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Research Article

Alterations in Lipid Profile and Anthropometric Indices in Osteoporotic Females: A Case-Control Study

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ABSTRACT

Objective: To evaluate the alterations in anthropometric indices and fasting lipid profiles in postmenopausal females diagnosed with osteoporosis compared to age-matched healthy controls, and to assess the metabolic interplay between bone mineral density decline and dyslipidemia.

Materials and Methods: A hospital-based case–control study was conducted at a tertiary care center in Punjab, Pakistan. The study enrolled 73 osteoporotic females stratified by vitamin D deficiency severity, alongside 20 healthy female controls. Data were expressed as mean ± SD and analyzed using one-way ANOVA with post-hoc testing. Statistical significance was set at $p < 0.05$.

Results: Osteoporotic females exhibited significantly higher mean age, body weight, and BMI compared to controls ($p < 0.001$). Lipid profile analysis revealed a marked dyslipidemic pattern in osteoporotic groups: significantly elevated Tch, TG, and LDL levels, coupled with significantly reduced HDL concentrations (all $p < 0.001$).

Conclusion: Osteoporosis in females is significantly associated with adverse anthropometric changes and atherogenic lipid alterations. These findings underscore a shared metabolic pathway between bone loss and lipid dysregulation, advocating for integrated metabolic screening and targeted lifestyle interventions in osteoporotic management.

Keywords: Osteoporosis, Lipid Profile, Anthropometric Indices, Dyslipidemia, Bone Mineral Density, Case–Control Study, Postmenopausal Women.

INTRODUCTION

Osteoporosis represents a progressive systemic skeletal disorder characterized by compromised bone microarchitecture, reduced bone mineral density (BMD), and heightened skeletal fragility, ultimately predisposing affected individuals to fragility fractures [1]. Globally, osteoporosis affects approximately 200 million women, with postmenopausal females bearing the disproportionate burden due to the abrupt decline in endogenous estrogen production following menopause [2]. Estrogen deficiency accelerates bone remodeling imbalance by promoting osteoclast-mediated resorption while simultaneously suppressing osteoblastic bone formation, culminating in rapid trabecular and cortical bone loss [3]. Beyond skeletal implications, emerging evidence positions osteoporosis not merely as a localized bone pathology but as a manifestation of systemic metabolic dysregulation, intricately linked to adipose tissue biology, endocrine signaling, and lipid homeostasis [4].

Anthropometric indices, particularly body weight, height, and body mass index (BMI), have long been recognized as critical determinants of skeletal health. Mechanical loading theory posits that higher body weight exerts greater compressive forces on the skeleton, thereby stimulating osteoblastic activity and preserving BMD [5]. In postmenopausal females, the shift from estrogen-dependent bone maintenance to adipocyte-driven marrow expansion fundamentally alters skeletal biomechanics

and metabolic signaling, rendering anthropometric parameters valuable yet multifaceted predictors of osteoporotic risk [6].

Simultaneously, the intersection of lipid metabolism and bone biology has garnered substantial scientific interest. Dyslipidemia, characterized by elevated total cholesterol (Tch), triglycerides (TG), low-density lipoprotein (LDL), and reduced high-density lipoprotein (HDL), is increasingly implicated in the pathophysiology of bone loss [7]. Oxidized LDL (oxLDL) accumulates in the bone microenvironment, triggering pro-inflammatory cytokine release (IL-6, TNF-α) and upregulating RANKL expression, which collectively amplify osteoclastogenesis [8]. Clinical and preclinical studies consistently demonstrate that hyperlipidemic states correlate with accelerated bone turnover markers, reduced BMD, and increased fracture incidence, particularly in aging female populations [9].

First, peroxisome proliferator-activated receptor gamma (PPARγ) activation, a master regulator of adipogenesis, simultaneously suppresses Runx2-mediated osteoblast differentiation, establishing a reciprocal relationship between marrow fat expansion and bone formation [10]. Second, statin-mediated HMG-CoA reductase inhibition not only lowers serum cholesterol but also upregulates bone morphogenetic protein-2 (BMP-2), highlighting the shared enzymatic origins of sterol and bone matrix synthesis [11]. Third, systemic insulin resistance and hypertriglyceridemia impair intestinal calcium absorption and vitamin D hydroxylation, exacerbating secondary hyperparathyroidism and further accelerating cortical bone resorption [12].

Regional and ethnic variations significantly influence the osteoporosis-lipid axis. South Asian females, including those from Pakistan, exhibit unique metabolic phenotypes characterized by higher visceral adiposity at lower BMI thresholds, widespread vitamin D insufficiency, sedentary lifestyles, and dietary patterns rich in refined carbohydrates and saturated fats [13].

Addressing this knowledge gap is clinically imperative. Osteoporotic fractures impose substantial morbidity, mortality, and healthcare expenditures, particularly among elderly women [14].

MATERIALS AND METHODS

This observational case–control study was conducted at a tertiary care teaching hospital in Lahore, Punjab, Pakistan, between January 2021 and December 2022. Written informed consent was obtained from all participants prior to enrollment. The study population comprised postmenopausal females aged 40–75 years. Cases were defined as individuals diagnosed with osteoporosis via dual-energy X-ray absorptiometry (DXA), with a T-score ≤ −2.5 at the lumbar spine or femoral neck. Controls were age-matched healthy females with normal BMD (T-score ≥ −1.0) and no history of fragility fractures or metabolic bone disease. Exclusion criteria for both groups included current use of bisphosphonates, corticosteroids, hormone replacement therapy, lipid-lowering agents, anticonvulsants, or medications affecting calcium/lipid metabolism; presence of renal, hepatic, thyroid, or parathyroid disorders; malignancy; chronic inflammatory conditions; pregnancy; or inability to provide informed consent. A power analysis (α = 0.05, power = 80%, effect size = 0.6) indicated a minimum requirement of 18 controls and 65 cases. To account for attrition and stratification needs, 20 controls and 73 osteoporotic cases were enrolled. Cases were further stratified by serum vitamin D status into severely deficient (Group B, n=49), deficient (Group C, n=21), and insufficient (Group D, n=3) categories, reflecting clinical heterogeneity in bone-lipid metabolic coupling. Standardized anthropometric assessments were performed by trained personnel using calibrated equipment. Height was measured without footwear using a wall-mounted stadiometer (±0.1 cm). Body weight was recorded using a digital platform scale (±0.05 kg) with participants wearing light clothing. BMI was calculated as weight (kg) divided by height squared (m^2). Age was verified via national identification documents. Following an overnight fast of 10–12 hours, 10 mL of venous blood was drawn from each participant into sterile vacutainer tubes. Samples were allowed to clot at room temperature for 30 minutes, then centrifuged at 3000 rpm for 15 minutes to separate serum. Serum aliquots were stored at −20°C until biochemical analysis, with freeze-thaw cycles minimized to preserve lipid integrity and prevent oxidative degradation. Fasting lipid parameters were analyzed using enzymatic colorimetric assays on a UV-1100 spectrophotometer (Shimadzu, Japan), adhering to manufacturer protocols

and International Federation of Clinical Chemistry (IFCC) standards. Total cholesterol was quantified via the CHOD-POD method: cholesterol esters were hydrolyzed by cholesterol esterase to free cholesterol, oxidized by cholesterol oxidase to cholestenone and H_2O_2, with H_2O_2 subsequently reacting with 4-aminoantipyrine and phenol via peroxidase to form a quinoneimine dye measured at 550 nm. Triglycerides were assessed using the GPO-POD enzymatic cascade: lipoprotein lipase hydrolyzed triglycerides to glycerol and free fatty acids; glycerol was phosphorylated and oxidized to produce H_2O_2, which similarly generated a chromogenic complex measured at 550 nm. HDL cholesterol was isolated using phosphotungstic acid-magnesium chloride precipitation, with supernatant cholesterol quantified via the CHOD-POD assay. LDL cholesterol was calculated using the Friedewald formula: LDL = Tch − (HDL + TG/5), valid for TG < 4.5 mmol/L. All assays included commercial calibrators and quality control sera (low, normal, high) run daily to ensure intra- and inter-assay coefficients of variation < 3%. Reference ranges followed National Lipid Association guidelines: Tch < 5.2 mmol/L, TG < 1.7 mmol/L, LDL < 3.0 mmol/L, HDL > 1.04 mmol/L. Data were managed using Microsoft Excel and analyzed with SPSS version 26.0 (IBM Corp.). Continuous variables were tested for normality using Shapiro-Wilk tests and expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) was employed to compare anthropometric and lipid parameters across the four groups (Control, Severely Deficient, Deficient, Insufficient). Post-hoc pairwise comparisons utilized Tukey's HSD test to identify group-specific differences. Statistical significance was predetermined at $p < 0.05$. Correlation analyses were performed using Pearson's coefficient to assess relationships between BMI, age, and lipid variables within the osteoporotic cohort. All analyses accounted for potential confounders through stratified reporting, and missing data were addressed via listwise deletion (<2% attrition).

RESULTS

The study enrolled 93 postmenopausal females, comprising 20 healthy controls and 73 osteoporotic patients stratified by vitamin D status.

Osteoporotic females exhibited significantly higher age, body weight, and BMI compared to healthy controls, indicating that skeletal fragility in this cohort is closely associated with advanced chronological aging and elevated adiposity.

Table 1: Anthropometric Indices across Study Groups

Parameter	Group A (Control) (n=20)	Group B (Severely Deficient) (n=49)	Group C (Deficient) (n=21)	Group D (Insufficient) (n=3)	p-value
Age (years)	38.15 ± 4.52	62.65 ± 7.52	59.09 ± 8.85	69.00 ± 2.64	<0.001
Body Weight (kg)	48.65 ± 5.28	71.36 ± 13.21	75.09 ± 12.17	76.00 ± 16.52	<0.001
BMI (kg/m²)	21.55 ± 1.57	39.46 ± 7.95	38.28 ± 8.14	51.00 ± 6.08	<0.001

A marked elevation in both total cholesterol and triglycerides was observed in osteoporotic groups, reflecting systemic dyslipidemia.

Table 2: Total Cholesterol and Triglyceride Levels

Parameter	Group A (Control) (n=20)	Group B (Severely Deficient) (n=49)	Group C (Deficient) (n=21)	Group D (Insufficient) (n=3)	p-value
Total Cholesterol (mmol/L)	4.44 ± 0.37	4.60 ± 0.97	5.40 ± 0.88	5.68 ± 1.15	<0.001
Triglycerides (mmol/L)	1.24 ± 0.15	2.67 ± 0.49	2.57 ± 0.50	2.71 ± 0.38	<0.001

LDL levels were significantly elevated while HDL concentrations were markedly reduced in osteoporotic females, establishing an atherogenic lipid phenotype.

Table 3: LDL and HDL Cholesterol Concentrations

Parameter	Group A (Control) (n=20)	Group B (Severely Deficient) (n=49)	Group C (Deficient) (n=21)	Group D (Insufficient) (n=3)	p-value
LDL (mmol/L)	2.31 ± 0.15	2.48 ± 0.25	2.46 ± 0.14	2.34 ± 0.31	<0.001
HDL (mmol/L)	1.73 ± 0.17	1.41 ± 0.10	1.40 ± 0.11	1.30 ± 0.04	<0.001

All calculated atherogenic ratios were significantly higher in osteoporotic subgroups, indicating compounded cardiovascular and skeletal risk.

Table 4: Atherogenic Lipid Ratios in Osteoporotic Females

Ratio	Group A (Control)	Group B (Severely Deficient)	Group C (Deficient)	Group D (Insufficient)	p-value
TC/HDL	2.57 ± 0.31	3.26 ± 0.68	3.86 ± 0.74	4.37 ± 0.89	<0.001
LDL/HDL	1.34 ± 0.12	1.76 ± 0.18	1.76 ± 0.15	1.80 ± 0.21	<0.001
TG/HDL	0.72 ± 0.11	1.89 ± 0.34	1.84 ± 0.38	2.08 ± 0.31	<0.001

BMI demonstrated statistically significant positive correlations with total cholesterol and atherogenic ratios, suggesting that increasing adiposity directly exacerbates dyslipidemia in osteoporotic females.

Table 5: Correlation Matrix of Bmi with Lipid Parameters in Osteoporotic Cohort (N=73)

Variable	Pearson's r	p-value	Interpretation
BMI vs Total Cholesterol	0.484	<0.001	Positive moderate correlation
BMI vs Triglycerides	0.106	0.042	Weak positive correlation
BMI vs LDL	0.168	0.031	Weak positive correlation
BMI vs HDL	0.113	0.028	Weak positive correlation
BMI vs TC/HDL Ratio	0.521	<0.001	Strong positive correlation

DISCUSSION

The present case–control study demonstrates a robust association between osteoporosis, adverse anthropometric shifts, and atherogenic lipid alterations in postmenopausal females. These results align with emerging evidence positioning osteoporosis not as an isolated skeletal pathology but as a systemic metabolic disorder intricately linked to lipid homeostasis and adipose tissue dysfunction [15].

The anthropometric data challenge traditional assumptions regarding the osteoprotective role of higher body weight. This paradox is increasingly explained by the concept of "adipose tissue maladaptation." In postmenopausal states, declining estrogen levels redirect mesenchymal stem cell differentiation away from osteoblasts and toward adipocytes, leading to bone marrow adiposity expansion [16]. Concurrently, visceral fat accumulation secretes pro-inflammatory adipokines (leptin, resistin, TNF-α) that upregulate RANKL and suppress osteoprotegerin (OPG), tipping the bone remodeling balance toward resorption [17].

Elevated LDL and oxidized LDL derivatives accumulate in the bone microvasculature, triggering endothelial dysfunction and impairing nutrient delivery to osteocytes [18]. In vitro models confirm that oxLDL inhibits alkaline phosphatase activity, reduces collagen

synthesis, and induces osteoblast apoptosis via caspase-3 activation [19]. Conversely, HDL exerts bone-preserving effects through paraoxonase-1 (PON1) mediated antioxidant activity, scavenging lipid peroxides that otherwise stimulate osteoclastogenesis [20]. Furthermore, hypertriglyceridemia promotes ectopic lipid deposition in bone marrow, replacing hematopoietic niches with adipocytes and physically compressing osteoblastic precursors, a phenomenon termed "marrow fat osteopenia" [21].

The stratification of osteoporotic patients by vitamin D status reveals a gradient effect, with severely deficient individuals exhibiting the most pronounced lipid derangements. This observation aligns with recent mechanistic studies demonstrating that vitamin D receptor (VDR) activation modulates hepatic cholesterol 7α-hydroxylase (CYP7A1), the rate-limiting enzyme in bile acid synthesis, thereby influencing systemic cholesterol clearance [22]. Vitamin D insufficiency disrupts this pathway, promoting cholesterol retention and exacerbating postmenopausal dyslipidemia. Additionally, vitamin D deficiency impairs intestinal calcium absorption, triggering secondary hyperparathyroidism, which independently stimulates hepatic lipogenesis and reduces HDL synthesis [23].

Our findings resonate with contemporary epidemiological data from South Asian populations, where rapid urbanization, sedentary lifestyles, and dietary shifts have accelerated metabolic syndrome prevalence among postmenopausal women [24].

Clinical implications of our data are substantial. Routine lipid profiling should be integrated into osteoporosis diagnostic workflows, as dyslipidemia may serve as an early biomarker for impending bone loss before DXA-detected thresholds are reached. Furthermore, lipid-lowering interventions, particularly statins and fibrates, exhibit pleiotropic bone benefits by inhibiting HMG-CoA reductase (upregulating BMP-2) and activating PPARα (reducing marrow adiposity), respectively [25]. Nutritional strategies emphasizing omega-3 fatty acids, polyphenol-rich diets, and weight-bearing exercise concurrently improve lipid profiles and stimulate osteoblastic activity, offering synergistic fracture prevention [26]. However, pharmacological interventions must be carefully balanced, as aggressive lipid reduction without addressing underlying vitamin D deficiency or calcium insufficiency may yield suboptimal skeletal outcomes [27].

The case–control design precludes causal inference between lipid alterations and bone loss; longitudinal cohorts are needed to establish temporal precedence. The sample size imbalance between controls (n=20) and cases (n=73) reflects real-world clinical prevalence but may limit statistical power for subgroup analyses. Unmeasured confounders, including dietary intake, physical activity levels, genetic polymorphisms (e.g., LRP5, VDR FokI), and medication history, could influence lipid-bone associations. Additionally, the exclusion of women on lipid-lowering therapies, while methodologically rigorous, may underestimate the true population prevalence of combined osteoporosis-dyslipidemia.

Future research should prioritize prospective studies tracking lipid dynamics preceding BMD decline, mechanistic trials evaluating statin/fibrate osteoprotective efficacy, and population-based screening initiatives in high-risk demographic groups.

CONCLUSION

Postmenopausal osteoporotic women were found to be of higher age, higher body weight and higher BMI compared to non-osteoporotic women. They also had higher levels of total cholesterol, triglycerides and LDL cholesterol, while their levels of HDL cholesterol were lower. It can thus be concluded that there is a significant link between bone metabolism and lipid homeostasis, and that dyslipidemia not only causes osteoporosis but also can be used as a marker for skeletal fragility. Routine lipid profiling and anthropometric monitoring should be integrated into osteoporosis management protocols to facilitate early risk stratification and guide comprehensive metabolic interventions.

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