%) | 0.993 |
| *Grade 1* | 6 (3.0%) | 4 (2.6%) | 2 (4.0%) | NA |
| *Grade 2* | 2 (1.0%) | 1 (0.7%) | 1 (2.0%) | NA |
| *Grade 3* | 2 (1.0%) | 2 (1.3%) | 0 (0.0%) | NA |
| *Wedged* | 8 (4.0%) | 6 (4.0%) | 2 (4.0%) | NA |
| *Biconcave* | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | NA |
| *Compression* | 1 (0.5%) | 0 (0.0%) | 1 (2.0%) | NA |
| L4 | 5 (2.5%) | 5 (3.3%) | 0 (0.0%) | 0.436 |
| *Grade 1* | 2 (1.0%) | 2 (1.3%) | 0 (0.0%) | NA |
| *Grade 2* | 3 (1.5%) | 3 (2.0%) | 0 (0.0%) | NA |
| *Grade 3* | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | NA |
| *Wedged* | 3 (1.5%) | 3 (2.0%) | 0 (0.0%) | NA |
| *Biconcave* | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | NA |
| *Compression* | 1 (0.5%) | 1 (0.7%) | 0 (0.0%) | NA |

*Indicates statistically significant *P* value of < 0.05. The *P* values are for the chi-square test (categorical data).

but with different odds ratios, (Table 3).

## 5. Discussion

In our study, we aimed to investigate the prevalence of vertebral compression fractures in patients with rheumatoid arthritis in Sulaymaniyah, Kurdistan, and detect confounding factors and effect modifiers that can contribute to those fractures. Men were more likely to have vertebral fractures than women ($P = 0.003$) although women mostly had higher disease activity DAS28 scores related to tenderness ($P = 0.004$), general health ($P < 0.001$), and ESR ($P < 0.001$). This contradicts the findings in another study which found that the risk of fracture increases with disease progression using DAS28 and Health Assessment Questionnaire (HAQ) scores.[22] Their findings correspond well with another study that found that increased disease activity correlates with axial bone density loss.[23,24] However, our study has included an effect modifier (sex) when calculating the risks of those patients. Moreover, in our study, we found that age, male sex, illiteracy, osteopenia, and osteoporosis significantly increase the risk of fractures using simple and multiple logistic regression models.

In a recent systematic review and meta-analysis, the summary point prevalence of osteoporosis among patients with rheumatoid arthritis was calculated to be 27.6% (95% CI: 23.9-31.3%).[25] This corresponds nicely to the reporting of 24.2% of the prevalence of having at least one vertebral fracture in another study.[22] But, Osteoporosis and at least one fracture were 22%, and 33.8%, respectively recorded in our study.

As osteoporosis is one of the leading causes of senile bone fractures,[26] in a study that included 865 patients from China, Tong et al, found that osteoporosis in rheumatoid arthritis is associated with large doses of daily corticosteroid ingestion, longer disease duration, older age, and female sex. Protective factors included BMI.[16] Moreover, another study has found the same results with age, glucocorticoids,

**Table 3.** Simple and Multiple Logistic Regression Models to Predict the Occurrence of Any Vertebral Fracture in Patients With Rheumatoid Arthritis

| Variables | Univariable Logistic Regression | | | Multiple Logistic Regression | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | *P* Value | OR | 95% CI | *P* Value |
| Age in years | 1.08 | 1.04 to 1.12 | <0.001* | 1.05 | 1.01 to 1.10 | 0.023* |
| Gender (male) | 2.81 | 1.46 to 5.47 | 0.002* | 3.10 | 1.37 to 7.20 | 0.007* |
| BMI | 0.97 | 0.92 to 1.02 | 0.305 | 1.00 | 0.93 to 1.06 | 0.970 |
| At least one comorbidity | 1.19 | 0.66 to 2.14 | 0.566 | 1.29 | 0.63 to 2.65 | 0.481 |
| Duration of disease | 1.00 | 0.99 to 1.01 | 0.588 | 1.00 | 0.99 to 1.01 | 0.569 |
| Education (reference: illiterate) | – | – | – | – | – | – |
| Primary school | 0.48 | 0.24 to 0.93 | 0.033* | 0.41 | 0.17 to 0.97 | 0.046* |
| Secondary school | 0.97 | 0.38 to 2.41 | 0.944 | 1.02 | 0.32 to 3.14 | 0.979 |
| University | 0.85 | 0.29 to 2.35 | 0.754 | 1.15 | 0.29 to 4.39 | 0.842 |
| Socioeconomic status (reference: low income) | 0.61 | 0.34 to 1.11 | 0.105 | 0.73 | 0.36 to 1.51 | 0.398 |
| DEXA scan (reference: normal) | – | – | – | – | – | – |
| Osteopenia | 3.18 | 1.50 to 7.18 | 0.004* | 2.84 | 1.17 to 7.26 | 0.024* |
| Osteoporosis | 6.70 | 2.87 to 16.59 | <0.001* | 4.05 | 1.48 to 11.61 | 0.007* |
| ACR classification (reference: Class I) | – | – | – | – | – | – |
| Class II | 0.69 | 0.26 to 1.88 | 0.461 | 0.63 | 0.20 to 2.04 | 0.437 |
| Class III | 1.19 | 0.50 to 3.03 | 0.711 | 0.76 | 0.23 to 2.53 | 0.651 |
| Class IV | 2.00 | 0.53 to 7.69 | 0.303 | 1.16 | 0.23 to 5.92 | 0.860 |

*Indicates statistical significance at the level of $P<0.05$.

and history of falls.[22] Although the higher risk in female patients may contradict our findings, our outcome assessment was vertebral compression fractures instead of the mere presence of osteoporosis. Moreover, it should be noted that people with rheumatoid arthritis are more likely to experience falls; and hence, are more likely to have peripheral or vertebral fractures.[27,28] Other factors that contribute to fractures in rheumatoid arthritis patients include positive anti-citrullinated protein antibody (ACPA), positive rheumatoid factor, or both.[24,29] But, in this study, these factors were not significantly affected in patients with rheumatoid arthritis. It is also important to note that although glucocorticoids can have harmful effects on bone mass density, they may provide some local and general benefits that limit the disability in the active phase of the disease.[30-34] Therefore, it is imperative in future studies to study the effect of the type and duration of glucocorticoid intake coupled with the stage of the disease. This was not feasible in our study due to some sample size limitations.

Although this is the first study to report these findings from Sulaymaniyah, Kurdistan, there are some limitations. Firstly, we do not have data about the incidence of vertebral fractures in the general population or postmenopausal women to compare with. Secondly, although, surprisingly, biological DMARDs may decrease bone loss[35] and decrease the incidence of fractures,[36] previous studies found that the incidence of fractures between people with rheumatoid arthritis and the general population is still comparable.[11,22] This makes it more difficult for our assessment as only 22.4% of our sample receives biological DMARDs. Thirdly, due to funding limitations, we were not able to link our findings to laboratory analyses for better risk prediction in the future.

## 6. Conclusion

People may present with single or multiple fractures, with at least one fracture affecting females and males at a rate of 27.8% and 52.0%, respectively. We also reported that age, male sex, illiteracy, osteopenia, and osteoporosis significantly increase the risk of fractures using simple and multiple logistic regression models. These factors should prompt further quantification to allow more accurate patient counseling about the risk of fractures. Further studies are needed to assess more factors in this population and other populations. Seeing that there are some published articles about this question, conducting a systematic review to properly assess all risk factors is now feasible.

### Acknowledgments

The authors are thankful to Dr. Hadi Omar Sofi Karim, who interpretate the X-ray finding. Also express their appreciation and gratitude to the Nursing staff of the rheumatology department at

### Research Highlights

**What Is Already Known?**

Rheumatoid arthritis is an autoimmune disease that affects synovial joints and has variable extra articular manifestations.

**What Does This Study Add?**

This study reported that age, sex, illiteracy, osteopenia, and osteoporosis significantly increase the risk of fractures among patients with rheumatoid arthritis and men were more likely to have vertebral fractures than women.

Shahid Hemn Teaching Hospital in Sulaymaniyah, Kurdistan/Iraq for their support and cooperation in conducting this study despite their busy schedules.

### Author Contributions

HHM contributed to the analysis, writing manuscript. RRM Contributed to the conception and design of this article. Both authors provided critical revision and the final approval for this article.

### Conflict of Interest Disclosures

The authors declare no conflict of interest.

### Ethical Approval

The Kurdistan Board of the Medical Specialties Research Protocol Ethics Committee approved all procedures involving human subjects in this study, which was carried out by the Declaration of Helsinki's principles (ethical approval number: 201). All subjects provided their written informed consent.

### Funding/Support

This research received no external funding.

### References

1. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet. 2016;388(10055):2023-2038. doi:10.1016/s0140-6736(16)30173-8.
2. Grassi W, De Angelis R, Lamanna G, Cervini C. The clinical features of rheumatoid arthritis. Eur J Radiol. 1998;27 Suppl 1:S18-24. doi:10.1016/s0720-048x(98)00038-2.
3. Shlobin NA, Dahdaleh NS. Cervical spine manifestations of rheumatoid arthritis: a review. Neurosurg Rev. 2021;44(4):1957-1965. doi:10.1007/s10143-020-01412-1.
4. Book C, Algulin J, Nilsson JA, Saxne T, Jacobsson L. Bone mineral density in the hand as a predictor for mortality in patients with rheumatoid arthritis. Rheumatology (Oxford). 2009;48(9):1088-1091. doi:10.1093/rheumatology/kep169.
5. Lin YC, Li YH, Chang CH, et al. Rheumatoid arthritis patients with hip fracture: a nationwide study. Osteoporos Int. 2015;26(2):811-817. doi:10.1007/s00198-014-2968-y.
6. van Staa TP, Geusens P, Bijlsma JW, Leufkens HG, Cooper C. Clinical assessment of the long-term risk of fracture in patients with rheumatoid arthritis. Arthritis Rheum. 2006;54(10):3104-3112. doi:10.1002/art.22117.
7. Cheng TT, Yu SF, Su FM, et al. Anti-CCP-positive patients with RA have a higher 10-year probability of fracture evaluated by FRAX®: a registry study of RA with osteoporosis/fracture. Arthritis Res Ther. 2018;20(1):16. doi:10.1186/s13075-018-1515-1.
8. Mori Y, Kuwahara Y, Chiba S, et al. Bone mineral density of postmenopausal women with rheumatoid arthritis depends on disease duration regardless of treatment. J Bone Miner Metab. 2017;35(1):52-57. doi:10.1007/s00774-015-0716-9.
9. Phuan-Udom R, Lektrakul N, Katchamart W. The association between 10-year fracture risk by FRAX and osteoporotic fractures with disease activity in patients with rheumatoid arthritis. Clin Rheumatol. 2018;37(10):2603-2610. doi 10.1007/s10067-018-4218-8.
10. Gough AK, Lilley J, Eyre S, Holder RL, Emery P. Generalised bone loss in patients with early rheumatoid arthritis. Lancet. 1994;344(8914):23-27. doi:10.1016/s0140-6736(94)91049-9.
11. Hauser B, Riches PL, Wilson JF, Horne AE, Ralston SH. Prevalence and clinical prediction of osteoporosis in a contemporary cohort of patients with rheumatoid arthritis. Rheumatology (Oxford). 2014;53(10):1759-1766. doi:10.1093/rheumatology/keu162.
12. Kroot EJ, Nieuwenhuizen MG, de Waal Malefijt MC, van Riel PL, Pasker-de Jong PC, Laan RF. Change in bone mineral density in patients with rheumatoid arthritis during the first decade of the disease. Arthritis Rheum. 2001;44(6):1254-1260. doi:10.1002/1529-0131(200106)44:6<1254::aid-art216>3.0.co;2-g.
13. Lodder MC, de Jong Z, Kostense PJ, et al. Bone mineral density in patients with rheumatoid arthritis: relation between disease severity and low bone mineral density. Ann Rheum Dis. 2004;63(12):1576-1580. doi:10.1136/ard.2003.016253.
14. Sambrook PN, Eisman JA, Champion GD, Yeates MG, Pocock NA, Eberl S. Determinants of axial bone loss in rheumatoid arthritis. Arthritis Rheum. 1987;30(7):721-728. doi:10.1002/art.1780300701.
15. Shibuya K, Hagino H, Morio Y, Teshima R. Cross-sectional and longitudinal study of osteoporosis in patients with rheumatoid arthritis. Clin Rheumatol. 2002;21(2):150-158. doi:10.1007/s10067-002-8274-7.
16. Tong JJ, Xu SQ, Zong HX, Pan MJ, Teng YZ, Xu JH. Prevalence and risk factors associated with vertebral osteoporotic fractures in patients with rheumatoid arthritis. Clin Rheumatol. 2020;39(2):357-364. doi:10.1007/s10067-019-04787-9.
17. Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX and the assessment of fracture probability in men and women from the UK. Osteoporos Int. 2008;19(4):385-397. doi:10.1007/s00198-007-0543-5.
18. Lindner L, Callhoff J, Alten R, et al. Osteoporosis in patients with rheumatoid arthritis: trends in the German National Database 2007-2017. Rheumatol Int. 2020;40(12):2005-2012. doi:10.1007/s00296-020-04593-6.
19. Kay J, Upchurch KS. ACR/EULAR 2010 rheumatoid arthritis classification criteria. Rheumatology (Oxford). 2012;51 Suppl 6:vi5-9. doi:10.1093/rheumatology/kes279.
20. Wells G, Becker JC, Teng J, et al. Validation of the 28-joint Disease Activity Score (DAS28) and European League Against Rheumatism response criteria based on C-reactive protein against disease progression in patients with rheumatoid arthritis, and comparison with the DAS28 based on erythrocyte sedimentation rate. Ann Rheum Dis. 2009;68(6):954-960. doi:10.1136/ard.2007.084459.
21. Genant HK, Wu CY, van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res. 1993;8(9):1137-1148. doi:10.1002/jbmr.5650080915.
22. Guañabens N, Olmos JM, Hernández JL, et al. Vertebral fractures are increased in rheumatoid arthritis despite recent therapeutic advances: a case-control study. Osteoporos Int. 2021;32(7):1333-1342. doi:10.1007/s00198-021-05824-7.
23. Vis M, Havaardsholm EA, Haugeberg G, et al. Evaluation of bone mineral density, bone metabolism, osteoprotegerin and receptor activator of the NFkappaB ligand serum levels during treatment with infliximab in patients with rheumatoid arthritis. Ann Rheum Dis. 2006;65(11):1495-1499. doi:10.1136/ard.2005.044198.
24. Stemmler F, Simon D, Liphardt AM, et al. Biomechanical properties of bone are impaired in patients with ACPA-positive rheumatoid arthritis and associated with the occurrence of fractures. Ann Rheum Dis. 2018;77(7):973-980. doi:10.1136/annrheumdis-2017-212404.
25. Moshayedi S, Tasorian B, Almasi-Hashiani A. The prevalence of osteoporosis in rheumatoid arthritis patient: a systematic review and meta-analysis. Sci Rep. 2022;12(1):15844. doi:10.1038/s41598-022-20016-x.
26. Coughlan T, Dockery F. Osteoporosis and fracture risk in older people. Clin Med (Lond). 2014;14(2):187-191. doi:10.7861/clinmedicine.14-2-187.
27. Armstrong C, Swarbrick CM, Pye SR, O'Neill TW. Occurrence and risk factors for falls in rheumatoid arthritis. Ann Rheum Dis. 2005;64(11):1602-1604. doi:10.1136/ard.2004.031195.
28. Clynes MA, Jameson K, Prieto-Alhambra D, Harvey NC, Cooper C, Dennison EM. Impact of rheumatoid arthritis and its management on falls, fracture and bone mineral density

in UK Biobank. Front Endocrinol (Lausanne). 2019;10:817. doi:10.3389/fendo.2019.00817.
29. Bugatti S, Bogliolo L, Vitolo B, Manzo A, Montecucco C, Caporali R. Anti-citrullinated protein antibodies and high levels of rheumatoid factor are associated with systemic bone loss in patients with early untreated rheumatoid arthritis. Arthritis Res Ther. 2016;18(1):226. doi:10.1186/s13075-016-1116-9.
30. Ibañez M, Ortiz AM, Castrejón I, et al. A rational use of glucocorticoids in patients with early arthritis has a minimal impact on bone mass. Arthritis Res Ther. 2010;12(2):R50. doi:10.1186/ar2961.
31. Habib GS, Haj S. Bone mineral density in patients with early rheumatoid arthritis treated with corticosteroids. Clin Rheumatol. 2005;24(2):129-133. doi:10.1007/s10067-004-0989-1.
32. Sambrook PN, Cohen ML, Eisman JA, Pocock NA, Champion GD, Yeates MG. Effects of low dose corticosteroids on bone mass in rheumatoid arthritis: a longitudinal study. Ann Rheum Dis. 1989;48(7):535-538. doi:10.1136/ard.48.7.535.
33. Blavnsfeldt AG, de Thurah A, Thomsen MD, Tarp S, Langdahl B, Hauge EM. The effect of glucocorticoids on bone mineral density in patients with rheumatoid arthritis: a systematic review and meta-analysis of randomized, controlled trials. Bone. 2018;114:172-180. doi:10.1016/j.bone.2018.06.008.
34. Güler-Yüksel M, Hoes JN, Bultink IEM, Lems WF. Glucocorticoids, inflammation and bone. Calcif Tissue Int. 2018;102(5):592-606. doi:10.1007/s00223-017-0335-7.
35. Zerbini CAF, Clark P, Mendez-Sanchez L, et al. Biologic therapies and bone loss in rheumatoid arthritis. Osteoporos Int. 2017;28(2):429-446. doi:10.1007/s00198-016-3769-2.
36. Ozen G, Pedro S, Wolfe F, Michaud K. Medications associated with fracture risk in patients with rheumatoid arthritis. Ann Rheum Dis. 2019;78(8):1041-1047. doi:10.1136/annrheumdis-2019-215328.