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The inter-relationship of the triad: osteoporosis, fracture risk, and obesity—a longitudinal multicenter analysis by the Egyptian Academy of Bone Health

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Abstract

Purpose To assess the relationship between the triad of obesity, fracture risk factors, and osteoporosis and its impact on fragility fractures.

Results Osteoporosis was least prevalent ($p < 0.001$) among the obese patients in comparison to overweight and normal body mass index patients. On the other hand, history of risk of falling as well as history of fall(s) in the last year, sarcopenia, and functional disability were significantly more prevalent (< 0.01, 0.05, and 0.05 respectively) among the obese patient cohort.

Conclusion Obesity was found to be associated with higher bone mineral density of the hip, lumbar spine, and distal forearm. This was significantly different in post-menopausal women, but not in men. Covariates such as sarcopenia, falls risk, and functional disability play an important factor in making the patient at high risk and prone to develop a fragility fracture.

Keywords Obesity, Hip fracture, Osteoporosis, DXA, Fracture risk, FRAX, Sarcopenia, Falls, FRAS, Egyptian Academy of Bone Health, Egypt

Background

The pace of population aging is much faster than any time passed. By 2050, worldwide, the number of older adults over 60 years old is expected to double (from 901 million in 2015 to 2.1 billion); 80% of them will be in low- and middle-income countries [1]. However, it is necessary that longevity is associated with healthy aging. Globally, the incidence of osteoporosis-related fractures has been predicted to increase with the expansion of aging population [2, 3]. In concordance, aging was reported to be associated with an increase in truncal obesity, a major contributor to metabolic syndrome and insulin resistance. Consequently,

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obesity has been linked to several of the age-related diseases and thus has become a serious concern for both the population and the policy makers [4]. Together, osteoporosis and obesity have been linked with excess mortality [5–7], besides being among the commonest causes of disability and morbidity worldwide [8].

Obesity was previously thought to have positive effect on age-related osteoporosis as overweight individuals possess higher bone mineral density. This positive effect has been explained by the high mechanical loading on bones, higher bone mineral density, and fat padding effect around the hips [9–12]. However, this assumption has recently been increasingly questioned. Lack of association between risk of vertebral fracture and body mass index (BMI) was reported in a meta-analysis of 6 studies [13]. Furthermore, several clinical risk factors besides age, gender, and menopausal status have been suggested as covariates that might have an impact on the development of low trauma fractures [14, 15]. This study examines the relationship between the triad of obesity, fracture risk factors, and osteoporosis and its impact on fragility fractures.

Methods

Study population

This was a population-based multicenter cross sectional prospective epidemiological study. Men and women of 50 years old and older who presented with a fragility fracture and managed under the fracture liaison service (FLS) program in Egypt were recruited for this work consecutively. All the patients were managed and monitored prospectively according to the Egyptian FLS standards [16]. Longitudinal analysis of the currently accessible 2-year data (2021–2023) recorded on the national register was carried out.

Case definition

Patients 50 + years old who attended the trauma clinic/accident and emergency as well as those who were admitted to the hospital with fragility fractures whether major osteoporotic fracture or hip fracture were recruited for this study.

Eligibility criteria

Inclusion criteria: Egyptian patients, either male or female, above 50 years of age, presenting with fragility fractures.

Exclusion criteria: we excluded persons with pathological fractures, with history of high impact trauma, and those on anti-osteoporotic medications.

Patients' assessment

Clinical evaluation

All patients were subjected to the following: (a) a structured baseline questionnaire that included complete history, including smoking history, alcohol use, current medications, previous fracture, or parents' history of fracture; (b) general clinical examination including the calculation of BMI and review of systems—according to the BMI, in kg/m^2, patients were classified into 4 classes: underweight (< 18.49), normal weight (18.5–24.99), overweight (25.0–29.9), and obese class I/II (> 30.0) [13]—(c) evaluation of the musculoskeletal system; (d) assessment of risk factors for fragility fractures including fracture risk assessment (FRAX) factors; (e) fall risk assessment was done using the falls risk assessment (FRAS) questionnaire [17]; (f) sarcopenia risk using sarcopenia self-reported (SARC-F) questionnaire [18]; (g) functional disability using Health Assessment Questionnaire (HAQ) [19].

Evaluation of bone mineral density

Dual x-ray absorptiometry (DXA) scanner was used to measure the bone mineral density (BMD) at two sites:the lumbar spine (L1 through L4) and non-dominant hip (femoral neck, trochanter, and total hip)—and *Z*-scores and *T*-scores were scored.

In case the patient may have more than one fragility fracture, analyses were adjusted for baseline FRAX parameters recorded at the time of first fragility fracture.

Outcomes

The primary outcome was comparison of fracture risk as identified by FRAX (Egypt FRAX) [20] (https://www.fraxplus.org/calculation-tool/) and bone mineral density in relation to the body mass index stratified into 3 categories: normal, overweight, and obese. Secondary outcomes were as follows: (1) assessing whether there are gender differences in relation to the body mass index and fracture risks and bone mineral density; (2) what are the covariants that might affect the relation between the BMI and osteoporotic fractures.

Statistical analysis

Statistical analyses were performed using the 26th version of SPSS. Data was checked for missing and consistency before statistical analysis was conducted. All collected categorical data were described as frequency

and percentages. Quantitative data were described as mean and standard deviation. Chi-square test was used for categorical variables to compare between different groups, and p value was always set at ≤ 0.05. Additionally, multivariate regression analysis was performed, Omnibus test was used to test the significance, and Hosmer and Lemeshow test was used for goodness of fit.

Results

Basic characteristics

Two hundred sixty-four patients were included in this study, 72 males and 192 females. The mean age of the men was 70.5 ± 9.415 years, whereas the mean age of the women was 71.03 ± 9.389 years. Analysis of the patients' data revealed that no patients with chronic liver or kidney diseases were included in the study. Glucocorticoid dose taken by the patients included in the study was in the range of 2.5–5 mg; there were no patients taking oral glucocorticoids more than 5 mg/day. Data showing systemic diseases as well as history of smoking among the patients included in the study are demonstrated in Table 1. Osteoporosis was the least prevalent among the obese patients in comparison to overweight and normal BMI patients (Table 2). On the other hand, history of fall(s) in the previous year, sarcopenia, and functional disability were more prevalent among the obese patient cohort.

Table 1 Risk factors among the studied groups

	Sex		Total No. = 264	*p* value
	Male No = 72	Female No = 192		
Diabetes mellitus	31 (23.2%)	55 (34.7%)	86 (32.5%)	**0.04**
Hypertension	18 (13%)	75 (39%)	93 (35.2%)	**< 0.001**
Rheumatoid arthritis	2 (2.7%)	8 (4.1%)	10 (3.78%)	1.000 NS
Low-dose glucocorticoid intake (less than 5 mg)	6 (8.3%)	17 (8.8%)	23 (8.7%)	0.913 NS
Smoking	28 (38.8%)	7 (3.6%)	52 (13.2%)	**< 0.001**

Bold values indicate statistical significance at $p \leq 0.05$

DXA scan results and gender differences

BMD was significantly higher in obese postmenopausal women at all sites: forearm, spine, hip, and neck of the femur (Table 2). In contrast, in men, there was no difference on comparing the BMD between the obese, overweight, and normal BMI patients. Table 4 shows a comparison of the fracture risks among the males and females included in this study stratified according to their BMI.

Risk factors

Although the fracture risk was lower in obese patients (Tables 2 and 3), sarcopenia risk, functional disability (Tables 3 and 4), and falls risk (Table 5) were significantly higher in the obese patients in comparison to the overweight and normal weight patients.

Though osteoporosis, defined as t-score ≤ 2.5, was less encountered among obese ($p < 0.01$), the incidence of fracture was higher but not significant among obese patients compared to the overweight and non-obese (47.8%, 46% and 33% respectively). Moreover, multivariable regression analysis showed no significant independent effect of obesity on the incidence of fracture

Table 2 Prevalence of osteoporosis (T-score < − 2.5 at either hip or spine) of the study cohort stratified according to their BMI

		Normal weight [*N* = 75] *N* (%)	Overweight [*N* = 87] *N* (%)	Obese [*N* = 90] *N* (%)	*p* value
Forearm OP	Male	11 (73.3)	9 (56.3)	5 (41.7)	0.249 NS
	Female	20 (76.9)	23 (82.1)	15 (44.1)	**0.003**
	Total	31 (75.6)	32 (72.7)	20 (43.5)	**0.002**
Spine OP	Male	6 (37.5)	7 (43.8)	4 (33.3)	0.353
	Female	22 (84.6)	22 (78.6)	11 (32.4)	**< 0.001**
	Total	28 (61.9)	29 (65.9)	15 (32.6)	**0.011**
Hip OP	Male	8 (50)	7 (43.8)	5 (41.7)	0.541 NS
	Female	17 (65.4)	10 (35.7)	12 (34.3)	**0.031**
	Total	23 (54.8)	17 (38.6)	19 (40.4)	0.257 NS
Neck of femur op	Male	4 (30.8)	0	1 (33.3)	0.357 NS
	Female	10 (55.6)	9 (42.9)	12 (60.0)	**0.03**
	Total	14 (45.2)	9 (34.6)	13 (56.5)	**0.03**

Bold values indicate statistical significance at $p \leq 0.05$

OP, osteoporosis *BMI*, body mass index

Table 3 Obesity and fractures: comparison of the fracture risks assessed by FRAX among the study cohort stratified according to their BMI

	Normal weight [*N* = 75] *N* (%)	**Overweight [*N* = 87] *N* (%)**	**Obese [*N* = 90] *N* (%)**	***p* value**
History of fragility fracture	25 (33.3)	40 (46.0)	43 (47.8)	0.134 NS
Last year fall	32 (42.7)	48 (55.2)	61 (78.8)	**0.01**
FRAX[a]				**0.007**
No risk	5 (10.2)	9 (10.3)	17 (18.9)	
Intermediate risk	12 (24.5)	19 (21.8)	35 (38.9)	
High risk	32 (65.3)	35 (40.2)	26 (28.9)	
Sarcopenia (high risk)	31 (40.8)	47 (54.0)	63 (70)	**0.05**
Functional disability (high risk) by HAQ	31 (40.8)	38 (43.7)	59 (65.6)	**0.05**
Osteoporosis (*T*-score ≤ 2.5)	38 (90.5)	42 (48.3)	32 (35.6)	**0.001**

Bold values indicate statistical significance at $p \leq 0.05$

BMI, body mass index; *FRAX*, fracture risk assessment; *HAQ*, health assessment questionnaire

[a] FRAX: no risk—major osteoporosis fracture risk < 10% and hip fracture risk < 1%; intermediate risk—major osteoporosis fracture risk 10– < 20% and hip fracture risk < 1– < 3%; high risk—major osteoporosis fracture risk ≥ 20% and hip fracture risk ≥ 3%)

Table 4 Comparison of the fracture risks assessed by FRAX among the males and females included in this study stratified according to their BMI

	Male				**Female**			
	Normal *N* (%)	**Overweight *N* (%)**	**Obese *N* (%)**	***p* value**	**Normal *N* (%)**	**Overweight *N* (%)**	**Obese *N* (%)**	***p* value**
History of fracture	7 (29.2)	17 (53.1)	11 (68.8)	**0.039**	18 (35.3)	23 (41.8)	32 (43.2)	0.656
Last year fall	7 (29.2)	17 (53.1)	12 (75)	**0.05**	25 (49.0)	31 (56.4)	49 (66.2)	**0.05**
FRAX								**0.039**
No risk	2 (10.0)	6 (20.7)	8 (50.0)	**0.010**	3 (10.3)	3 (8.8)	9 (14.5)	
Intermediate risk	6 (30.0)	11 (37.9)	7 (43.8)		6 (20.7)	8 (23.5)	28 (45.2)	
High risk	12 (60.0)	12 (41.4)	1(6.3)		20 (69.0)	23 (67.6)	25 (40.3)	
Sarcopenia (high risk)	5 (20.8)	12 (37.5)	10 (62.5)	**0.03**	26 (50.0)	35 (63.6)	53 (71.6)	**0.05**
Functional disability (high risk) by HAQ	6 (25.0)	11 (34.4)	11 (68.8)	**0.05**	25 (48.1)	27 (49.1)	48 (64.9)	**0.05**
Osteoporosis (*T*-score ≤ − 2.5)	13 (81.3)	15 (93.8)	9 (75.0)	0.377 NS	25 (96.2)	27 (96.4)	23 (67.6)	**0.001**

Bold values indicate statistical significance at $p \leq 0.05$

BMI, body mass index; *FRAX*, fracture risk assessment; *HAQ*, health assessment questionnaire

Table 5 Comparison of the falls risk in both males and females included in this study stratified according to their BMI

	Falls risk	**Normal *N* (%)**	**Overweight *N* (%)**	**Obese *N* (%)**	***p* value**
Male	< 2.50 no risk	12 (52.2)	12 (37.5)	3 (18.8)	0.477 NS
	2.5– < 3.5 moderate risk	4 (17.4)	7 (21.9)	2 (12.5)	
	= > 3.5 high risk	7 (30.4)	13 (40.6)	11 (68.8)	**0.03**
Female	< 2.50 no risk	18 (34.6)	17 (30.9)	16 (21.6)	0.387 NS
	2.5– < 3.5 moderate risk	9 (17.3)	9 (16.4)	11 (14.9)	
	= > 3.5 high risk	25 (48.1)	29 (52.7)	47 (63.5)	**0.05**

Bold values indicate statistical significance at $p \leq 0.05$

BMI, body mass index

controlling for smoking and parental history of fracture. The model was found to be significant (Omnibus test p value = 0.031), and Hosmer and Lemeshow test for goodness of fit was found to be insignificant ($p = 0.955$). The model was able to explain 60.7% of the variability in the incidence of fracture (Table 6).

Discussion

Aging and obesity are two sides of the same coin. By middle age, obesity predisposes an individual to age-related conditions, illness, and disease. Later, in older adult stage, obesity may cause the muscles to age faster, and for its impact on the person's activities of daily living as well as systemic health, it enhances frailty and consequently

Table 6 Multivariable regression analysis showing the effect of obesity on the incidence of fracture controlling for smoking and parental history of fracture

	B	*B* (SE)	Wald	*p* value	OR	95% C.I. for OR	
						Lower	Upper
Obesity (BMI ≥ 30)	−0.294	0.272	1.165	0.281	0.746	0.437	1.271
Parental history of fracture	1.055	0.484	4.742	**0.029**	2.872	1.111	7.422
Smoking	0.614	0.362	2.868	0.090	1.848	0.908	3.760
Constant	−0.302	0.215	1.985	0.159	0.739		

Bold values indicate statistical significance at $p \leq 0.05$

OR, odds ratio *CI*, confidence interval

fractures. The aim of this study was to assess the relationship between the triad of obesity, fracture risk factors, and osteoporosis and its impact on fragility fractures.

This study showed that, though the prevalence of osteoporosis was significantly less in obese and overweight patients, there was no statistically significant difference in the incidence of fragility fractures in relation to the BMI category. Therefore, the high bone mineral content seems not enough as a protective factor on the fracture risk. Results of this work agree with the outcomes of previous studies which documented the positive association between obesity and high bone mass [21–23]. This was attributed to increased levels of the obesity-related insulin, leptin, and estrogen which inhibit bone remodeling and stimulate bone growth. This protective effect of obesity is called the "obesity paradox" or "reverse epidemiology" [24]. On the other hand, a negative association between body mass and osteoporosis has been reported in other studies [25–29].

The prevalence of osteoporosis and the rate of fractures revealed gender differences in the studied cohort of patients. The total fat mass was positively associated with high BMD; hence, the obesity paradox was only found in postmenopausal women and not in men. Yet, there was a significant difference in men reflecting higher prevalence of low impact trauma fractures in comparison to women. A relatively few research studies have included both genders aiming to assess gender-based dissimilarities in the association between BMD and the obesity paradox which remains controversial. Ley et al. [30] attributed this to the difference in body fat distribution between males and females. In contrast, Katzmarzyk et al. [31] did not report any gender differences between BMD and either abdominal subcutaneous tissue or visceral adiposity tissue in African-American and white men versus women, whereas the work done by Taaffe [32] and colleagues reported a positive association between femoral neck BMD and the fat mass in women but not in men. These contradictory results highlight the important action of the other covariates. The discrepancy between the prevalence of low trauma fracture and the bone mineral density between males and females raises the question of the optimum interventional threshold for men and whether this should be different from post-menopausal women.

One of the most interesting findings in the current study is that although the fracture risk probability assessed by FRAX calculator was significantly lower in obese patients, the effect of obesity on the incidence of fracture controlling the other factors was not significant among different BMI groups. This highlights the fact that obesity may not be protective against the occurrence of fragility fracture. Several studies investigated this debated issue. They postulated that obesity may be protective against hip fractures, but obese patients may be more at risk for distal radial, upper humeral, and ankle fractures [33, 34]. Another study conducted on Japanese postmenopausal female patients revealed that the incidence of vertebral fractures was significantly lower in underweight and normal weight females compared to overweight and obese females if BMD and other risk factors were adjusted [35]. It is worth noting that FRAX assessment may be improved if fracture sites are taken into consideration.

Results of this work underlined the principal role of obesity as an important covariate. Obesity was correlated significantly with sarcopenia and fractures. Sarcopenia is one of the conditions associated with aging [36]. Several causes have been postulated to explain sarcopenic obesity in elderly people including alteration of skeletal muscle lipid metabolism, induction of insulin resistance, and stimulation of inflammatory pathways. Both sarcopenia and obesity are cut from the same cloth where they share similar pathophysiologic factors, including lifestyle behaviors, hormonal changes, and immunological factors, all of which may synergistically increase the risk of developing a series of adverse health problems, functional waning, and consequently disability [37]. Scott and colleagues [38] reported in their study that both

men and women with both obesity and sarcopenia were found to have lower-leg muscle density and lower balance, consequently at high risk of falling. These findings agree with the results of this work which revealed significantly higher falls risk in the cohort with obesity and sarcopenia. Similarly, Follis et al. [39] reported that people with obesity and sarcopenia had 1.35-folds and 1.21-folds increased fall risk in age group 50 to 64 years old and 65 to 79 years old respectively. These findings reflect the double impact of sarcopenia and obesity. Such double phenomenon highlights the importance of considering these covariates when managing older adults with sarcopenic obesity, putting in consideration the possible high risks of osteoporosis and falls.

In addition to falls risk and sarcopenia, this study highlighted the important role of physical inactivity/disability, as an important covariate in the of occurrence of fragility fractures. While most research focus on the functional decline after fragility fractures [40], less attention has been paid to physical disability as a contributing factor for fragility fractures. However, indirectly, several studies revealed elevated risk of fragility fractures in patients living with diseases such as Parkinsonism [41] and stroke [42] who are known to have significant physical disability. Bone cells and fat have a common cellular origin (the same bone marrow stem cells) [43], and both aging and low physical activity induce osteoporosis and obesity [44]. In addition, these two disorders synergistically induce functional impairments and physical disabilities [24, 45] which suggest a complex effect of obesity on bone health. These results of this work are in favor of the FRAXplus and its important role in including the important risk factors for the calculation of the individual patient's fracture risk.

Limitations of the study

This study relied on the FRAX as a tool for the assessment of fracture risk. Given that obesity is usually associated with other comorbidities that might have an impact on bone health, this could be a limitation of the study. Assessment of the FRAXplus risk is advisable to be carried out in a future study. Additionally, obesity is suggested to affect bone quality rather than bone mass; thus, it would be more reasonable to study the impact of obesity on altered bone microarchitecture by assessing the trabecular bone score that predicts fractures independently of other clinical risk factors and BMD [46].

Conclusion

In conclusion, progressive aging and increasing life expectancy of the population translates into a higher prevalence of diseases and disorders associated with old age. Obesity was found to be associated with BMD of the hip and lumbar spine as well as distal forearm. Similarly, overweight and obese individuals had similar degrees of osteoporosis. There was a statistically significant difference in post-menopausal women but not in men. Covariates such as sarcopenia, falls risk, and functional disability play an important factor in making the patient at high risk of developing a low impact fracture.

Abbreviations

BMD	Bone mineral density
BMI	Body mass index
DXA	Dual energy X-ray absorptiometry
FLS	Fracture liaison service
FRAS	Falling risk assessment score
FRAX	Fracture risk assessment
HAQ	Health Assessment Questionnaire

Duplicate publication

This is to confirm that the content of the manuscript has not been published or submitted for publication elsewhere.

Mini abstract

This work studies the relationship between the triad of obesity, fracture risk factors, and osteoporosis and its impact on fragility fractures. While obesity was found to be associated with higher BMD of the hip and lumbar spine as well as distal forearm, there was no significant difference on comparing the fragility of fractures.

Authors' contributions

All authors contributed to the study methodology, analysis, and interpretation of the data and outcomes as well as the manuscript writing, reading, and approval of the final version.

Availability of data and materials

The data will be available upon reasonable request.

Declarations

Ethics approval and consent to participate

This study is in agreement with the ethical guidelines of the Declaration of Helsinki, and it follows the ethical standards of Alexandria Faculty of Medicine, IRB NO: 00012098. An informed written consent was obtained from all patients in accordance with the local ethical committee. Privacy of all patients' data was granted as there was a code number for every patient file that included all investigations.

Consent for publication

Not applicable.

Competing interests

The authors declare that Mohammed H Abu-Zaid is an associate editor in the Egyptian Rheumatology and Rehabilitation. Waleed Hassan, Safaa Mahran, Naglaa GadAllah, and Yasser El Miedany are from the editorial board of the journal.

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