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Original article

Assessment of Risk Factors of Osteoporotic Fractures among Egyptian Patients

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Abstract

Aim: To study and assess the risk factors for fractures in the osteoporotic Egyptian patients older than 40 years. **Methods:** Forty eight persons (> 40 years old) were included. They underwent complete clinical evaluation and laboratory analyses of serum calcium (Ca^{+2}) and vitamin D (Vit. D) levels, with assessment of the bone mineral density (BMD) using the Dual Energy X-ray Absorptiometry scanner (DEXA). They were divided into two groups: a **patients' group** including 27 osteoporotic patients having fractures and **a control group** including 21 osteoporotic cases without fractures. **Results:** The percentage of females was higher in both groups (74.1% and 61.9%. p=0.36).The mean age was significantly higher in the patients' group (mean ± SD 62.11 ± 6.6 ***vs***53.48 ±6.7 years), while the mean height was significantly lower (p<0.05). The weight and body mass index (BMI) were comparable between both groups (p>0.05). About 70.4% of osteoporotic patients had their fractures from minor traumas; meanwhile the control had no fractures even with minor or moderate traumas. The T-score, Z-score and the BMD were significantly lower in the patients (p<0.05). In addition, Vit. D and Ca^{+2} levels were significantly lower (p<0.05). A positive family history of fractures was significantly higher in the patients (p=0.013), while no other risk factor was significantly different between both groups. **Conclusion:** An advanced age, a short stature, a positive family history, traumas, and low Vit. D and Ca^{+2} levels are major risk factors associated with a low BMD and osteoporotic fractures in the adult Egyptian population.

Keywords: Osteoporosis; Vit. D; fractures; trauma

Introduction

Osteoporosis (OP) is defined as a systemic skeletal disease characterized by a decreased bone strength leading to an increased risk of fracture ***(1)***. The disease can cause a significant physical disability ***(2)*** and is associated with an increased mortality ***(3)***.

Osteoporotic fractures are a major and an increasing cause of morbidity that pose a considerable burden on health services ***(4)***. Risk factors are present before the occurrence of fractures and often provide insights regarding the etiology of bone fragility and fracture. For osteoporotic fractures, there are at least two etiologic mechanisms: low bone density and the frequency and type of falls. Intervention to modify etiologic risk factors can help to prevent fractures. Risk factors for fracture can also be used to identify which persons are at greatest risk that would benefit from preventive therapy before fractures occur. Low bone density is an important risk factor for osteoporotic fractures, and its association with fracture risk is discussed elsewhere in this issue ***(5)***.

OP is asymptomatic until fracture occurs but may be diagnosed using DEXA. Most countries have adopted a case-finding strategy whereby persons with one or more risk factors for OP may be referred for a DEXA scan. This strategy, however, does not perform well, because OP remains underdiagnosed and undertreated in the world ***(6)***. However, intervention thresholds determined on hip fracture risk alone would neglect many other fractures that occur, particularly in younger age groups where the pattern of fractures differs from the elderly. Even in the elderly, hip fractures represent less than 50% of all fractures in men and women aged 80 years or more ***(7)***.

Thus, public health measures that focus on hip fracture underestimate considerably the burden of other fractures ***(8)***.

Patients and Methods

Design and population:

This prospective study was conducted on patients with OP; it was carried out at Benha university hospitals in the period from December 2019 to May 2021. Total number of included population was 48 more than 40 years old. After completing the clinical and investigational assessment, patients were divided into two groups; **a patients' group** that included 27 osteoporotic patients with fractures (in the hip, spine or forearm) and **a**

control group that included 21 osteoporotic cases without fractures.

Ethics and Inclusion/ Exclusion criteria:

The Ethics and Research Committee of the Benha Faculty of Medicine gave an approval to our study (MS 17-11-2019). Patients who presented with osteoporotic fractures to the Rheumatology, Rehabilitation and Physical medicine department or the Orthopedic department of Benha university hospital were enrolled in the study. The method of our study was explained to all the patients, and they signed a written informed consent to participate in the study.

Inclusion criteria:

- Proven cases to have OP by radiological studies.
- Age > 40 years.
- Cases with or without fractures either in the hip, spine, or forearm.

Exclusion criteria:

- Patients with a medical history of any chronic illness.
- Patients with impaired renal or liver functions.
- Patients with a history of medications that may predispose to OP such as corticosteroids, anticonvulsants, or gonadotropin-releasing hormone agonists.
- Pregnant women.
- Patients presented with violent traumas or pathological fractures.

Methods:

All the patients were subjected to complete history taking and clinical evaluation including:

- The history of smoking(current, past, or never), alcohol use, medications (such as steroids: oral glucocorticoids > 3 months duration at a dose of prednisolone ≥ 5 mg daily or equivalent doses of other glucocorticoids),
- Previous fractures(including a fracture occurring spontaneously or due to a trauma that would not cause fracture in an otherwise healthy individual with classification of their type of trauma as minor, moderate or severe) or a family history of fractures in the first-degree relatives,
- Consumption of dairy products, degree of sun exposure (poor for non-exposure,

fair for once per week exposure of arms and legs, good for twice or more exposure of arms and legs between the hours of 10 am and 3 pm),

- Medical history of rheumatoid arthritis (RA), history of medication use, history of previous fracture was taken. Also,
- General clinical examination for all the patients including height, body weight and BMI (calculated according to the formula: weight in kg /height in m^2) that stratified into four categories: Underweight<18.5 kg/m^2, Normal 18.5 to 24.9 kg/m^2, Overweight 25.0 to 29.9 kg/m^2 and Obese ≥30.0 kg/m^2 ***(9)***.
- Laboratory investigation**:** serum calcium (total and ionized) ***(10)*** and Vit. D levels that were measured according to thefollowing ranges for the classification of 25-OH Vit. D status: Deficiency; 0-20 ng/ml, Insufficiency; 21-29 ng/ml, Sufficiency; 30-100 ng/ml and Toxicity; > 100 ng/ml ***(11)***.
- Assessment of the BMD measured by the dual X-ray absorptiometry scanner (Medilink Medix DR System) at the forearm (wrist, distal radius, and distal ulna), the lumbar spine (L1 through L4) and the non-dominant hip (femoral neck, trochanter, and total hip), calculation of the T-scores representing comparisons with young adults: [(Normal: ≥ –1.0 SD), (Osteopenia: < –1.0 > –2.5 SD), (Osteoporosis ≤ –2.5 SD) and (severe osteoporosis: ≤ –2.5 SD with a fragility fracture and of the Z-scores representing comparisons with age-matched norms ***(6)***.
- Presence of other major osteoporotic fractures (within the spine or forearm) had been defined.

Data management and Statistical Analysis

Data were collected and entered to the computer using SPSS (Statistical Package for Social Science) program for statistical analysis (Chicago, Inc, Illinois, program for statistical analysis version 18). Data were entered as numerical or categorical as appropriate.

Quantitative data were shown as mean± standard deviation (SD) (minimum-maximum). Qualitative data were expressed as frequency and percent (%).Chi- square test and Fisher exact test were used to measure association between qualitative variables. The Mann Whitney U test was done to compare 2 sets of quantitative data non-parametrically distributed. Independent

sample t- test was done to compare 2 sets of quantitative data parametrically distributed and the Spearman correlation test was used to assess the correlation between quantitative variables. Multivariate logistic regression analysis was done to predict the independent risk factors for the occurrence of fractures in osteoporotic patients. P (probability) value was considered of a statistical significance if it is ≤ 0.05.

Results

In all the studied groups 33 patients (68.8%) were females and 15 patients (31.3%) were males with a mean age of 58.3 ± 7.9 years ***(Table 1)***. The mean age was significantly higher in patients with fractures (p<0.05), while the gender was comparable between both groups (p>0.05).

In group of osteoporotic patients with fractures (case group) included 27 patients divided into 12 spine fractures (44.4%), 8 hip fractures (29.6%), 7 forearm (25.9%).

Fractures from minor traumas were more significantly prevalent in the patients' group (p<0.05) with a significantly higher positive family history of fractures (p<0.05). Other risk factors such as smoking, sun exposure, BMI, and comorbidities were comparable between both groups (p>0.05) ***(Table 2)***.

The mean height, vitamin-D and calcium levels were significantly lower in patients with fractures (p<0.05), ***Figure (1)***, while the weight and BMI were comparable between both groups (P>0.05),

The T-score of forearm and spine, the Z-score of the forearm and the BMD of the spine were significantly lower in the patients with fractures (p<0.05) ***(Figure 2; Table 3)***.

A correlative analysis of the BMD with the patients' parameters showed a significant positive correlation between the patients' height and the BMD of the forearm (***r***= 0.29, p= 0.041), spine (***r***=0.34, p= 0.02) and the femur (***r***=0.31, p= 0.03). The total Ca^{+2} level also positively correlated significantly with the BMD of the forearm (***r***=0.35, p=0.01) and spine (***r***= 0.33, p= 0.02). A highly significant negative correlation of the patients' age was only found with the forearm BMD (***r***= -0.54, p= <0.0001) (***Table 4).***

Multivariate regression analysis showed that the patients' height, Ca^{+2} level, and the T-score are independent risk factors for the occurrence of fractures (***Table 5).***

Table 1: Sex and age distribution in osteoporotic patients with and without fractures

		Group			
		Patients N=27	Controls N=21	X^{2*}	P-value**
Sex	Males	7 (25.9%)	8 (38.1%)	0.814	0.367
	Females	20 (74.1%)	13 (61.9%)		
Age (years)	Mean ± SD	62.11 ± 6.6	53.48 ± 6.76	t= 4.448	<0.0001

*chi- square test

**P (probability) value was considered to be of statistical significance if it is ≤0.05

Table 2: Proposed risk factor of fractures in patients with and without fractures

		Group		X^{2*}	P-value**
		Patients N=27	Controls N=21		
Smoking	Non-smoker	21 (77.8%)	15 (71.4%)	0.254	0.614
	Smoker	6 (22.2%)	6 (28.6%)		
Sun exposure	Good	5 (18.5%)	6 (28.6%)	2.259	0.323
	Fair	10 (37%)	10 (47.6%)		
	Poor	12 (44.4%)	5 (23.8%)		
BMI	Obese	11 (40.7%)	10 (47.6%)	1.431	0.489
	Overweight	12 (44.4%)	6 (28.6%)		
	Normal	4 (14.8%)	5 (23.8%)		
Comorbidities	No comorbidity	5 (18.5%)	10 (47.6%)	5.849	0.119
	DM	1 (3.7%)	0 (0%)		
	HTN	8 (29.6%)	6 (28.6%)		
	HTN−DM	13 (48.1%)	5 (23.8%)		
Type of trauma	Minor trauma	19 (70.4%)	5 (23.8%)	10.24	0.001
	Moderate trauma	8 (29.6%)	16 (76.2%)		
Family history of fractures	Present	13 (48.15%)	3 (14.29%)	6.1	0.013
	Absent	14 (51.85%)	18 (85.71%)		

*chi- square test

**P (probability) value was considered to be of statistical significance if it is ≤0.05

Table 3: Bone mineral density scores in patients with and without fractures

	Patients N=27 Mean ± SD	Controls N=21 Mean± SD	Mann-Whitney U test	P-value
T score (forearm)	-2.64 ± 1.32	-1.16 ±0.85	4.448	<0.0001
Z score (forearm)	-1.42 ± 1.19	-0.447 ±1.02	3.003	0.004
BMD	0.32 ± 0.48	0.499 ±0.058	1.648	0.106
T score_A (spine)	-2.44 ± 1.039	-1.43 ±1.32	2.962	0.005
Z score_A (spine)	-1.54 ± 1.105	-0.881 ±1.25	1.944	0.058
BMD_A	0.709 ±0.112	0.839 ±0.177	3.113	0.003
T score_B(femur)	-0.57 ±2.038	-0.128 ±1.003	0.917	0.364
Z score_B(femur)	0.066 ± 2.32	0.266 ±0.946	0.370	0.713
BMD_B	0.938 ±0.35	0.976±0.152	0.468	0.642

*by Mann-Whitney U test
*Abbreviations: BMD; bone mineral density, SD; standard deviation.
*P value is significant if it is ≤ 0.05.

Table 4: Correlations of the BMD score with the patients' parameters

	Correlations					
	BMD (Forearm)		**BMD-A (Spine)**		**BMD-B (Femur)**	
	r	**P**	***r***	**P**	***r***	**P**
Age	-0.540	<0.0001	-0.251	0.086	-0.226	0.123
Weight	0.031	0.833	0.141	0.340	0.051	0.731
Height	0.296	0.041	0.337	0.019	0.309	0.033
BMI	-0.103	0.485	-0.069	0.642	-0.100	0.501
Vit.D	0.269	0.064	0.128	0.387	0.271	0.063
Total Ca	0.352	0.014	0.330	0.022	0.269	0.064
Ionized Ca	0.216	0.140	0.177	0.228	0.074	0.618

*BMI= body mass index, P>0.05= insignificant difference.

Table 5: Multivariate regression analysis for risk factors of fractures

	B	S.E.	Wald	df	Sig.	Exp(B)
Age	-0.142	0.156	0.827	1	0.363	0.868
Height	0.472	0.240	3.848	1	0.050	1.603
Vit.D	0.036	0.073	0.236	1	0.627	1.036
Total Ca	4.629	1.867	6.145	1	0.013	102.3
Ionized Ca	1.758	0.990	3.457	1	0.046	5.80
T score	6.735	3.032	4.934	1	0.026	841.5
Z score	-3.382	1.767	3.963	1	0.048	0.034
T score A	1.129	0.985	1.314	1	0.252	3.093
BMD-A	25.806	15.774	2.676	1	0.102	1.612

* P>0.05= insignificant difference, P<0.05= significant difference.

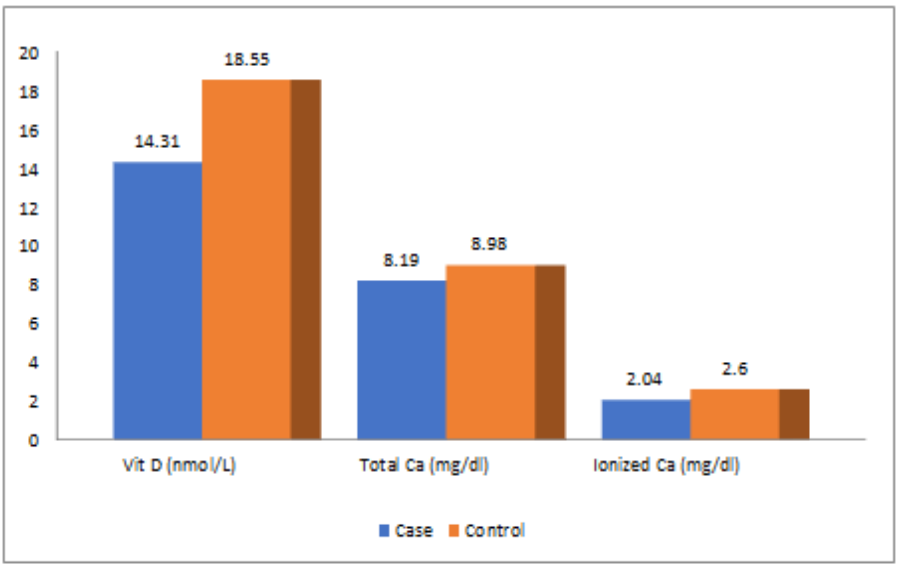

Figure 1: Bar chart showing the vitamin-D and calcium levels in patients with and without fractures

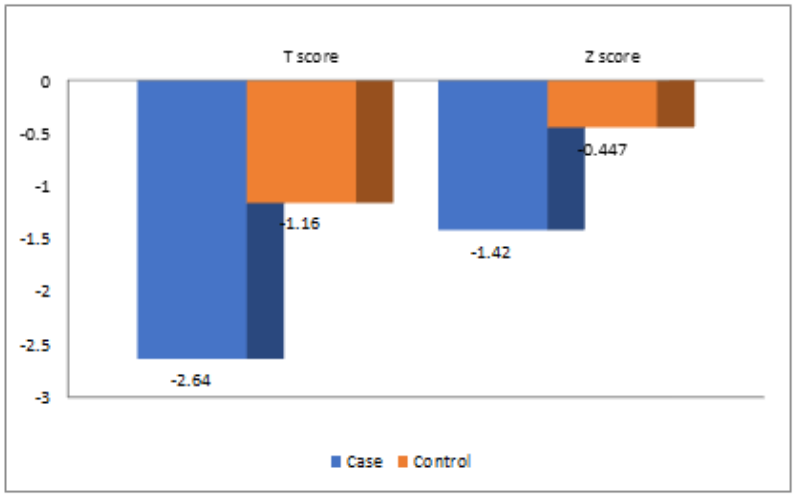

Figure 2: Bar chart showing the T and Z scores in patients with and without fractures

Discussion:

Osteoporotic fractures are defined as fractures associated with a low BMD and they clinically include spine, hip, forearm, and shoulder fractures ***(12)***.

The development of intervention thresholds for OP requires a consideration of the threshold of fracture risk at which intervention is appropriate ***(13)***.

Our study was conducted to assess the risk factors for osteoporotic fractures in Egyptian patients older than 40 years.

Regarding our demographic data, the mean age was significantly higher in patients with fractures ($p<0.05$), while the gender was comparable between both groups ($p>0.05$).

Fragility fractures are a significant public health problem in the entire world. The incidence of OP-related fractures, especially hip fractures, increases with age and are associated with significant reductions in the quality of life and high mortality ***(14)***.

Smoking is one of the most important lifestyle factors that reduce bone mass ***(15)***. It is a modifiable risk factor that should be appraised when assessing individual fracture risk ***(16)***. However, in our study only 25% of patients were smokers. This is concordant with a similar study on osteoporotic patients which also reported that 3.8% of their studied group were smokers ***(17)***.

Remarkably, another study reported that current smoking was associated with a significantly increased risk of any fracture compared with non-smokers***(4)***. Consequently, current smoking was included as a risk factor in the World Health Organization methodology for calculating the absolute risk of fracture with Fracture Risk Assessment Tool (FRAX) ***(15)***.

Our study showed that the mean of the height was significantly lower in the patients with fractures ($p<0.05$), while the weight and BMI were comparable between both groups ($p>0.05$).

Compared to a previous study ***(17),*** their subjects had markedly lower BMI, with 8.4 % underweight and 2.0 % obesity, and a higher incidence rate of vertebral fracture.

In our study, 5 patients (18.5%) had no co-morbidities, 11 (40.7%) were obese and 13 (48.1%) had a combined diabetes mellitus (DM) and hypertension compared to 10 (47.6%), 10 (47.6%) and 5 (23.8%) respectively in the control group.

According to a previous study ***(18)***, DM was associated with fractures in both the case and control groups. Osteoporotic fracture rates were greater in cases than in the controls.

In our study, a positive family history of fractures was significantly higher in the patients' group ($p<0.05$).

A previous study***(19)*** confirmed a high prevalence of Vit. D insufficiency in patients with hip fractures and showed that Vit. D plays an important role in the occurrence of hip fractures in these patients, and especially when they also suffer from osteoporosis.

In the patients' group, fractures occurred in 70.4% significantly more ($p<0.05$) due to minor traumas.

A former study ***(20)*** showed that in Western cohorts of older women and men, annual prevalence rates of low-impact falls were within the range of (0.217–0.625). Fall prevalence rates were 20% lower in men than in women. A median of 4.1% of low-impact falls resulted in fractures in cohorts of Western women and men. The percentages of all low-trauma fractures attributable to low-impact falls and all fractures that were osteoporotic were similar, ranging from 86.0 to 95.0% and 71.6 to 92.4%, respectively.

The BMD is one of the major determinants of fracture risk. Interestingly, it was shown that, compared with Caucasians, the Asian women usually had similar or somewhat lowered BMD, but a comparable rate of spinal fractures, and even a much-lowered rate of hip fractures; this may be an effect of body/bone size ***(21)***.

The DEXA scan was used in our study, and it is currently the test of choice for measuring BMD ***(22)*.**

Our results for measuring the BMD in the forearm, hip and spine in the Egyptian population showed that the forearm mean BMD was $0.32 \pm 0.48 gm/cm^2$. The spine mean BMD was 0.709 ± 0.112 gm/cm^2. The femur mean BMD was 0.938 ± 0.35 gm/cm^2. The BMD of the spine was significantly lower in patients with fractures ($p<0.05$). These results matched other studies ***(23&24).***

Limitations of the study:

- Small number of studied cases.
- The Fracture Risk Algorithm (FRAX) which is a diagnostic tool used to

evaluate the probability of bone fracture was not used in our study.

- In this study, we should have included some basic laboratory investigations e.g., serum creatinine, alkaline phosphatase, phosphorus, testosterone in men, thyroid stimulating hormone and 24 hours urinary Ca.

Conclusion and Recommendation

An advanced age, a short stature, a positive family history, traumas and a low Vit. D and Ca^{+2} levels were major risk factors associated with a low BMD and osteoporotic fractures.

The clinical use of these parameters to identify patients at a higher risk for fractures might be a reasonable strategy to decrease the impact of OP on the community.

We recommend formulating of public health policies for the prevention and early treatment strategies of OP and resource allocations to minimize the direct and indirect costs associated with osteoporotic fractures.

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