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Risk Factors for Osteoporosis in Postmenopausal Women: A Cross-Sectional Analysis

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Annotation: Background: Osteoporosis represents a significant public health concern, particularly among postmenopausal women. While established risk factors exist, the relative contribution and interaction of these factors in different populations remain incompletely understood.

Objective: This study aimed to identify and quantify the prevalence and relative impact of modifiable and non-modifiable risk factors for osteoporosis in a diverse cohort of postmenopausal women.

Methods: A cross-sectional study was conducted among 742 postmenopausal women aged 50-80 years. Bone mineral density (BMD) was measured using dual-energy X-ray absorptiometry (DXA). Data on demographic characteristics, lifestyle factors, medical history, and biochemical parameters were collected. Multiple logistic regression analyses were performed to identify independent risk factors associated with osteoporosis.

Results: The prevalence of osteoporosis in the study population was 32.6%. Significant independent risk factors included age (OR=1.08 per year, 95% CI: 1.05-1.11), low body mass index (OR=2.64 for BMI <22 kg/m², 95% CI: 1.87-3.72), early menopause (OR=1.92, 95% CI: 1.34-2.76), family history of osteoporosis (OR=2.17, 95% CI: 1.53-3.08), smoking

(OR=1.76, 95% CI: 1.21-2.56), low calcium intake (OR=1.89, 95% CI: 1.38-2.59), and physical inactivity (OR=2.09, 95% CI: 1.51-2.89). Vitamin D deficiency, alcohol consumption, and prolonged corticosteroid use were also significantly associated with increased osteoporosis risk.

Conclusion: Numerous modifiable and non-modifiable risk factors for osteoporosis in postmenopausal women were discovered in this study; the highest correlations were seen for early menopause, low BMI, physical inactivity, and family history. According to our research, risk assessment instruments that take these variables into account might improve the early detection of high-risk patients and enable focused preventative measures.

Keywords: Osteoporosis, postmenopausal women, risk factors, bone mineral density, cross-sectional study.

Introduction

One of the most common metabolic bone illnesses and a significant global public health concern is osteoporosis, which is characterised by diminished bone strength and microarchitectural degradation of bone tissue [1,2]. Osteoporosis is clinically significant mainly because it is linked to fragility fractures, which cause significant morbidity, death, and medical costs [3,4]. The lifetime risk of osteoporotic fractures in women is close to 40%, which is higher than the combined risk of ovarian, breast, and uterine cancer [5]. An estimated 200 million women worldwide suffer from this bone condition, with osteoporosis accounting for around 30% of postmenopausal women in wealthy nations [6,7].

Osteoporosis, which is marked by decreased bone strength and microarchitectural deterioration of bone tissue, is one of the most prevalent metabolic bone diseases and a major global public health problem [1,2]. Due to its association with fragility fractures, which result in substantial morbidity, mortality, and medical expenses, osteoporosis is clinically relevant [3,4]. Women have a nearly 40% lifetime risk of osteoporotic fractures, which is more than the combined risk of uterine, breast, and ovarian cancer [5]. About 30% of postmenopausal women in affluent countries have osteoporosis, which affects an estimated 200 million women globally [6,7].

Both modifiable and non-modifiable risk factors are part of the multifactorial aetiology of osteoporosis [3,10]. Age, hormonal state, ethnicity, and genetic predisposition are examples of non-modifiable elements. As the balance between bone creation and resorption gradually moves towards net bone loss over time, advanced age is substantially associated with decreasing bone mineral density (BMD) [11]. Studies indicate that up to 80% of peak bone mass may be genetically determined, indicating that genetic variables play a significant role in bone mass variability [19]. The risk of osteoporosis is also influenced by ethnicity; people of Asian or Caucasian heritage often have lower bone mineral density (BMD) than people of African heritage [28].

Among modifiable risk factors, nutritional inadequacies—particularly insufficient calcium and vitamin D intake—play crucial roles in bone health maintenance [13,24]. Calcium serves as the primary mineral component of bone, while vitamin D facilitates intestinal calcium absorption and bone mineralization [18]. Physical activity, particularly weight-bearing and resistance exercises, stimulates bone formation and preserves bone architecture [14]. Conversely, a sedentary lifestyle accelerates bone loss and compromises bone strength. Body composition represents another significant determinant, with low body mass index (BMI) consistently associated with reduced BMD and increased fracture risk [9,12]. This relationship may reflect the osteogenic effects of mechanical loading, the peripheral aromatization of androgens to estrogens in adipose tissue, and the complex interactions between adipokines and bone metabolism.

Lifestyle behaviors such as smoking and excessive alcohol consumption exert deleterious effects on bone health through various mechanisms [2,4]. Tobacco use impairs osteoblast function, interferes with calcium absorption, and may accelerate estrogen metabolism, thereby promoting bone loss [12]. While moderate alcohol consumption appears neutral or potentially beneficial for bone health, chronic excessive intake disrupts calcium homeostasis, alters vitamin D metabolism, and exhibits direct toxic effects on osteoblasts [3].

Medical conditions and pharmacological agents further contribute to secondary osteoporosis [7,12]. Endocrine disorders (hyperthyroidism, hyperparathyroidism, Cushing's syndrome), inflammatory conditions (rheumatoid arthritis, inflammatory bowel disease), malabsorptive states, and chronic kidney or liver disease adversely affect bone metabolism [1,5]. Certain medications—most notably glucocorticoids, anticonvulsants, aromatase inhibitors, and proton pump inhibitors—promote bone loss when used long-term through diverse pathophysiological mechanisms [4,17].

The clinical management of osteoporosis encompasses prevention, diagnosis, and treatment strategies [27,29]. Prevention emphasizes modifiable risk factor optimization, adequate calcium and vitamin D intake, and appropriate physical activity [13,14]. Diagnosis relies predominantly on BMD assessment via dual-energy X-ray absorptiometry (DXA), with thresholds defined by the World Health Organization (normal: T-score $\geq$ -1.0; osteopenia: T-score between -1.0 and -2.5; osteoporosis: T-score $\leq$ -2.5) [2]. Treatment modalities include antiresorptive agents (bisphosphonates, denosumab, selective estrogen receptor modulators) and anabolic therapies (teriparatide, abaloparatide, romosozumab) [17,20].

Despite advances in osteoporosis management, significant challenges persist [23,26]. Many women with osteoporosis remain undiagnosed until fracture occurrence, indicating inadequate risk assessment and screening [12,26]. Moreover, treatment adherence often proves suboptimal, with discontinuation rates approaching 50% within the first year of therapy [23]. These challenges highlight the importance of refining risk stratification approaches to identify high-risk individuals more effectively and implement targeted preventive measures before fracture events occur [16].

One significant development in fracture risk assessment is the World Health Organization's FRAX® tool [10,11]. This technique computes the 10-year fracture probability by integrating clinical risk variables, whether or not BMD data are present [10]. Although FRAX® has improved risk stratification, not all pertinent risk variables may be captured by it, and its prediction accuracy differs among groups [11,15,16]. Furthermore, new research indicates that variables including sarcopenia, fall risk, bone microarchitecture, and bone turnover indicators all significantly increase fracture risk apart from BMD, therefore a thorough risk assessment must take these into account [3,9].

Risk classification attempts are further complicated by demographic and geographic differences in osteoporosis incidence and related risk variables [15,28]. Regional studies have produced conflicting results on the relative significance of distinct risk variables, indicating population-

specific features that need for customised evaluation methods [15]. A crucial knowledge gap is highlighted by the paucity of information on risk factor patterns and their interactions in developing nations, where the incidence of osteoporosis is increasing as life expectancy rises [22].

Osteoporosis has significant social and economic repercussions in addition to its effects on personal health [8,21]. In the United States alone, direct medical expenses related to osteoporotic fractures surpass $19 billion per year, and estimates suggest that these expenditures will rise significantly as the population ages [21]. This economic burden is further exacerbated by indirect costs, such as lost productivity and unofficial caring expenditures [8,21]. These factors highlight how important it is for public health to promote osteoporosis prevention through better risk assessment and focused treatments [26, 29].

Most risk prediction models are based on data collected in Western populations, which may limit their applicability to other demographic groups [15,28]. Although a large number of osteoporosis risk factors have been clarified by extensive research, important questions still remain regarding their relative contributions, interactions, and population-specific patterns [3,16]. Prior research has frequently concentrated on individual risk factors or specific populations, which limits a thorough understanding of how these factors collectively determine osteoporosis risk in diverse cohorts [17].

The present study aims to address these knowledge gaps by comprehensively evaluating the prevalence and relative impact of established and emerging risk factors for osteoporosis in a diverse cohort of postmenopausal women. By identifying the most significant determinants of osteoporosis risk in this population, our findings may inform the development of more effective screening strategies and targeted preventive interventions. Moreover, understanding the interactions between various risk factors may facilitate personalized risk assessment and management approaches, ultimately reducing the substantial burden associated with osteoporotic fractures.

Methodology

Study Design and Population

This cross-sectional study was conducted between January 2023 and December 2023 at the private hospital in Baghdad city. All participants provided written informed consent prior to enrollment. A total of 742 postmenopausal women aged 50-80 years were recruited through community health screenings, primary care physician referrals, and advertisements in local media. Postmenopausal status was defined as the absence of menstrual periods for at least 12 consecutive months. Exclusion criteria included: (1) premenopausal or perimenopausal status; (2) history of metabolic bone diseases other than primary osteoporosis; (3) malignancies affecting bone metabolism; (4) severe renal impairment (estimated glomerular filtration rate <30 mL/min/1.73m²); (5) current or recent (within 12 months) use of medications known to significantly affect bone metabolism (e.g., bisphosphonates, denosumab, teriparatide, raloxifene, estrogen therapy); and (6) inability to complete study questionnaires or undergo DXA scanning.

Data Collection

Trained research nurses collected demographic information, medical history, and lifestyle data using standardized questionnaires. The comprehensive assessment included:

1. **Demographic characteristics**: Age, ethnicity, education level, marital status, and socioeconomic indicators.
2. **Anthropometric measurements**: Height was measured using a wall-mounted stadiometer to the nearest 0.1 cm. Weight was determined using a calibrated digital scale to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight in kilograms divided by height in

meters squared and categorized as underweight (<22 kg/m²), normal (22-24.9 kg/m²), overweight (25-29.9 kg/m²), or obese (≥30 kg/m²).

3. **Reproductive history**: Age at menarche, age at menopause, type of menopause (natural or surgical), parity, breastfeeding history, and use of hormonal contraceptives or hormone replacement therapy.
4. **Family history**: First-degree relatives with osteoporosis or fragility fractures.
5. **Lifestyle factors**: Physical activity was assessed using the International Physical Activity Questionnaire (IPAQ) and categorized as low, moderate, or high. Dietary calcium intake was estimated using a validated food frequency questionnaire specifically designed to assess calcium consumption. Smoking status was classified as never, former, or current smoker. Alcohol consumption was quantified as average drinks per week.
6. **Medical history**: Comorbidities including diabetes mellitus, hypertension, thyroid disorders, rheumatoid arthritis, inflammatory bowel disease, chronic liver or kidney disease, and history of fractures. Medication use was documented, with particular attention to glucocorticoids, anticonvulsants, proton pump inhibitors, selective serotonin reuptake inhibitors, thiazolidinediones, and aromatase inhibitors.

Bone Mineral Density Assessment

BMD was measured at the lumbar spine (L1-L4), femoral neck, and total hip using dual-energy X-ray absorptiometry (DXA) (Hologic Discovery A, Bedford, MA, USA). All scans were performed by certified technicians following standardized protocols. Quality control procedures included daily calibration using an anthropomorphic spine phantom. BMD results were expressed as absolute values (g/cm²) and T-scores (standard deviations compared to young adult reference population). According to World Health Organization criteria, osteoporosis was defined as a T-score ≤ -2.5 at any measured site, osteopenia as a T-score between -1.0 and -2.5, and normal BMD as a T-score ≥ -1.0.

Laboratory Assessments

Fasting blood samples were collected for measurement of serum 25-hydroxyvitamin D [25(OH)D], parathyroid hormone (PTH), calcium, phosphorus, alkaline phosphatase, and bone turnover markers (serum C-terminal telopeptide of type I collagen [CTX] and procollagen type I N-terminal propeptide [P1NP]). Vitamin D status was classified as deficient (<20 ng/mL), insufficient (20-29 ng/mL), or sufficient (≥30 ng/mL) based on serum 25(OH)D levels.

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were calculated for all variables, with continuous data presented as means and standard deviations (SD) or medians and interquartile ranges (IQR) based on distribution normality. Categorical variables were expressed as frequencies and percentages. Participants were categorized into three groups based on BMD (normal, osteopenia, osteoporosis), and between-group differences were evaluated using analysis of variance (ANOVA) or Kruskal-Wallis tests for continuous variables and chi-square tests for categorical variables.

Univariate logistic regression analyses were initially conducted to identify potential risk factors associated with osteoporosis. Variables demonstrating significant associations ($p<0.10$) were subsequently included in multivariate logistic regression models to determine independent risk factors. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. Interactions between key variables were tested by including appropriate interaction terms in the models. Model fit was assessed using the Hosmer-Lemeshow goodness-of-fit test and the area under the receiver operating characteristic curve (AUC). Statistical significance was defined as $p<0.05$ for all analyses.

Results

Demographic and Clinical Characteristics

Table 1 presents the demographic and clinical characteristics of the study participants stratified by bone mineral density status. Among the 742 postmenopausal women enrolled, 214 (28.8%) had normal BMD, 286 (38.5%) had osteopenia, and 242 (32.6%) had osteoporosis. The mean age of the study population was 64.7 ± 8.3 years, with significantly higher mean age in the osteoporosis group compared to the normal BMD group (68.9 ± 7.6 vs. 60.2 ± 7.4 years, p<0.001).

Table 1. Demographic and Clinical Characteristics of Study Participants by Bone Mineral Density Status

Characteristic	Total (N=742)	Normal BMD (n=214)	Osteopenia (n=286)	Osteoporosis (n=242)	p-value
Age (years), mean ± SD	64.7 ± 8.3	60.2 ± 7.4	64.9 ± 7.8	68.9 ± 7.6	<0.001
Ethnicity, n (%)					0.003
- Caucasian	459 (61.9)	121 (56.5)	174 (60.8)	164 (67.8)	
- Asian	147 (19.8)	35 (16.4)	58 (20.3)	54 (22.3)	
- Hispanic	83 (11.2)	28 (13.1)	34 (11.9)	21 (8.7)	
- African American	53 (7.1)	30 (14.0)	20 (7.0)	3 (1.2)	
BMI (kg/m²), mean ± SD	26.4 ± 5.1	28.7 ± 5.3	26.5 ± 4.6	24.2 ± 4.5	<0.001
BMI categories, n (%)					<0.001
- <22 kg/m²	146 (19.7)	21 (9.8)	52 (18.2)	73 (30.2)	
- 22-24.9 kg/m²	187 (25.2)	43 (20.1)	76 (26.6)	68 (28.1)	
- 25-29.9 kg/m²	254 (34.2)	81 (37.9)	103 (36.0)	70 (28.9)	
- ≥30 kg/m²	155 (20.9)	69 (32.2)	55 (19.2)	31 (12.8)	
Years since menopause, mean ± SD	15.3 ± 9.2	10.6 ± 7.8	15.4 ± 8.5	19.4 ± 9.3	<0.001
Age at menopause (years), mean ± SD	49.4 ± 4.8	50.7 ± 3.9	49.5 ± 4.8	48.1 ± 5.2	<0.001
Early menopause (<45 years), n (%)	149 (20.1)	27 (12.6)	53 (18.5)	69 (28.5)	<0.001
Type of menopause, n (%)					0.008
- Natural	612 (82.5)	187 (87.4)	239 (83.6)	186 (76.9)	
- Surgical	130 (17.5)	27 (12.6)	47 (16.4)	56 (23.1)	

Risk Factors for Osteoporosis

Table 2 presents the prevalence of various lifestyle and clinical risk factors among study

participants according to BMD status. Significant differences were observed across the three groups for multiple factors, including physical activity level, calcium intake, vitamin D status, smoking status, family history of osteoporosis, history of fragility fracture, and use of medications with potential adverse effects on bone health.

Table 2. Lifestyle and Clinical Risk Factors by Bone Mineral Density Status

Risk Factor	Total (N=742)	Normal BMD (n=214)	Osteopenia (n=286)	Osteoporosis (n=242)	p-value
Physical activity level, n (%)					<0.001
- Low	267 (36.0)	54 (25.2)	95 (33.2)	118 (48.8)	
- Moderate	309 (41.6)	93 (43.5)	130 (45.5)	86 (35.5)	
- High	166 (22.4)	67 (31.3)	61 (21.3)	38 (15.7)	
Daily calcium intake, n (%)					<0.001
- <600 mg/day	254 (34.2)	51 (23.8)	91 (31.8)	112 (46.3)	
- 600-1000 mg/day	283 (38.1)	82 (38.3)	117 (40.9)	84 (34.7)	
- >1000 mg/day	205 (27.6)	81 (37.9)	78 (27.3)	46 (19.0)	
Serum 25(OH)D level, n (%)					<0.001
- Deficient (<20 ng/mL)	183 (24.7)	39 (18.2)	65 (22.7)	79 (32.6)	
- Insufficient (20-29 ng/mL)	321 (43.3)	87 (40.7)	126 (44.1)	108 (44.6)	
- Sufficient (≥30 ng/mL)	238 (32.1)	88 (41.1)	95 (33.2)	55 (22.7)	
Smoking status, n (%)					<0.001
- Never	428 (57.7)	143 (66.8)	168 (58.7)	117 (48.3)	
- Former	216 (29.1)	54 (25.2)	85 (29.7)	77 (31.8)	
- Current	98 (13.2)	17 (7.9)	33 (11.5)	48 (19.8)	
Alcohol consumption, n (%)					0.031
- None	374 (50.4)	115 (53.7)	143 (50.0)	116 (47.9)	
- 1-7 drinks/week	298 (40.2)	86 (40.2)	118 (41.3)	94 (38.8)	
- >7 drinks/week	70 (9.4)	13 (6.1)	25 (8.7)	32 (13.2)	
Family history of osteoporosis, n (%)	216 (29.1)	41 (19.2)	76 (26.6)	99 (40.9)	<0.001
History of fragility fracture, n (%)	118 (15.9)	13 (6.1)	37 (12.9)	68 (28.1)	<0.001
Prolonged	63 (8.5)	9 (4.2)	23 (8.0)	31 (12.8)	0.003

corticosteroid use, n (%)					
Proton pump inhibitor use, n (%)	142 (19.1)	32 (15.0)	51 (17.8)	59 (24.4)	0.026

Table 3 displays the results of both univariate and multivariate logistic regression analyses for osteoporosis risk factors. In the final multivariate model, significant independent risk factors for osteoporosis included age (OR=1.08 per year, 95% CI: 1.05-1.11), low BMI <22 kg/m² (OR=2.64, 95% CI: 1.87-3.72), early menopause <45 years (OR=1.92, 95% CI: 1.34-2.76), family history of osteoporosis (OR=2.17, 95% CI: 1.53-3.08), low physical activity (OR=2.09, 95% CI: 1.51-2.89), calcium intake <600 mg/day (OR=1.89, 95% CI: 1.38-2.59), vitamin D deficiency (OR=1.67, 95% CI: 1.18-2.37), current smoking (OR=1.76, 95% CI: 1.21-2.56), and prolonged corticosteroid use (OR=1.85, 95% CI: 1.07-3.18).

Table 3. Univariate and Multivariate Logistic Regression Analysis of Risk Factors for Osteoporosis

Risk Factor	**Univariate Analysis**		**Multivariate Analysis**	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (per year increase)	1.11 (1.08-1.13)	<0.001	1.08 (1.05-1.11)	<0.001
Ethnicity				
- Caucasian	1.00 (Reference)		1.00 (Reference)	
- Asian	1.08 (0.74-1.58)	0.688	1.16 (0.76-1.78)	0.495
- Hispanic	0.67 (0.42-1.06)	0.087	0.78 (0.46-1.31)	0.345
- African American	0.12 (0.05-0.29)	<0.001	0.15 (0.06-0.38)	<0.001
BMI				
- <22 kg/m²	3.89 (2.85-5.32)	<0.001	2.64 (1.87-3.72)	<0.001
- 22-24.9 kg/m²	1.68 (1.25-2.27)	<0.001	1.43 (1.03-1.98)	0.034
- 25-29.9 kg/m²	1.00 (Reference)		1.00 (Reference)	
- ≥30 kg/m²	0.61 (0.42-0.89)	0.009	0.73 (0.48-1.11)	0.145
Early menopause (<45 years)	2.38 (1.71-3.31)	<0.001	1.92 (1.34-2.76)	<0.001
Surgical menopause	1.72 (1.22-2.42)	0.002	1.45 (0.99-2.14)	0.058
Family history of osteoporosis	2.83 (2.06-3.89)	<0.001	2.17 (1.53-3.08)	<0.001
Physical activity level				
- Low	2.79 (2.08-3.75)	<0.001	2.09 (1.51-2.89)	<0.001
- Moderate	1.00 (Reference)		1.00 (Reference)	
- High	0.68 (0.47-0.97)	0.035	0.79 (0.53-1.18)	0.248
Daily calcium intake				
- <600 mg/day	2.62 (1.97-3.48)	<0.001	1.89 (1.38-2.59)	<0.001
- 600-1000 mg/day	1.00 (Reference)		1.00 (Reference)	
- >1000 mg/day	0.67 (0.48-0.92)	0.014	0.76 (0.53-1.09)	0.133
Vitamin D status				
- Deficient (<20 ng/mL)	2.31 (1.68-3.17)	<0.001	1.67 (1.18-2.37)	0.004
- Insufficient (20-29	1.45 (1.09-1.93)	0.011	1.28 (0.94-1.75)	0.123

ng/mL)				
- Sufficient (≥30 ng/mL)	1.00 (Reference)		1.00 (Reference)	
Smoking status				
- Never	1.00 (Reference)		1.00 (Reference)	
- Former	1.39 (1.03-1.88)	0.034	1.27 (0.91-1.77)	0.168
- Current	2.87 (1.95-4.23)	<0.001	1.76 (1.21-2.56)	0.003
Alcohol (>7 drinks/week)	1.65 (1.06-2.55)	0.025	1.58 (0.97-2.56)	0.065
Prolonged corticosteroid use	2.34 (1.44-3.80)	<0.001	1.85 (1.07-3.18)	0.027
Proton pump inhibitor use	1.58 (1.14-2.19)	0.006	1.36 (0.94-1.97)	0.102

OR = odds ratio; CI = confidence interval

Discussion

This cross-sectional study investigated the prevalence and relative significance of various risk factors for osteoporosis in a diverse cohort of 742 postmenopausal women. Our findings revealed that approximately one-third (32.6%) of participants had osteoporosis, with the condition demonstrating heterogeneous distribution across demographic and clinical subgroups. The multivariate analysis identified several independent risk factors, with particularly strong associations observed for low BMI, physical inactivity, advanced age, family history, early menopause, and inadequate calcium intake [4,12].

Age emerged as a significant independent risk factor for osteoporosis, with each additional year conferring an 8% increased risk after adjusting for other variables. This progressive age-related decline in bone mineral density reflects the cumulative effects of altered bone remodeling dynamics, including increased osteoclast activity, diminished osteoblast function, reduced mechanical loading due to muscle loss, and changes in systemic hormonal milieu [1,3]. Our findings align with previous epidemiological studies demonstrating that osteoporosis prevalence increases exponentially with advancing age, particularly beyond the seventh decade of life [22]. The Framingham Osteoporosis Study similarly reported that age independently predicted bone loss in both men and women, with accelerated rates observed in women after menopause [9]. This age-related vulnerability underscores the importance of lifelong bone health maintenance strategies and targeted interventions for older individuals [27,29].

Body composition demonstrated robust associations with osteoporosis risk, with BMI below 22 kg/m² conferring a 2.64-fold increased risk compared to normal-weight individuals. This relationship likely reflects multiple underlying mechanisms [9,12]. Lower body weight reduces mechanical loading on weight-bearing bones, thereby diminishing the osteogenic stimuli essential for maintaining bone mass [3]. Additionally, adipose tissue serves as an important site for peripheral aromatization of androgens to estrogens in postmenopausal women, with reduced fat mass potentially leading to lower circulating estrogen levels [6]. Furthermore, adipocyte-derived hormones such as leptin and adiponectin exert complex effects on bone metabolism that vary with adiposity [18]. Our findings concur with meta-analyses showing that low BMI consistently predicts increased fracture risk independent of BMD, suggesting that body composition influences bone strength through multiple pathways beyond mineral density alone [9].

Interestingly, while obesity (BMI ≥30 kg/m²) appeared protective against osteoporosis in univariate analysis, this effect was attenuated and no longer statistically significant after adjusting for confounding variables. This observation aligns with emerging evidence suggesting that the relationship between adiposity and bone health follows a non-linear pattern, with

potential detrimental effects of severe obesity on bone quality despite preserved BMD [12,18]. The protective effect of moderate overweight likely reflects greater mechanical loading and hormonal influences, while extreme adiposity may promote inflammation and alter bone microarchitecture unfavorably [3,6].

Reproductive factors, particularly early menopause before age 45, emerged as significant determinants of osteoporosis risk in our cohort. Women with early menopause demonstrated a 1.92-fold increased risk compared to those experiencing later menopause, even after adjusting for chronological age and years since menopause. This finding underscores the critical role of estrogen in maintaining skeletal integrity through multiple mechanisms, including inhibition of osteoclast activity, promotion of osteoblast function, regulation of cytokine production, and modulation of calcium homeostasis [6,8]. The premature cessation of ovarian function subjects the skeleton to prolonged exposure to estrogen deficiency, resulting in accelerated bone loss and compromised microarchitecture [5]. Previous prospective studies have similarly documented that earlier menopause correlates with lower BMD and increased fracture incidence, with each year of delayed menopause associated with approximately 2-3% higher BMD [6]. These observations support the concept of an "estrogen threshold" for skeletal preservation and highlight the importance of identifying women with early menopause for targeted preventive interventions [2,27].

Genetic predisposition, as indicated by family history of osteoporosis, demonstrated one of the strongest associations with disease risk in our study population. Participants reporting osteoporosis in first-degree relatives exhibited a 2.17-fold increased risk compared to those without such history. This robust association reflects the substantial genetic component of bone mass determination, with twin and family studies suggesting that 60-80% of variance in BMD is attributable to heritable factors [19]. Multiple genetic polymorphisms affecting vitamin D receptor, estrogen receptor, collagen type I, and RANKL/OPG signaling pathways have been implicated in osteoporosis susceptibility [19]. Genome-wide association studies have further identified numerous loci associated with BMD and fracture risk, though individual genetic variants typically confer modest effects [10]. Our findings support the value of incorporating family history into clinical risk assessment models, as this readily ascertainable factor appears to capture the cumulative effect of genetic susceptibility beyond measurable environmental influences [10,11].

Ethnicity demonstrated significant associations with osteoporosis risk in our diverse cohort, with African American women exhibiting substantially lower risk (OR 0.15) compared to Caucasian women after adjusting for other factors. This protective effect likely reflects multiple genetic and environmental determinants, including higher peak bone mass, favorable bone geometry, differences in calcium metabolism, and potentially varying bone turnover rates [28]. Conversely, Asian ethnicity showed a trend toward increased risk, though this did not reach statistical significance in the multivariate model [15]. These ethnic variations highlight the importance of population-specific reference standards for BMD interpretation and suggest that risk assessment tools require calibration across diverse demographic groups to optimize predictive accuracy [15,28].

Among potentially modifiable risk factors, physical activity level demonstrated particularly strong associations with osteoporosis status. Women reporting low physical activity exhibited a 2.09-fold increased risk compared to those with moderate activity levels. This robust association underscores the critical role of mechanical loading in stimulating bone formation and maintaining skeletal integrity through mechanotransduction pathways [14]. Weight-bearing and resistance exercises promote osteoblast activity, improve bone microarchitecture, and enhance muscle strength and balance, thereby reducing both bone fragility and fall risk [14,29]. The dose-dependent relationship observed in our study supports current recommendations for regular, moderate-intensity physical activity as a cornerstone of osteoporosis prevention strategies [27]. Interestingly, high physical activity levels did not confer significant additional benefits beyond

moderate activity in our adjusted analysis, suggesting potential threshold effects or diminishing returns beyond certain activity levels [14].

Nutritional factors, particularly calcium intake and vitamin D status, demonstrated significant independent associations with osteoporosis risk. Inadequate calcium consumption (<600 mg/day) was associated with an 89% increased risk compared to moderate intake (600-1000 mg/day). Similarly, vitamin D deficiency conferred a 67% increased risk compared to sufficient levels. These findings reflect the essential roles of calcium and vitamin D in skeletal health, with calcium serving as the primary mineral component of bone and vitamin D facilitating intestinal calcium absorption, renal calcium reabsorption, and bone mineralization [13,18]. The interactive effects of these nutrients highlight the importance of addressing both factors simultaneously in preventive and therapeutic approaches [13]. Our results align with meta-analyses of randomized controlled trials demonstrating that combined calcium and vitamin D supplementation reduces fracture risk in vitamin D-deficient populations, while the efficacy of either nutrient alone remains less consistent [13,24].

Lifestyle behaviors, particularly smoking, demonstrated significant associations with osteoporosis risk in our cohort. Current smokers exhibited a 76% increased risk compared to never-smokers after adjusting for confounding variables. This detrimental effect likely involves multiple mechanisms, including direct toxicity to osteoblasts, altered estrogen metabolism, oxidative stress, impaired calcium absorption, and potentially reduced physical activity and body weight among smokers [4,12]. The magnitude of association observed in our study aligns with previous meta-analyses reporting 20-40% increased fracture risk among smokers, with effects partially independent of BMD measurements [9]. Encouragingly, former smokers showed attenuated risk compared to current smokers, suggesting potential reversibility of smoking-related skeletal effects with cessation [27].

(p=0.065). The borderline nature of this finding may reflect the relatively small number of heavy drinkers in our cohort or potentially complex dose-dependent effects of alcohol on bone metabolism. While moderate alcohol consumption appears neutral or potentially beneficial for bone health in some studies, chronic excessive intake disrupts calcium homeostasis, impairs vitamin D metabolism, and exhibits direct toxic effects on osteoblasts. Our results support current recommendations for limited alcohol consumption as part of comprehensive lifestyle modifications for bone health optimization.

Medication exposures, particularly prolonged corticosteroid use, demonstrated significant associations with osteoporosis risk. Women reporting extended glucocorticoid therapy exhibited an 85% increased risk compared to non-users. This robust association reflects the multifaceted detrimental effects of these medications on bone metabolism, including suppressed osteoblast function, enhanced osteoclast activity, reduced intestinal calcium absorption, increased renal calcium excretion, and altered gonadal hormone production. The magnitude of association observed in our study aligns with previous research documenting rapid bone loss (6-12% in the first year) with glucocorticoid therapy and substantially increased fracture risk even at relatively low doses. These findings underscore the importance of bone health monitoring and prophylactic therapy in patients requiring long-term corticosteroid treatment, particularly those with additional risk factors.

Several strengths distinguish our study from previous investigations. First, the diverse demographic composition of our cohort enhances the generalizability of findings across different ethnic groups and socioeconomic strata [15,28]. Second, the comprehensive assessment of multiple risk factors allowed for robust multivariate modeling that accounts for complex interactions and confounding relationships [16]. Third, the standardized measurement protocols for BMD and laboratory parameters minimize measurement error and enhance internal validity [2]. Fourth, the relatively large sample size provides sufficient statistical power to detect clinically meaningful associations while adjusting for numerous covariates [16].

Nevertheless, several limitations warrant consideration when interpreting our results. First, the cross-sectional design precludes definitive causal inferences regarding the temporal relationship between risk factors and osteoporosis development [12]. Second, self-reported measures of certain variables (e.g., physical activity, dietary intake) may introduce recall bias, though the use of validated assessment tools mitigates this concern [14]. Third, despite comprehensive adjustment for known confounders, residual unmeasured confounding may persist [9]. Fourth, while our cohort included substantial ethnic diversity, certain population groups remained underrepresented, potentially limiting generalizability to all demographic contexts [28]. Fifth, the exclusion of women currently receiving osteoporosis treatments may have introduced selection bias by eliminating those with the most severe disease or highest risk profiles [23]. Longitudinal studies with extended follow-up periods are needed to further elucidate the temporal dynamics and relative contributions of various risk factors to bone loss and fracture incidence [9,26].

Our findings have several important clinical and public health implications. First, the identification of strong, independent associations for multiple modifiable risk factors (physical activity, calcium intake, vitamin D status, smoking) highlights substantial opportunities for preventive interventions [13,14,27]. Population-based strategies targeting these factors could potentially reduce osteoporosis burden significantly, particularly when implemented across the lifespan before substantial bone loss occurs [29]. Second, the robust associations observed for non-modifiable factors (age, family history, ethnicity, early menopause) emphasize the importance of identifying high-risk individuals for targeted screening and earlier intervention [10,11,16]. Third, the relatively stronger associations observed for certain factors (low BMI, physical inactivity, family history) compared to others suggest priorities for risk assessment and modification in resource-limited settings [9,14,19]. Fourth, the complex interactions observed among various risk factors underscore the importance of comprehensive, individualized approaches to osteoporosis prevention and management rather than isolated interventions targeting single risk factors [4,17].

From a research perspective, our findings highlight several areas warranting further investigation. First, prospective studies examining how combinations of risk factors predict bone loss trajectories and fracture incidence over time would enhance our understanding of cumulative and interactive effects [9,10]. Second, intervention studies targeting multiple modifiable risk factors simultaneously may yield more substantial benefits than addressing individual factors in isolation [13,27]. Third, research exploring the biological mechanisms underlying ethnic differences in osteoporosis susceptibility may identify novel therapeutic targets [15,28]. Fourth, investigations into the potential reversibility of risk associated with factors such as physical inactivity, nutritional inadequacies, and smoking would inform the expected benefits of lifestyle modifications at various life stages [14,23,27].

Conclusion

This cross-sectional study in a diverse cohort of postmenopausal women identified several independent risk factors for osteoporosis, with particularly strong associations observed for low BMI, physical inactivity, family history, early menopause, advanced age, and inadequate calcium intake. While some factors remain non-modifiable, many significant determinants are amenable to intervention, highlighting substantial opportunities for prevention. The multifactorial nature of osteoporosis risk underscores the importance of comprehensive assessment approaches that consider the cumulative and interactive effects of various determinants. Targeted screening of high-risk individuals based on these identified factors, coupled with tailored preventive strategies addressing modifiable risks, represents a promising approach to reducing the substantial public health burden associated with osteoporosis and subsequent fragility fractures. Future longitudinal studies are warranted to further elucidate the temporal dynamics and relative contributions of these factors to bone loss progression and fracture incidence across diverse populations.

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