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**Original Article**

# Positive Association of Obesity and Insulin Resistance With Bone Mineral Density in Tunisian Postmenopausal Women

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## Abstract

The association of bone mineral density (BMD) with obesity and insulin resistance remains unclear. This study aimed to explore these associations in Tunisian menopausal women. Eighty-one postmenopausal women were recruited. Data were analyzed for obese (N = 57) and non-obese women (N = 24) and for insulin-resistant (N = 43) and non insulin-resistant women (N = 36). Anthropometric and biochemical parameters were recorded. BMD in different sites and body composition were measured using dual-energy X-ray absorptiometry. Higher BMD was observed in obese women than those non-obese in the left femur ($p = 0.0067$), right femur ($p = 0.0108$), total hip ($p = 0.0077$), and the whole body ($p = 0.0276$). Also BMD was significantly greater in insulin-resistant women than in non–insulin-resistant women when measured in the left femur and total hip. Positive correlations were recorded between BMD and anthropometric parameters, body composition parameters, and glycemia ($r = 0.249$, $p < 0.05$). Multiple linear regression analysis shows that only trunk fat ($p < 0.05$) and lean mass ($p < 0.05$) were independently and positively related to BMD, and the waist circumference was the only anthropometric parameter independently and negatively associated to BMD. BMD is improved in obese and insulin-resistant women. Also, trunk fat and lean mass are likely to be key positive independent factors for BMD.

**Key Words:** Bone mineral density; fat; insulin resistance; lean mass; obesity.

## Introduction

Osteoporosis is a major public health problem characterized by a decrease in bone mineral density (BMD) and an alteration of bone quality *(1)*. Obesity, another common disease, has been demonstrated to be closely related with osteoporosis *(2,3)*. Despite their sedentary lifestyle, several studies have demonstrated that obese subjects present higher BMD than normal-weight subjects *(4,5)* and increased body weight or body mass index (BMI) is related to higher BMD and reduced fracture risk *(6)*.

In postmenopausal women, obesity has been considered a protective factor for bone loss and osteoporosis, likely for increases in the number of adipocytes, which are important sources of estrogen derived from aromatization, resulting in increased BMD *(7,8)*. Although there is a little doubt that body weight has an effect on bone, whether it is the effect of fat mass or lean mass that influences BMD is disputed. Studies in postmenopausal women have suggested that fat mass plays a key role *(9,10)*, and both fat and lean mass have been reported to be significant predictors of BMD *(11,12)*. However, there is also

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disagreement in the literature on the positive effect of lean and fat mass on BMD *(10,13)*.

In addition to obesity, there have been conflicting reports about the relation between insulin-resistance and BMD. Some authors have reported elevated BMD in the presence of insulin resistance *(14,15)*, whereas some have reported decreased BMD *(16,17)*. Because of the discrepancies in the results, the association between insulin resistance and bone mass remains unclear, and further studies are needed to explain this relationship.

Prevalence of osteoporosis and metabolic syndrome greatly increases in the Tunisian population. It was estimated that 31.6% of women develop the metabolic syndrome *(18)* and 23.4% are osteoporotic *(19)*. Based on the conflicting studies results and the high prevalence of these diseases in Tunisia, we evaluate the relationship between BMD and obesity at different bone sites in a cohort of Tunisian postmenopausal women. We also investigate other factors related to body composition (leg fat, trunk fat, total fat, lean mass) in order to identify those potentially associated with BMD. We also sought to determine the association between insulin resistance and bone mass in normal-weight women.

## Patients and Methods

### *Patients*

A total of 81 postmenopausal women (age range: 50–83 years) were recruited consecutively between June 2014 and April 2015 from the Endocrinology Department of the National Institute of Nutrition of Tunis, Tunisia, during visits for routine checkups. The study was approved by the local ethic committee of National Institute of Nutrition of Tunis and written or oral consent was obtained from all the patients before the study. Written consents were not possible in all cases because the majority of eligible subjects in our study were unable to read or write. The consent includes the agreement of patients to participate in the clinical study and to undergo free densitometry examination.

Original inclusion criteria were age >50, postmenopausal (defined as cessation of menstruation for at least 1 year), and no previous osteoporotic fracture or known diagnosis of osteoporosis. Women with liver or renal disease, inflammatory disease, parathyroid and thyroid, chronic inflammatory rheumatism, early natural menopause before age 40, and receiving medicine known to influence bone metabolism, such as corticosteroids, heparin, anticonvulsants, vitamin D or calcium supplementations, and bisphosphonates, were not included.

Participants were questioned about their age, age at the onset of menopause, education, occupation, family history of osteoporosis, history of peripheral traumatic fractures, weight history, smoking habits, level of physical activity, and current medication use. Smoking habit was categorized as non-smoker and current smoker. Physical activity was self-graded by participants and categorized as sedentary, moderate, and important.

### *Anthropometric Measurements*

Body weight was measured to the nearest 0.1 kg and height was determined to the nearest centimeter. BMI was calculated as the weight (kg) divided by the square of height ($m^2$). Patients were considered as non-obese if BMI < 30 kg/$m^2$ and as obese if BMI ≥ 30 kg/$m^2$ according to the World Health Organization (WHO) definition *(20)*. Waist circumference was measured at the narrowest part of the abdomen, that is, at the natural indentation between the 10th rib and the iliac crest (minimum waist).

### *Biochemical Analysis*

Fasting blood samples were taken after fasting for at least 12 h. Venous blood samples were taken from an antecubital vein and placed into heparinized or non-heparinized tubes. Tubes were centrifuged at 3000 × *g* for 10 min.

Serum fasting blood glucose, glycated hemoglobin (HbA1c), lipid levels (total cholesterol, triglycerides, and high-density lipoprotein cholesterol) were determined by well-validated laboratory routine methods. Serum low-density lipoprotein cholesterol values were estimated using the Friedwald formula *(21)*.

Fasting blood samples were collected in non-heparinized tube for the serum insulin concentrations measurement. The tube was left for 30 min at room temperature (to allow clot formation) then centrifuged at 1000 × *g* for 15 min. The serum was separated and stored in microtubes of 250 µL at 80°C until the day of manipulation. After adequate thawing, insulin was measured by enzyme-linked immunosorbent assay (ALPCO kit, Salem, NH). Insulin resistance was measured according to the following formula: HOMA-IR (homeostasis model assessment of insulin resistance) = fasting insulin (µU/mL) × fasting glucose (mmol/L)/22.5 *(22)*. Patients were considered as insulin resistant when HOMA-IR ≥ 2.6 and non-insulin resistant when HOMA-IR < 2.6.

### *Dual-energy X-ray Absorptiometry (DXA) Measurements*

Densitometry examination of patients was realized at the Rheumatology Department of the Rabta Hospital of Tunis. Lumbar (anteroposterior projection at L1–L4), femur, femoral neck, total hip, and whole body BMD as well as fat (leg, trunk, and total) and total lean mass were measured by DXA using GE-Lunar PRODIGYTM device. Quality control procedures were carried out in accordance with the manufacturer's recommendations. Instrument variation was determined by a daily calibration procedure using a phantom supplied by manufacturer. The precision error was <2.0% for each measured sites at standard speed based on repeated scans in a random sample of 30 subjects. BMD values were expressed in grams per square centimeter (g/$cm^2$), and fat and lean mass values were expressed in grams.