Original Article

Exploring Adiponectin and Leptin Levels as Potential Biomarkers in Osteoporosis Pathogenesis

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Abstract

Background: Accurate and early diagnosis of osteoporosis, a skeletal disorder characterized by low bone density and increased fracture risk, is crucial for effective management. This study aimed to evaluate the diagnostic potential of adiponectin and leptin levels as biomarkers for osteoporosis. **Objectives:** The primary objective of this study was to investigate whether adiponectin and leptin levels could serve as biomarkers for diagnosing osteoporosis and distinguishing it from healthy individuals. **Materials and Methods:** A total of ninety participants, including healthy individuals (n = 30) and patients with osteoporosis (n = 30) or osteopenia (n = 30), underwent comprehensive evaluations. Demographic, clinical, hormonal, and lipid profiles were assessed. Additionally, bone mineral density (BMD) was measured using dual-energy X-ray absorptiometry. Enzyme-linked immunosorbent assays were conducted to measure adiponectin and leptin levels in serum samples. **Results:** Significant differences were observed between osteoporosis patients and healthy controls in several parameters. Osteoporosis patients were older and had a lower body mass index compared to healthy individuals. Furthermore, BMD was significantly lower in osteoporosis patients. Hormonal and lipid profiles also differed significantly between the two groups. Notably, adiponectin levels were lower, whereas leptin levels were higher in osteoporosis patients compared to healthy controls. These findings suggest that adiponectin and leptin levels may have diagnostic potential for osteoporosis. **Conclusion:** Adiponectin and leptin levels exhibit promise as biomarkers for the accurate diagnosis of osteoporosis and differentiation from healthy individuals. Further research and validation studies are warranted to confirm their utility in clinical practice.

Keywords: Adiponectin, biomarkers, leptin, osteoporosis diagnosis, predictive analysis

Introduction

Osteoporosis is a chronic condition that is widespread, and it is characterized by low bone mass and degeneration of bone tissue, leading to a higher risk of fractures. It affects millions of individuals globally, especially postmenopausal women, and it places a substantial burden on healthcare systems and quality of life. The timely diagnosis of osteoporosis is critical for implementing preventive measures and initiating prompt treatment interventions.[1] Nonetheless, the existing diagnostic techniques, such as dual-energy X-ray absorptiometry (DEXA), have constraints in precisely detecting individuals who are prone to developing osteoporosis.[2] Over the past few years, there has been an increasing focus on exploring potential biomarkers that could improve the precision of diagnosing and predicting osteoporosis. Among these promising candidates, adiponectin and leptin have emerged as notable contenders. Adiponectin and leptin are two hormones derived from adipose tissue, and they have attracted attention due to their involvement in bone metabolism and their potential as biomarkers for various diseases. Adiponectin, primarily secreted by adipocytes, possesses anti-inflammatory properties and aids in improving insulin sensitivity.[3] Leptin, on the other hand, plays a vital role in regulating

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appetite and maintaining energy balance. The potential of adiponectin and leptin as predictive biomarkers for diagnosing osteoporosis has been extensively studied. One noteworthy study conducted by Zhang *et al*.[4] explored the connection between adiponectin and bone mineral density (BMD) in postmenopausal women. The results unveiled a negative association between adiponectin levels and BMD, indicating that higher adiponectin levels could potentially contribute to bone loss and an elevated risk of osteoporosis. Several studies have indicated that low levels of adiponectin are associated with a reduction in bone mineral density and an increased risk of fractures. For instance, Kanazawa *et al*.[5] conducted a study that found a negative correlation between serum adiponectin levels and lumbar spine bone mineral density in postmenopausal women. The findings indicate that adiponectin may have the potential to serve as a biomarker for diagnosing osteoporosis. Likewise, the role of leptin in osteoporosis has been investigated in several research studies.[6] A study by Philbrick *et al*.[7] demonstrated a positive correlation between leptin levels and BMD in postmenopausal women. The study suggested that lower concentrations of leptin may contribute to increased bone turnover and reduced bone mass, thereby increasing the risk of developing osteoporosis.[8,9] The correlation among adiponectin, leptin, and osteoporosis has been investigated in a previous research.[10,11] One study found a notable link among elevated serum adiponectin levels, decreased BMD, and an elevated risk of vertebral fractures in postmenopausal women. Conversely, Martínez-Morillo *et al*.[12] conducted a study that did not identify a significant association between adiponectin levels and BMD in postmenopausal women. In relation to leptin, a study conducted by Ansari *et al*.[13] revealed a positive correlation between leptin levels and BMD in postmenopausal women. These studies, along with others, have provided valuable insights into the potential of adiponectin and leptin as predictive biomarkers for Osteoporosis. However, further research is required to validate their utility in larger cohorts and diverse populations. Therefore, the objective of the current study titled "Predictive Analysis of Adiponectin and Leptin Levels as Potential Biomarkers for Osteoporosis Diagnosis" is to investigate the association among adiponectin, leptin, and bone density in a cross-sectional analysis of postmenopausal women. By measuring the levels of these hormones and evaluating bone density using DEXA, this study aims to contribute to the existing knowledge and potentially enhance early detection and risk assessment of Osteoporosis.

The identification of reliable biomarkers for early diagnosis of Osteoporosis is essential for improving patient outcomes and reducing the burden of this debilitating condition. Adiponectin and leptin have emerged as potential biomarkers with promising associations with bone density and Osteoporosis risk. The present study aims to further investigate the predictive value of adiponectin and leptin levels in postmenopausal women, thereby adding to the growing body of research in this field.

Materials and Methods

Ninety individuals were recruited between October 2022 and March 2023 at Al-Sader Teaching Hospital to participate in this study. The participants were divided into two groups:[1] healthy individuals n = (30) and n = (60) patients, including Osteoporosis n = (30) and Osteopenia n = (30).

Specific exclusion criteria were applied to ensure the study's objectives were met. In the context of osteoporosis, the following exclusion criteria were utilized: (1) Existing medical conditions: Excluding individuals with specific medical conditions or diseases that may confound the study results or affect bone health independently. This could include chronic kidney disease, hyperparathyroidism, hyperthyroidism, malignancies, or other conditions that affect bone metabolism. (2) Medication use: Excluding individuals who are currently taking medications that may affect bone health or the interpretation of study results. This could include long-term corticosteroid use, hormonal therapies, certain anticonvulsant medications, or specific osteoporosis treatments. (3) History of bone diseases or fractures: Excluding individuals who have a history of significant bone diseases (other than osteoporosis) or recent fractures, as these conditions may affect bone density or introduce confounding factors. (4) Pregnancy and breastfeeding: Excluding pregnant or breastfeeding women due to the potential impact of hormonal changes on bone health. (5) Substance abuse or alcoholism: Excluding individuals with a history of substance abuse or alcoholism, as these factors may independently affect bone health.

All participants completed a standardized questionnaire to capture clinical and demographic data. Blood samples were collected after a 10-hour or longer overnight fast to measure various factors including adiponectin, leptin, parathyroid hormone (PTH), blood lipids, and certain minerals. Enzyme-linked immunosorbent assays were employed to measure the concentrations of adiponectin, leptin, and PTH in the serum. Spectrophotometry was utilized to measure levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, as well as serum levels of calcium (Ca), phosphorus (Pi), and magnesium (Mg). DEXA was employed to collect data on BMD, T-scores, and Z-scores.

The statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 24.0 (SPSS, IBM Company, Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation, whereas

categorical variables were presented as frequencies and percentages. Group characteristics were compared using Student's *t*-tests for independent samples and one-way analysis of variance test. Correlation analysis, specifically Pearson Correlation, was performed to determine the correlation coefficients between variables.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal consent before samples were taken.

Results

Comparison study between osteoporosis patients and controls

Comparisons of age and body mass index (BMI) were made between the osteoporosis and healthy groups

Table 1 presents the mean values and standard deviations (SD) of age and body mass index (BMI) for the osteoporosis group and the healthy group. The results indicate statistically significant differences in age and BMI between the osteoporosis group and the healthy group, as observed in the participants involved in the study.

Age

The difference in age between the osteoporosis patients and healthy controls was found to be statistically significant (P = 0.0001). The average age of osteoporosis patients was 61.32 years (SD = 10.55), whereas the average age of healthy controls was 46.50 years (SD = 8.48).

BMI

There was a statistically significant difference in BMI between the two groups (P = 0.003). The average BMI of osteoporosis patients was 29.26 kg/m² (SD = 5.71), whereas the average BMI of healthy controls was 26.26 kg/m² (SD = 3.63).

The bone density data obtained from a DEXA scan, including BMD, T-scores, and Z-scores, were compared between the osteoporosis and healthy groups.

The analysis of the given data reveals in Table 2 significant differences in BMD, *T*-scores, and *Z*-scores between individuals with osteoporosis (OP) and healthy controls (HT).

The average BMD in the OP group is (0.69 ± 0.09), whereas in the HT group, it is (1.08 ± 0.08). The *P*-value of (<0.0001) indicates a highly significant distinction between the two groups. This suggests that individuals diagnosed with osteoporosis have lower BMD compared to those who are healthy. The mean *T*-scores in the OP group are (–2.73 ± 0.82), whereas in the HT group, they are (1.09 ± 0.37). The *P*-value of (<0.0001) suggests a highly significant difference. It indicates that individuals with osteoporosis have lower *T*-scores, which signify more severe bone loss, compared to healthy controls. The mean *Z*-scores in the OP group are (–1.32 ± 0.97), whereas in the HT group, they are (1.23 ± 0.78). The *P*-value of (<0.0001) suggests a highly significant difference.

Comparison of adipocytokines levels between osteoporosis patients and controls

Table 3 presents the results of adiponectin and leptin levels in healthy controls and patients. Considering the data provided in the table, the analysis reveals the following:

Adiponectin: The *P*-value of (<0.0001) suggests a highly significant difference in adiponectin levels between individuals diagnosed with osteoporosis and

Table 1: The demographic data for the healthy controls and subjects with osteoporosis

Parameters	Control N = (30)	Patients N = (60)	Df	t	P-value	Decision
Age (yrs)	46.50 ± 8.48	61.32 ± 10.55	1/88	–6.679	0.0001	Significant
BMI (kg/m²)	26.26 ± 3.63	29.26 ± 5.71	1/88	–2.613	0.003	Significant

df = degree of freedom, BMI = body mass index
Significant (P-value ≤ 0.05)

Table 2: BMD, *T*-scores, and *Z*-scores are used to compare the bone density between the osteoporosis and healthy groups in DEXA scan data

Aspects	Mean ± SD		t	P-value
	(OP) n = (60)	(HT) n = (30)		
BMD	0.69 ± 0.09	1.08 ± 0.08	20.31	<0.0001
T-scores	–2.73 ± 0.82	1.09 ± 0.37	24.07	<0.0001
Z-scores	–1.32 ± 0.97	1.23 ± 0.78	13.42	<0.0001

BMD = bone mineral density
Significant (P-value ≤ 0.05)

healthy controls. The average adiponectin level among osteoporosis patients is (2.72) µg/mL with a standard deviation of (0.56), whereas healthy controls have an average adiponectin level of (4.77) µg/mL with a standard deviation of (1.51). These findings indicate that individuals with osteoporosis have significantly lower adiponectin levels than healthy controls.

Leptin: The *P*-value of (<0.0001) indicates a highly significant difference in leptin levels between individuals diagnosed with osteoporosis and healthy controls. The average leptin level among osteoporosis patients is (3.73) ng/mL with a standard deviation of (1.12), whereas healthy controls have an average leptin level of (2.38) ng/mL with a standard deviation of (0.50). These results suggest that individuals with osteoporosis have significantly higher leptin levels compared to healthy controls.

Osteoporosis is a systemic skeletal disorder characterized by reduced bone mass and deterioration of bone tissue, resulting in increased vulnerability to fractures and bone fragility. It is a prevalent condition, particularly among postmenopausal women and older individuals. Although the exact causes of osteoporosis are multifactorial, several studies have investigated the potential involvement of adipokines, such as adiponectin and leptin, in the development of this disease. Adiponectin, primarily secreted by adipose tissue, plays a crucial role in regulating glucose and lipid metabolism, while also exerting anti-inflammatory and anti-atherogenic effects.

Comparisons of the serum parathyroid hormone and minerals (Ca, Mg, Pi) between osteoporosis and healthy groups

In accordance with the revised [Table 4], here are the results for the serum PTH and mineral levels (Ca, Mg, Pi) between patients with osteoporosis and healthy controls.

The provided table presents the findings from comparing serum levels of PTH and minerals (calcium, magnesium, phosphate) between individuals with osteoporosis and healthy controls. The analysis reveals significant differences in PTH, calcium, and phosphate levels, whereas no significant difference is observed for magnesium levels.

First, there is a significant difference ($P < 0.0001$) in serum PTH levels between osteoporosis patients and healthy controls. Osteoporosis patients exhibit a mean PTH level of (40.78 ± 8.69) pg/mL, whereas the control group has a significantly lower mean of (18.72 ± 6.02) pg/mL. These findings suggest that individuals with osteoporosis have elevated PTH levels compared to healthy controls.

Second, there is a significant difference ($P < 0.0001$) in serum calcium levels between the two groups. Osteoporosis patients have a mean calcium level of (6.01 ± 0.99) mg/dL, whereas the control group has a significantly higher mean of (8.94 ± 0.66) mg/dL. This indicates that patients with osteoporosis have lower serum calcium levels compared to healthy controls.

Third, there is no significant difference ($P = 0.421$) in serum magnesium levels between osteoporosis patients and healthy controls. Both groups show similar mean magnesium levels, with patients having a mean of (0.71 ± 0.11) mmol/L and controls having a mean of (0.73 ± 0.07) mmol/L. Thus, magnesium levels do not appear to be associated with the presence of osteoporosis.

Lastly, there is a significant difference ($P < 0.0001$) in serum phosphate levels between the two groups. Osteoporosis patients have a mean phosphate level of

Table 3: Serum adiponectin and leptin levels of osteoporosis subjects and healthy controls

Adipocytokines	Control *N* = (30)	Patients *N* = (60)	Df	*T*	*P*-value	Decision
Adiponectin µg/mL	4.77 ± 1.51	2.72 ± 0.56	1/88	-7.87	<0.0001	Significant
Leptin ng/mL	2.38 ± 0.50	3.73 ± 1.12	1/88	-9.21	<0.0001	Significant

Values expressed as mean ± SD

Significant differences at *P*-value ≤ 0.05

*Highly significant (*P*-value < 0.001)

Table 4: Serum parathyroid hormone (PTH) and minerals (Ca, Mg, and Pi) levels of osteoporosis and healthy controls

Biomarker	Control *N* = (30)	Patients *N* = (60)	df	*t*	*P*-value	Decision
PTH (pg/mL)	18.72 ± 6.02	40.78 ± 8.69	1/88	–12.46	<0.0001	Significant
Ca (mg/dL)	8.94 ± 0.66	6.01 ± 0.99	1/88	14.58	<0.0001	Significant
Mg (mmol/L)	0.73 ± 0.07	0.71 ± 0.11	1/88	0.80	0.421	Non-Significant
Pi (mmol/L)	0.71 ± 0.32	1.28 ± 0.30	1/88	–8.27	<0.0001	Significant

PTH = parathyroid hormone

Values expressed as mean ± SD

Significant differences at *P*-value ≤0.05

(1.28 ± 0.30) mmol/L, whereas the control group has a significantly lower mean of (0.71 ± 0.32) mmol/L. These results indicate that patients with osteoporosis have elevated serum phosphate levels compared to healthy controls.

Comparison of lipid profile between osteoporosis and healthy groups

The results of lipid profile in healthy controls and patients are presented in Table 5. As per the provided table comparing serum lipid profile levels between individuals with osteoporosis and healthy controls:

Comparisons were made between the serum lipid profile levels of individuals with osteoporosis and healthy controls, revealing notable differences in various lipid parameters.

Total cholesterol (TC): The calculated *P*-value of (0.005) indicates a significant difference in TC levels between individuals with osteoporosis and healthy controls. The osteoporosis group exhibited an average TC level of (196.09) mg/dL (standard deviation: 49.48), whereas the healthy controls had an average TC level of (163.48) mg/dL (standard deviation: 49.48). This finding suggests significantly higher TC levels among individuals with osteoporosis compared to healthy controls.

TG: The calculated *P*-value of <0.0001 indicates a highly significant difference in TG levels between individuals with osteoporosis and healthy controls. The osteoporosis group showed an average TG level of 203.98 mg/dL (standard deviation: 93.92), whereas the healthy controls had an average TG level of 130.06 mg/dL (standard deviation: 77.29). Individuals with osteoporosis exhibited significantly higher TG levels compared to healthy controls.

HDL-C: The calculated p-value of <0.0001 indicates a highly significant difference in HDL-C levels between individuals with osteoporosis and healthy controls. The osteoporosis group demonstrated an average HDL-C level of (32.72) mg/dL (standard deviation: 7.96), whereas the healthy controls had an average HDL-C level of (46.39) mg/dL (standard deviation: 11.48). Individuals with osteoporosis exhibited significantly lower HDL-C levels compared to healthy controls.

LDL-C: The calculated *P*-value of (<0.0001) indicates a highly significant difference in LDL-C levels between individuals with osteoporosis and healthy controls. The osteoporosis group displayed an average LDL-C level of 204.16 mg/dL (standard deviation: 62.15), whereas the healthy controls had an average LDL-C level of (143.10) mg/dL (standard deviation: 62.22). Individuals with osteoporosis exhibited significantly higher LDL-C levels compared to healthy controls.

Comparison study between osteopenia and osteoporosis patients and controls

The comparisons of age and body mass index between osteopenia and osteoporosis with healthy groups.

Table 6 presents the demographic data of healthy controls, subjects with osteopenia, and subjects with osteoporosis. The accompanying *P*-values indicate the statistical significance of the observed differences among the groups.

The age parameter is listed first, and the results indicate a significant difference in age among the three groups ($P < 0.0001$). The mean age of the osteoporosis group (62.43 ± 11.60 years) is higher than that of the osteopenia group (59.10 ± 7.86 years), which, in turn, is higher than that of the healthy control group (46.50 ± 8.48 years). The second parameter listed is BMI, and the results also show

Table 5: The serum lipid profile levels of individuals with osteoporosis were compared to those of healthy controls

Biomarker	Control *N* = (30)	Patients *N* = (60)	Df	*t*	*P*-value	Decision
TC (mg/dL)	163.48 ± 49.48	196.09 ± 49.48	1⁄88	–2.94	0.005	Significant
TG (mg/dL)	130.06 ± 77.29	203.98 ± 93.92	1⁄88	–3.72	<0.0001	Significant
HDL-C (mg/dL)	46.39 ± 11.48	32.72 ± 7.96	1⁄88	6.59	<0.0001	Significant
LDL-C (mg/dL)	143.10 ± 62.22	204.16 ± 62.15	1⁄88	–4.39	<0.0001	Significant

TC = total cholesterol, LDL-C = low-density lipoprotein cholesterol, TG: triglyceride; HDL-C = high-density lipoprotein cholesterol

Values expressed as mean ± SD

Significant differences at *P*-value ≤0.05

*Highly significant (*P*-value < 0.0001)

Table 6: Demographic information of healthy controls and subjects with osteopenia and osteoporosis

Parameters	Control *N* = (30)	Osteopenia *N* = (30)	Osteoporosis *N* = (30)	*P*-value
Age (yrs.)	46.50 ± 8.48	59.10 ± 7.86	62.43 ± 11.60	<0.0001
BMI (kg/m^2)	26.26 ± 3.63	31.19 ± 6.77	28.29 ± 4.92	0.004

BMI = body mass index

Significant (*P*-value ≤0.05)

a significant difference among the groups ($P = 0.004$). The mean BMI of the osteoporosis group (28.29 ± 4.92 kg/m²) is lower than that of the osteopenia group (31.19 ± 6.77 kg/m²), which, in turn, is lower than that of the healthy control group (26.26 ± 3.63 kg/m²).

The bone density data from a DEXA scan are presented, including BMD, *T*-scores, and Z-scores, for comparisons among the osteopenia, osteoporosis, and healthy groups.

The data presented in Table 7 indicate significant differences in bone density measurements among the osteoporosis, osteopenia, and control groups. All parameters show *P*-values of less than 0.0001, indicating the statistical significance of these differences.

The osteoporosis group exhibited the lowest BMD values with a mean of (0.64 ± 0.07). The osteopenia group had slightly higher BMD values with a mean of (0.79 ± 0.03), whereas the control group had the highest BMD values with a mean of 1.08 ± 0.08. The *T*-scores, which indicate how many standard deviations the BMD values are from the mean of a young healthy population, were also lowest in the osteoporosis group (–3.12 ± 0.71), followed by the osteopenia group (–1.95 ± 0.31), and highest in the control group (1.09 ± 0.37). The *Z*-scores, which indicate how many standard deviations the BMD values are from the mean of the same age and gender, were also lowest in the osteoporosis group (–1.53 ± 1.07), followed by the osteopenia group (–0.90 ± 0.54), and highest in the control group (1.23 ± 0.78).

Comparison of adipocytokines levels among osteopenia, osteoporosis patients, and controls

The provided data in Table 8 show significant differences in serum adiponectin and leptin levels among individuals with osteoporosis, osteopenia, and healthy controls.

Comparisons of the serum parathyroid hormone and minerals (Ca, Mg, Pi) among osteoporosis, osteopenia, and healthy groups

Table 9 demonstrates significant differences in serum PTH and mineral levels, including calcium (Ca), magnesium (Mg), and phosphorus (Pi), among individuals with osteoporosis, osteopenia, and healthy controls.

Comparison of lipid profile among osteopenia, osteoporosis, and healthy groups

Table 10 presents a comparison of serum lipid profile levels among individuals with osteopenia, osteoporosis, and healthy controls. The associated *P*-values signify the statistical significance of the observed variations in biomarker levels across the three groups.

Table 7: The comparisons of bone density data from a DEXA scan are reported as BMD, *T*-scores and *Z*-scores; among the osteopenia, osteoporosis, and healthy groups

Parameters	Control *N* = 30	Osteopenia *N* = 30	Osteoporosis *N* = 30	*P* value
BMD	1.08 ± 0.08	0.79 ± 0.03	0.64 ± 0.07	<0.0001
T-scores	1.09 ± 0.37	–1.95 ± 0.31	–3.12 ± 0.71	<0.0001
Z-scores	1.23 ± 0.78	–0.90 ± 0.54	–1.53 ± 1.07	<0.0001

Significant (*P*-value ≤ 0.05)

BMD = bone mineral density

Table 8: Serum adiponectin and leptin levels of osteopenia, osteoporosis subjects and healthy controls

Adipocytokines	Control *N* = (30)	Osteopenia *N* = (30)	Osteoporosis *N* = (30)	*P* value
Adiponectin (µg/mL)	5.12 ± 1.61	4.59 ± 1.45	2.72 ± 0.56	<0.0001
Leptin (ng/mL)	2.38 ± 0.50	3.49 ± 0.87	3.85 ± 1.22	<0.0001

Values expressed as mean ± SD

Significant differences at *P*-value ≤ 0.05

*Highly significant (*P*-value < 0.001)

Table 9: Serum parathyroid hormone and minerals (Ca, Mg, Pi) levels of osteoporosis, osteopenia, and healthy controls

Biomarker	Control N=(30)	Osteopenia N=(30)	Osteoporosis N=(30)	p-value
PTH (pg/mL)	18.72±6.02	40.96±9.58	40.70±8.34	<0.0001
Ca (mg/dL)	8.94±0.66	5.57±1.39	6.23±0.62	<0.0001
Mg (mmol/L)	0.73±0.07	0.65±0.16	0.74±0.06	0.005
Pi (mmol/L)	0.71±0.32	1.26±0.29	1.29±0.30	<0.0001

PTH = parathyroid hormone

Values expressed as mean ± SD

Significant differences at *P*-value ≤ 0.05

The results indicate that the osteoporosis group exhibits significantly higher TC levels compared to the control group (192.39 ± 48.59 mg/dL vs. 163.48 ± 49.48 mg/dL, P = 0.012). The osteopenia group also shows higher TC levels compared to the control group, although the difference is not statistically significant (203.50 ± 51.66 mg/dL vs. 163.48 ± 49.48 mg/dL, $P > 0.05$). Both the osteoporosis and osteopenia groups demonstrate significantly elevated TG levels in comparison to the control group (187.93 ± 85.71 mg/dL and 236.07 ± 103.36 mg/dL vs. 130.06 ± 77.29 mg/dL, $P < 0.0001$). Furthermore, the osteoporosis and osteopenia groups exhibit significantly lower HDL-C levels compared to the control group (32.32 ± 7.55 mg/dL and 33.52 ± 8.87 mg/dL vs. 46.39 ± 11.48 mg/dL, $P < 0.0001$). The osteoporosis group demonstrates significantly higher LDL-C levels compared to the control group (197.65 ± 58.64 mg/dL vs. 143.10 ± 62.22 mg/dL, $P < 0.0001$). Similarly, the osteopenia group shows higher LDL-C levels compared to the control group, although the difference is not statistically significant (217.19 ± 68.32 mg/dL vs. 143.10 ± 62.22 mg/dL, $P > 0.05$).

ROC Study

Study of the biomarker for diagnostic characteristics of osteoporosis

The results in correlation between the biomarkers and receiver operating characteristic for diagnosis of osteoporosis are presented in Figure 1 and Table 11.

The ROC analysis for diagnosing osteoporosis from healthy controls is presented for two biomarkers, adiponectin and leptin. Adiponectin has a sensitivity of 96.7% and specificity of 76.7% with an AUC of 0.942 (95% CI: 0.897–0.987, $P < 0.0001$) and a Youden's J statistic of 0.734. The cut-off level is set at 3.0842 µg/mL. Leptin has a sensitivity of 86.7% and specificity of 86.7% with an AUC of 0.925 (95% CI: 0.866–0.985, $P < 0.0001$) and a Youden's J statistic of 0.734. The cut-off level is set at 2.8404 ng/mL. Both biomarkers exhibit good sensitivity and specificity and show promising diagnostic potential for differentiating individuals with osteoporosis from healthy controls.

Discussion

Multiple research studies have consistently demonstrated a significant association between age and osteoporosis. The risk of developing osteoporosis tends to rise with advancing

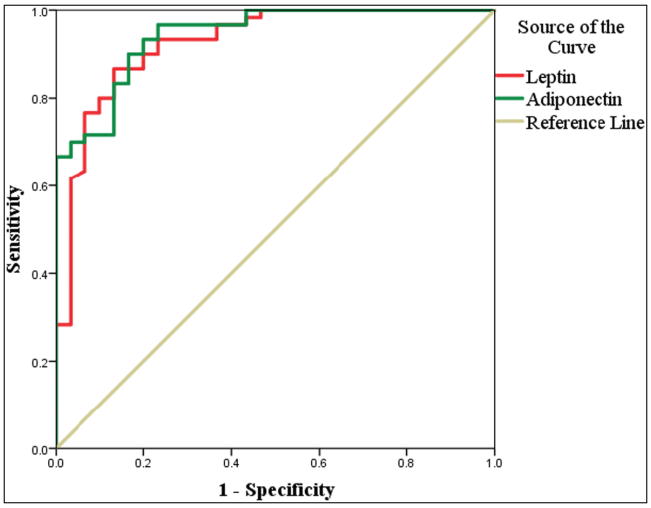

Figure 1: Illustrates the receiver operating characteristic (ROC) analysis, specifically the area under the curve (AUC), for the measured biomarkers in diagnosing Osteoporosis in comparison to healthy controls

Table 10: Comparisons of serum lipid profile levels of Osteopenia, Osteoporosis and healthy controls

Biomarker	Control N = (30)	Osteopenia N = (30)	Osteoporosis N = (30)	P-value
TC (mg/dL)	163.48 ± 49.48	203.50 ± 51.66	192.39 ± 48.59	0.012
TG (mg/dL)	130.06 ± 77.29	236.07 ± 103.36	187.93 ± 85.71	<0.0001
HDL-C (mg/dL)	46.39 ± 11.48	33.52 ± 8.87	32.3 2 ± 7.55	<0.0001
LDL-C (mg/dL)	143.10 ± 62.22	217.19 ± 68.32	197.65 ± 58.64	<0.0001

TC = total cholesterol, LDL-C = low-density lipoprotein cholesterol, TG = triglyceride, HDL-C = high-density lipoprotein cholesterol

Values expressed as mean ± SD

Significant differences at P-value ≤ 0.05

*Highly significant (P-value < 0.0001)

Table 11: The results of the receiver operating characteristic (ROC) analysis, specifically the area under the curve (AUC), for the measured biomarkers in diagnosing osteoporosis in comparison to healthy controls

Variable	Cut-off level	Sensitivity %	Specificity %	Youden's J statistics	AUC	95% CI of AUC	P-value
Adiponectin (µg/mL)	3.0842	96.7	76.7	0.734	0.942	0.897–0.987	<0.0001
Leptin (ng/mL)	2.8404	86.7	86.7	0.734	0.925	0.866–0.985	<0.0001

* Significant differences at P-value <0.05

AUC = area under curve, CI = confidence interval

age as a result of natural bone loss and declining bone mineral density. A noteworthy investigation published in the *Journal of Clinical Densitometry* thoroughly explored the relationship between age and bone mineral density, specifically focusing on a substantial cohort of postmenopausal women.[14] The results of the study revealed a robust and statistically significant negative correlation between age and bone mineral density. This finding indicates that as individuals grow older, their bone density tends to decrease, leading to an elevated risk of developing osteoporosis. Another critical factor associated with osteoporosis is BMI. Numerous studies have consistently demonstrated an inverse relationship between BMI and the likelihood of osteoporosis.[15] A comprehensive systematic review and meta-analysis, published in the *Journal of Bone and Mineral Research*, thoroughly investigated the influence of BMI on fracture risk specifically in postmenopausal women.[16] The findings of the study demonstrated a noteworthy association between higher BMI and a decreased risk of osteoporotic fractures. This suggests that increased body weight and fat mass play a protective role in maintaining bone health. In summary, the available evidence strongly supports the presence of significant disparities in age and BMI between individuals diagnosed with osteoporosis and healthy controls. Advanced age is widely recognized as a well-established risk factor for osteoporosis, whereas higher BMI is correlated with a reduced risk of osteoporotic fractures. These findings emphasize the significance of considering age and BMI as crucial factors when evaluating the risk and implementing management strategies for osteoporosis.

These findings are consistent with previous studies that have demonstrated an association among age, BMI, and the development of osteoporosis. Age is a well-established risk factor for osteoporosis, as bone density tends to decline with increasing age. Higher BMI has been linked to higher bone density, which may serve as a protective factor against osteoporosis.[15,17] However, excessive weight can also increase the risk of falls and fractures, which can lead to osteoporosis.

This indicates that individuals with osteoporosis have lower *Z*-scores, which indicate lower bone density compared to their age-matched peers, compared to healthy controls. Overall, the analysis demonstrates substantial and statistically significant differences in BMD, *T*-scores, and *Z*-scores between individuals with osteoporosis and healthy controls. The results support the assertion that individuals with osteoporosis exhibit significantly lower bone density and more severe bone loss compared to healthy individuals.[18] In a study published by Rinonapoli *et al*. in the *International Journal of Molecular Sciences* in 2021, the researchers examined and compared the BMD and *Z*-scores of men with and without osteoporosis. The findings of the study indicated that men diagnosed with osteoporosis had notably lower BMD and *Z*-scores when compared to men without osteoporosis.[19] The results align with the diagnostic guidelines for osteoporosis, which characterize the condition as a BMD measuring 2.5 standard deviations or more below the average for healthy young adults (equivalent to a *T*-score of –2.5 or lower). Numerous studies and diagnostic criteria have consistently demonstrated that individuals with osteoporosis exhibit lower BMD, *T*-scores, and *Z*-scores compared to healthy individuals. These findings emphasize the significance of BMD testing in the diagnosis and treatment of osteoporosis.

Overall, these findings suggest that individuals with osteoporosis have the lowest bone density measurements and are at the highest risk for fractures, followed by those with osteopenia. The control group has the highest bone density measurements and is at the lowest risk for fractures. Multiple studies have consistently demonstrated that individuals diagnosed with osteoporosis exhibit markedly lower BMD when compared to those without the condition. BMD, measured using DEXA, serves as a well-established parameter for assessing bone density and is widely utilized in the diagnosis of osteoporosis and evaluation of fracture risk. Reduced BMD is a characteristic feature of osteoporosis and is closely linked to an elevated vulnerability to fractures.[20] To summarize, scientific literature consistently confirms that individuals diagnosed with osteoporosis typically exhibit lower bone density measurements and are at an increased risk of fractures. BMD, *T*-scores, and fracture risk assessment tools play crucial roles in diagnosing osteoporosis, evaluating fracture risk, and informing treatment strategy.

Adiponectin and leptin are two adipocytokines that exert significant influences on bone metabolism. Adiponectin has been found to have beneficial effects on bone health, whereas leptin has been associated with detrimental effects on bone health.[11,21,22] Taking into account the provided data, individuals diagnosed with osteoporosis exhibit notably lower serum levels of adiponectin compared to those with osteopenia and healthy controls. This finding suggests a potential negative impact on bone health within the osteoporosis group. Conversely, individuals with osteopenia display significantly higher serum adiponectin levels when compared to those with osteoporosis and healthy controls, indicating a possible compensatory response to bone loss in this particular group. In terms of leptin levels, individuals with osteoporosis exhibit significantly higher serum levels of leptin compared to those with osteopenia and healthy controls,[23] implying a potential adverse effect on bone health within the osteoporosis group. Conversely, individuals with osteopenia have significantly lower serum leptin levels when compared to those with osteoporosis and healthy controls, suggesting a compensatory response to bone loss in this particular group. Overall, the data demonstrate

significant variations in serum adiponectin and leptin levels among individuals diagnosed with osteoporosis, osteopenia, and healthy controls. These differences may reflect variances in bone metabolism and provide valuable insights into potential mechanisms involved in the development and progression of osteoporosis.

Numerous studies have explored the association between adiponectin and osteoporosis, consistently demonstrating that individuals with osteoporosis have lower levels of adiponectin compared to healthy controls. Adiponectin and leptin are two significant adipokines implicated in the regulation of bone metabolism. Adiponectin, known for its insulin-sensitizing properties, has been shown to promote the differentiation of osteoblasts (cells responsible for bone formation) and inhibit the formation of osteoclasts (cells responsible for bone resorption), thus promoting bone formation and preventing bone loss.[24] In contrast, leptin is a hormone that regulates appetite and energy expenditure, but it also plays a significant role in bone metabolism. Research has demonstrated that leptin stimulates the proliferation and differentiation of osteoblasts, the cells responsible for bone formation. Additionally, it inhibits osteoclastogenesis, the process by which osteoclasts are formed, thereby promoting bone formation. Numerous studies have examined the association between adiponectin and leptin levels and osteoporosis. In one particular study, serum levels of adiponectin and leptin were compared between postmenopausal women with and without osteoporosis. The results indicated that individuals in the osteoporosis group had significantly lower levels of adiponectin and significantly higher levels of leptin compared to those without osteoporosis.[25] Another study reported similar findings in a group of older men with osteoporosis.[11] The precise mechanisms that explain the connections among adiponectin, leptin, and osteoporosis are not yet fully comprehended. Nonetheless, various hypotheses have been proposed to shed light on this matter. It is suggested that reduced levels of adiponectin might contribute to increased bone resorption and decreased bone formation due to its anti-inflammatory and anti-osteoclastogenic properties. Conversely, elevated levels of leptin may have detrimental effects on bone health by inhibiting osteoblast activity and promoting the formation and activity of osteoclasts. It is important to acknowledge that the relationship among adiponectin, leptin, and osteoporosis is intricate and influenced by multiple factors, including age, gender, BMI, and hormonal status. Moreover, inconsistencies have been observed across existing studies, underscoring the need for further research to fully comprehend the mechanisms and clinical implications of these associations. In summary, several studies have reported significantly lower adiponectin levels and significantly higher leptin levels in individuals with osteoporosis compared to healthy individuals. These findings suggest a potential role of adiponectin and leptin in the development of osteoporosis. However, additional research is necessary to gain a comprehensive understanding of the underlying mechanisms and establish the clinical significance of these associations.

In results findings are consistent with previous research indicating that individuals with osteoporosis tend to have higher TC, TG, and LDL-C levels, as well as lower HDL-C levels, compared to healthy individuals. For instance, a study published in the *Journal of BMC Musculoskeletal Disorders* investigated lipid profiles in postmenopausal women with osteoporosis and reported similar trends of elevated TC, TG, and LDL-C levels, along with decreased HDL-C levels, in the osteoporosis group when compared to healthy controls. A study conducted by Alfahal *et al*.,[26] published in the journal African Health Sciences, examined the lipid profiles of elderly individuals with osteoporosis. The study revealed findings consistent with previous research, indicating elevated levels of TC, TG, and LDL-C, as well as reduced levels of HDL-C, in this population. Although the exact mechanisms connecting altered lipid profiles and osteoporosis are not yet fully comprehended, dyslipidemia is thought to be involved in the development and progression of osteoporosis through several pathways. For instance, increased LDL-C levels have been linked to heightened inflammation and oxidative stress, which can have adverse effects on bone health.[27] Moreover, decreased levels of HDL-C may adversely affect the role of HDL particles in promoting bone formation and inhibiting bone resorption.[28] It is crucial to acknowledge that the presented findings indicate an association between lipid abnormalities and osteoporosis, but they do not provide conclusive evidence of a causal relationship. Additional research is necessary to unravel the intricate interplay between dyslipidemia and bone health. Collectively, the existing studies support the notion that individuals with osteoporosis generally display higher levels of TC, TG, and LDL-C, along with lower levels of HDL-C, compared to healthy individuals. Gaining a better understanding of these lipid alterations may have implications for identifying individuals at risk for osteoporosis and exploring potential therapeutic strategies.

In conclusion, the analysis reveals significant differences in serum PTH, calcium, and phosphate levels between individuals with osteoporosis and healthy controls, suggesting potential associations with the condition. However, no significant difference is found in serum magnesium levels, indicating that it may not be directly related to osteoporosis.[29,30] The elevation in PTH levels is frequently accompanied by a reduction in serum calcium levels, as PTH promotes the release of calcium from the bones into the bloodstream. Furthermore, individuals with osteoporosis may experience elevated serum phosphate levels, as PTH stimulates the kidneys

to reabsorb more phosphate, resulting in increased levels in the blood.[31] In a study published in the *Journal of Current and Advance Medical Research*, researchers discovered that postmenopausal women diagnosed with osteoporosis exhibited significantly elevated PTH levels and decreased serum calcium levels in comparison to postmenopausal women who were deemed healthy.[32] In a study conducted by Tsvetov *et al*.[33] and published in the journal Osteoporosis International, consistent findings were observed in both men and women diagnosed with osteoporosis. The study revealed elevated levels of PTH and phosphate, as well as reduced serum calcium levels, among individuals with osteoporosis.

Serum PTH plays a crucial role in maintaining the balance of calcium and phosphorus in the body. Increased PTH levels are frequently linked to bone loss and are recognized as a risk factor for osteoporosis. The data provided support this association, as individuals with osteoporosis and osteopenia display significantly higher serum PTH levels in comparison to healthy controls. These findings suggest an imbalance in calcium metabolism within these groups, which aligns with the conclusions drawn from the referenced study.[34] Calcium (Ca) is a vital mineral crucial for maintaining optimal bone health, and its levels are carefully controlled by various factors including PTH. The provided data demonstrate that individuals with osteoporosis and osteopenia exhibit considerably lower serum calcium levels in comparison to healthy controls. These findings indicate potential disruptions in calcium homeostasis within these groups, underscoring the importance of maintaining adequate calcium levels for maintaining bone health.[35] Magnesium (Mg) is a significant mineral that plays a crucial role in bone metabolism and interacts with calcium and PTH. The provided data reveal a notable finding: individuals diagnosed with osteoporosis exhibit significantly lower serum magnesium levels when compared to healthy controls. However, it is worth noting that the difference in magnesium levels between the osteopenia group and the control group did not reach statistical significance. This suggests a potential association between low serum magnesium levels and the presence of osteoporosis, highlighting the importance of magnesium in bone health.[36] Phosphorus (Pi) is a vital mineral that plays a critical role in bone formation and mineralization. The provided data indicate a noteworthy finding: individuals with osteoporosis and osteopenia exhibit significantly higher serum phosphorus levels in comparison to healthy controls. This increase in phosphorus levels could potentially be a compensatory response to the impaired bone metabolism observed in these groups. It suggests that elevated phosphorus levels may be associated with the pathophysiology of osteoporosis and osteopenia, highlighting the intricate relationship between phosphorus and bone health.[35] In summary, the data presented provide evidence of dysregulation in PTH and mineral levels, specifically calcium, magnesium, and phosphorus, among individuals with osteoporosis and osteopenia in comparison to healthy controls. These findings emphasize the intricate interaction between hormonal and mineral factors in maintaining optimal bone health. The observed disturbances in these parameters further support the understanding that imbalances in PTH and mineral levels contribute to the onset and advancement of osteoporosis.

This study findings indicate that both osteoporosis and osteopenia are associated with unfavorable lipid profile levels characterized by elevated TG and LDL-C levels and decreased HDL-C levels. These lipid profile alterations are recognized risk factors for cardiovascular disease, aligning with the outcomes reported in the study.[37]

The ROC analysis compared two biomarkers, adiponectin and leptin, for diagnosing osteoporosis from healthy controls. Adiponectin showed a sensitivity of 96.7%, whereas leptin exhibited a sensitivity of 86.7%. Both biomarkers displayed promising diagnostic potential for distinguishing individuals with Osteoporosis from healthy controls. These associations are supported by researches.[38]

Conclusion

This study presents compelling evidence demonstrating substantial disparities in age, BMI, bone density, hormonal and lipid profiles, as well as adiponectin and leptin levels between individuals with osteoporosis and healthy controls. The associations observed among adiponectin, leptin, and various parameters provide insights into their potential involvement in the development of osteoporosis. Moreover, the diagnostic value of adiponectin and leptin is underscored by their ability to distinguish osteoporosis patients from healthy individuals, and provide insights into the interplay between adiponectin and various parameters in the context of osteoporosis.

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Author contributions

Manal F. Al-Khakani contributed to the design and conceptualization of the study, as well as the execution and planning of the statistical analysis. Muna Sadeq Hameed provided the data for the study. The authors take full responsibility for all aspects of the research, including addressing any concerns regarding the accuracy or integrity of any part of the study and conducting appropriate investigations.

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Conflicts of interest

There are no conflicts of interest.

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