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Relationship between Biochemical Parameters and Bone Mineral Density in Postmenopausal Women of Karachi, Pakistan

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ABSTRACT

Background: Postmenopausal Osteoporosis is a significant public health concern, primarily due to estrogen decline, leading to metabolic changes and vasomotor symptoms. Common comorbidities in postmenopausal women include Diabetes Mellitus and Hypertension. This study aimed to assess the relationship between bone mineral density (BMD) and biochemical parameters in postmenopausal women to identify risk factors for osteoporosis and fractures.

Methods: This analytical cross-sectional study was conducted at a tertiary care hospital in Karachi from November 2023 to June 2024. After ethical approval, 150 postmenopausal women were enrolled and categorized into Normotensive, Non-Diabetic Hypertensive, and Hypertensive Diabetic (n=50 each). Investigated parameters included plasma glucose, HbA1c, lipid profile, and BMD. Data were analyzed using SPSS version 22.0. Pearson correlation assessed relationships between T-scores, Z-scores, and lipid parameters, with statistical significance set at $p<0.05$.

Results: Mean FBS, HbA1c, and total cholesterol were significantly higher in hypertensive diabetic women ($p=0.0001$). BMD analysis showed significantly lower T and Z-scores in hypertensive diabetic women ($p=0.0001$). Significant correlations were observed between Z-score and triglycerides ($p=0.008$) in normotensive women, T-score and Z-score ($p=0.000$) in hypertensive women, and T-score and triglycerides ($p=0.011$) in hypertensive diabetic women. Osteoporosis (76%) and fracture risk (64%) were significantly higher in hypertensive diabetic women ($p=0.0001$).

Conclusion: Hypertensive diabetic postmenopausal women exhibit significantly lower BMD, higher glucose and cholesterol levels, and increased fracture risk, underscoring their heightened osteoporosis susceptibility.

Keywords: Bone Mineral Density, Menopause, Hypertension, Diabetes, Osteoporosis.

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INTRODUCTION

One of the most prevalent health issues impacting older women globally is Osteoporosis (OP)[1]. Its main feature is low Bone Mineral Density (BMD), which can be brought on by a variety of reasons such as low vitamin D levels, aging, gender, low Body Mass Index, and inadequate dietary calcium consumption[1]. One of the main causes of OP in women is Menopause, which is marked by decreased estrogen levels that result in vasomotor symptoms and metabolic changes. The main symptoms of Postmenopausal Osteoporosis include decreased bone mass and weakening bones[2]. Hypo-estrogenic situations like Postmenopausal status are associated with reduced levels of high-density lipoprotein, also referred to as cardio-protective cholesterol and high levels of low-density lipoprotein[3]. Previous research has indicated that there is a possibility of a strong link between postmenopausal women's BMD & Lipid Profile. Increased Calcium loss from bone is the result of secondary Parathyroid gland activation brought on by Hypertension[3]. Hypertension can affect the kidney's capacity to metabolize Calcium and also the age-related excessive decrease in BMD. Additionally, it has been noted that elevated levels of Angiotensin II cause an increase in bone demineralization and resorption, which can have detrimental implications on Hypertension patients[4, 5]. Several studies have shown a negative correlation between hypertension and BMD[6, 7].

A prospective study using repeated Bone Mineral Density assessments on 3000 older women found that High Blood Pressure was linked to greater femoral neck bone loss after three years of follow-up[8]. According to research, Insulin Resistance and Bone Metabolism are also related. Apart from its function in controlling Glucose levels, Insulin can also have an impact on the production and breakdown of Bone [9]. Blood Glucose levels that are too high can negatively impact bone marrow Mesenchymal cells' ability to differentiate into Adipocytes. Elevated glucose levels cause the peroxisome proliferator-activated receptor gamma to be up-regulated and the non-canonical Wnt/protein kinase C pathway to be stimulated, which increases Adipogenesis and Bone loss[9].

Hormonal changes impact BMD and raise the risk of osteoporosis in Postmenopausal women. BMD and fracture risk may be influenced by biochemical indicators, including Lipid profiles and Glucose levels. By identifying the relationship between these parameters with BMD, we provided important information on the risk factors that contribute to Osteoporosis in the postmenopausal women.

METHODS

This analytical cross-sectional study was conducted at the Outpatient clinic of Medicine department at a tertiary care hospital in Karachi, from November 2023 to June 2024. Karachi Institute of Medical Sciences' Institutional Review Board approved the(Ref # 07/23/IRB/KIMS). One hundred and fifty Postmenopausal Women were enrolled in this study by using simple random sampling technique.

Declaration of Helsinki's guiding principles were followed throughout the research process[10]. 150 women, aged 50 years or older, who had attained menopause were divided into three groups: Normotensive, Hypertensive Non-Diabetic (with BP ≥ 140 /90mmHg or on antihypertensive medication were labelled hypertensive), and Hypertensive Diabetic (with BP ≥140 /90 mmHg and/or on antihypertensive or Oral Hypo-Glycemic were labelled as Hypertensive Diabetics). Exclusions from the study included females with gastrointestinal disorders, thyroid or parathyroid disorders and females taking estrogen therapy. After obtaining informed consent, following demographic information was entered into the questionnaire: Age, Height, Weight, Blood Pressure, Parity, Family and Medical history.

Sample size of this study was calculated by Sample Size Calculators for designing clinical research, using 23% positive correlation between T Scores lumbar spine and LH after adjusting for age and Menopause time at 95% confidence interval [11]. We required at least n=136 samples for this study. Weight by height meter squared was divided (kg/ m2) to determine the BMI[12].

Using the Glucose Oxidase-Phenol-Aminophenazone method (GODPAP), Serum Glucose was measured in the Fasting condition [13]. Using high-performance liquid chromatography, HbA1c levels were ascertained [14]. Commercially available Merck, France kits, Spectrophotometry (from Tokyo, Japan Model number AE-350, Erma Inc) was used to measure Triglycerides by glycerol-3-phosphate oxidase (GPO). Cholesterol and HDL-C by Cholesterol Oxidase phenol Aminophenazone (CHOD-PAP). LDL-C was estimated by using the formula by Friedwald[15].The Bone Density measurements were performed by trained staff. The Calcaneus (heel) bone Mineral Density was assessed using the DEXA-T Peripheral Ultrasonography Bone Densitometry (Stille AB, Stockholm, Sweden) [16]. The device software from the manufacturer converted the BMD measurement results, which were expressed in g/cm2, into T & Z-scores. A T-score of -1 or higher was regarded as normal. A score of -2.5 and below was labeled as Osteoporosis. Osteopenia was labelled as -1.1 to -2. 416.SPSS Version 22 was used to analyze the data (SPSS Inc., Chicago, IL, USA).

Quantitative variables with a normal distribution were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The Shapiro-Wilk test was used to assess whether continuous variables followed a normal distribution. To compare continuous numerical variables, the ANOVA test was applied for normally distributed data, whereas the Kruskal-Wallis test was used for non-normally distributed data. The Chi-square test was employed to compare categorical variables across the three groups. Correlations between T-scores, Z-scores, and lipid parameters were evaluated using the Pearson correlation test, with a significance level set at $p < 0.05$ and a 95% confidence interval.

RESULTS

The majority of study subjects were under 60 years old (57.3%). Most were overweight (48%), and 21.3% were obese. In the Hypertensive Diabetic group, 76% had a history of Osteoporosis, and 64% had a history of fractures, highlighting the detrimental effects of both conditions on bone health **(Table 1).**

Table 1: Frequency Distribution of Study Variables

Variables		Overall (n=150)	Normotensive (n=50)	Non- diabetic Hypertensive (n=50)	Diabetic Hypertensive (n=50)	p-value
Age groups	<60 years	86(57.3%)	44(88%)	26(52%)	16(32%)	0.101
	60 or more	64(42.7%)	6(12%)	24(48%)	34(68%)	
BMI	Normal weight	46(30.7%)	26(52%)	13(26%)	7(14%)	0.05
	Over-weight	72(48%)	16(32%)	34(68%)	22(44%)	
	Obese	32(21.3%)	8(16%)	3(6%)	21(42%)	
Osteoporosis history		78(52%)	11(22%)	29(58%)	38(76%)	0.0001
Fractures		53(35.3%)	4(8%)	17(34%)	32(64%)	0.001

N (%), Chi square test applied, Significance level <0.05.

Table 2: Comparison of Demographic Characteristics, Biochemical Markers, and Lipid Profile among The Study Groups

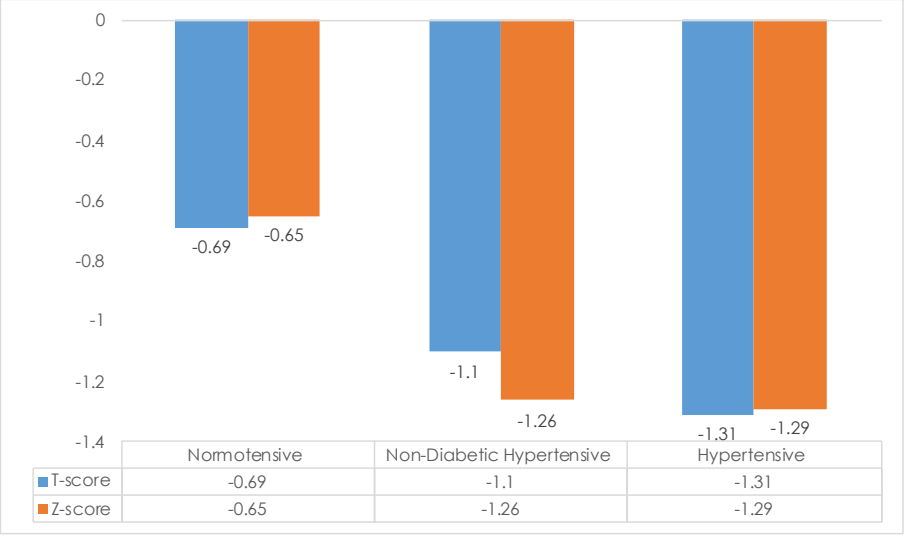
Variables	Normotensive (n=50)	Hypertensive Non-diabetics (n=50)	Hypertensive & Diabetics (n=50)	P-Value
Age in years	54.38+/-3.71	59.16+/-3.75	61.02+/-3.74	0.060
Weight (kg)	62.66+/-7.00	65.67+/-5.18	67.39+/-8.53	0.101
Height (meters)	1.56+/-0.09	1.58+/-0.45	1.53+/-0.05	0.051
Body Mass Index (kg/m^2)	25.64+/-3.34	26.36+/-2.58	28.71+/-3.60	0.081
Age at time of Marriage (years)	17.6+/-7.97	29.8/-4.18	22.34+/-4.94	0.015
No. of Children	3.26+/-1.67	5.08+/-1.61	2.34+/-0.47	0.214

FBS (mg/dl)	86.9+/-23.97	86.42+/-19.80	154.9+/-23.97	0.0001
HbA1c (%)	5.21+/-0.28	5.33+/-0.18	7+/-0.36	0.0001
Total Cholesterol (mg/dL)	167.6+/-47.15	174.08+/-22.23	205.48+/-43.02	0.001
Triglyceride (mg/dL)	147.14+/-37.18	217.74+/-38.86	225.18+/-52.49	0.012
HDL Cholesterol (mg/dL)	45.84+/-5.47	32.02+/-2.7	39.9+/-7.17	0.017
LDL Cholesterol (mg/dL)	126.62+/-8.59	129.5+/-5.11	133.04+/-8.77	0.110
VLDL (mg/dL)	25.74+/-7.40	29.32+/-2.16	31.2+/-1.62	0.018

Mean+/-SD, Anova test, Kruskal Wallis test applied, Significance level <0.05.

This study found significant differences in Biochemical Parameters among the groups. Mean Fasting Blood Sugar levels were 86.9±23.97 in Normotensive, 86.42±1.61 in Non-Diabetic Hypertensive, and 154.9±23.97 in Hypertensive Diabetic patients (p=0.0001). Mean HbA1c levels were 5.21±0.28, 5.33±0.18, and 7±0.36 respectively (p=0.0001). Mean Total Cholesterol levels were 167.6±47.15, 174.08±22.23, and 205.48±43.02 respectively (p=0.001) **(Table 2).**

Significantly low T-scores and Z-scores were found in Hypertensive Diabetic patients compared to Normotensive and Non-Diabetic Hypertensive groups (p=0.0001) **(Figure 1).**



Mean+/-SD, Anova test, Kruskal Wallis test applied, Significance level <0.05.

Figure 1: Comparison of T & Z-Score Among Three Groups

Table 3: Correlation Between Study Variables

Parameters	Normotensive (n=50)				Non-diabetics hypertensive (n=50)				Diabetic Hypertensive (n=50)			
	T-score		Z-score		T-score		Z-score		T-score		Z-score	
	correlation (r)	Sig.	correlation (r)	Sig.	correlation (r)	Sig.	correlation (r)	Sig.	correlation (r)	Sig.	correlation (r)	Sig.
T-score	1	---	-.129	.372	1	---	1.000**	0.000	1	---	.117	.420
Z-score	-.129	.372	1	---	1.000**	0.000	1	---	.117	.420	1	---
FBS	-.081	.577	-.184	.202	-.082	.570	-.082	.570	-.263	.065	-.291*	.040
HbA1c	-.043	.769	.092	.526	.125	.387	.125	.387	.036	.802	.093	.521
Total cholesterol (mg/dL)	-.003	.984	-.265	.063	.206	.151	.206	.151	.066	.649	.222	.121
Triglyceride (mg/dL)	.070	.628	-.372**	.008	-.081	.574	-.081	.574	.355*	.011	.195	.174
HDL cholesterol (mg/dL)	.068	.637	-.179	.213	.123	.393	.123	.393	-.100	.490	-.250	.080

Mean+/-SD, Pearson coefficient Correlation test applied, Significance level <0.05.

The study observed correlations of T and Z scores with Lipid Profile, HbA1c, and FBS in all three groups. In the normotensive group, a significant correlation was found between Z score and Triglycerides (r=-0.0372, P=0.008). In the Non-Diabetic Hypertensive group, T and Z scores were significantly correlated (r=-0.1, P=0.000). In the Hypertensive Diabetic group, T score was significantly correlated with Triglycerides (r=0.355, P=0.011), and Z score with FBS (r=-0.291, P=0.040) **(Table 3).**

DISCUSSION

The current study showed significant differences between Fasting Blood Sugar, HbA1c, Total Cholesterol, Triglycerides, LDL, and VLDL levels in the Diabetic Hypertensive group compared to two other groups. It was also found that a history of fractures was more common in the Hypertensive Diabetic group. In addition, the history of Osteoporosis was also more common in the Diabetic Hypertensive group and Non-Diabetic Hypertensive group compared to the Normotensive group along with a statistically significant difference between the three groups. The BMI of the individuals from the Diabetic Hypertensive group was higher as compared to the Non-Diabetic Hypertensive group and the Normotensive group, similar findings were found in another study by in 2023[17].

Correlations between BMD and various parameters range from weak to moderate across different groups. Research conducted in Korean women found out that BMD of lumbar, femur neck, and femur trochanter with Serum Glucose was positively correlated[18]. Our study showed a moderate negative relationship between FBS and Z levels in Hypertensive diabetic groups. In addition to the above, a weak positive correlation was found between HbA1c and Z score in the individuals having Diabetes and Hypertension. On the contrary, a study done on 434 post-menopausal T2DM, patients aged 46–87 years, hospitalized at the Department of Endocrinology of a Medical University, China, from Jan 2016 to Dec 2018, showed that higher HbA1c levels were associated with low Bone Mineral Density[19].This could be the result of the fact that better glycemic control leads to a better trabecular bone score. The possible effects of chronic hyperglycemia, which is frequently linked to diseases like type 2 diabetes, on bone health have been studied. Elevated blood sugar levels have been linked to alterations in bone turnover and BMD[9, 20]. Furthermore, hyperglycemia and inflammation are linked. Because it promotes bone resorption, chronic inflammation may be detrimental to bone health. Increased blood sugar levels have the potential to produce advanced glycation end products, which may have an impact on the composition and functionality of bone proteins[21, 22].

In the current study, a positive significant correlation is found between Total Cholesterol and BMD in two groups (Non-Diabetic Hypertensive and Diabetic Hypertensive), which is contrary to the study that showed that the levels of Serum Total Cholesterol and LDL-C were inversely correlated with BMD in two groups of women (355 postmenopausal and 375 premenopausal). The reason for this could be that

both in vitro and in vivo osteoblast functional activities are impacted by Total Cholesterol and its metabolites[23]. Because of this fact it is notable that a weak negative correlation is present in the current study between LDL and VLDL Cholesterol with Z score in all the groups. In another case–control study at an outpatient clinic conducted between 2012 till 2015 in Taiwan, 452 Postmenopausal women were evaluated and showed a negative correlation between LDL levels and BMD measurements[2]. In a Meta-analysis, different articles were evaluated that showed that 14.87% of post-menopausal females developed fracture. Among the 12 statistically significant parameters, two were hypertension and diabetes mellitus[24]. Additionally, diabetes mellitus and steroid use were found to raise the risk of first-incident hip fracture. It was widely accepted that common chronic conditions like diabetes mellitus and hypertension were associated with an increased risk of falls in the elderly[25]. The current research also showed that 76% females from Hypertensive Diabetic group, had a history of Osteoporosis, and 64% had a history of fractures. Osteoporosis-related fractures are more prevalent among postmenopausal women compared to premenopausal women or men, primarily due to the rapid bone loss accompanied by the decline of ovarian function in the menopausal transition [26].

The main limitation of the study was that we were unable to gather data from the post-menopausal women of the same age. There was a slight variation in the ages of the women of all three groups. Multicenter studies should be done to cover a large population.

CONCLUSION

BMD in Postmenopausal Women with Hypertension and Diabetes should be monitored more closely due to the increased risk of Fractures and Osteoporosis. Gaining a better understanding of the connection between Diabetes, Hypertension and Osteoporosis may help prevent fractures in the post-Menopausal women.

CONFLICT OF INTEREST

There is no conflict of interest

FUNDING

None

ETHICAL APPROVAL

The study was approved by the Institutional Review Board of the Karachi Institute of Medical Sciences, CMH, Malir Cantt, under reference number (Ref # 07/23/IRB/KIMS)/on 24-10-23

AUTHORS' CONTRIBUTIONS

MS and RF contributed to the conception and design of the study. Data collection and assembly were carried out by **RF and FF**, while **FP and AR** were responsible for data analysis and interpretation. **TA and MS** drafted the manuscript, with **TA and MS** also handling its revision. Statistical expertise was provided by **FF and FP**. The final approval and guarantors of the article were **FF, AR, and TA**.

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