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ORIGINAL ARTICLE

Association of Use of Drugs with Bone Mineral Density in Postmenopausal Women with Diabetes Mellitus

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ABSTRACT

Background: *Postmenopausal osteoporosis is a significant public health concern, characterized by reduced bone mineral density (BMD) and an increased risk of fragility fractures. In women with type 2 diabetes mellitus (T2DM), the interplay between metabolic dysregulation, microvascular complications, and pharmacological treatments may further influence bone health. This study aims to evaluate the association between the use of antidiabetic medications and bone mineral density in postmenopausal women with type 2 diabetes mellitus.* ***Methods & Materials:*** *This cross-sectional study was conducted in the Medicine Department of Sir Salimullah Medical College and Mitford Hospital, from July 2023 to June 2024. A total of 120 cases were included in this study according to the selection criteria. Data were processed and analyzed by SPSS 22.0. A p-value of <0.05 was considered statistically significant.* ***Result:*** *Among the 120 postmenopausal women studied, those with diabetes were older, had a longer duration since menopause, and showed a significantly higher prevalence of osteoporosis (63.3% vs. 40.0%) compared to non-diabetics. In the diabetic group, the mean duration of diabetes was 10.53 ± 5.09 years, with over half having poor glycemic control (HbA1c > 7%), and treatment was almost equally divided between oral agents alone and oral agents plus insulin. However, no significant differences in bone mineral density were observed between the two treatment groups.* ***Conclusion:*** *This study demonstrates that postmenopausal women with diabetes mellitus have a significantly higher prevalence of osteoporosis compared to their non-diabetic counterparts, a difference likely influenced by longer duration since menopause and suboptimal glycemic control. However, no significant association was observed between bone mineral density and the type of antidiabetic treatment (oral agents alone vs. oral agents plus insulin).*

Keywords: *Bone Mineral Density, Use of Drug, Postmenopausal Women, Diabetes Mellitus*

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INTRODUCTION

Postmenopausal women with type 2 diabetes mellitus (T2DM) face a distinctive skeletal phenotype marked by heightened fracture risk despite often normal—or even higher—bone mineral density (BMD) compared with non-diabetic peers. This "diabetic bone paradox" is attributed to qualitative deficits in bone material properties (e.g., increased cortical porosity, collagen glycation, microvascular compromise) and low bone turnover that are not fully captured by areal BMD on dual-energy X-ray absorptiometry (DXA) [1,2]. In this context, the pharmacotherapies commonly prescribed to manage hyperglycaemia may independently modify bone metabolism, BMD, and fracture risk, making medication exposure an important, potentially modifiable determinant of skeletal health in postmenopausal women with diabetes [1]. Among antidiabetic agents, thiazolidinediones (TZDs) have the most consistent adverse skeletal signal. Multiple syntheses of randomized and observational data demonstrate an increased risk of fractures—particularly in women—accompanied by measurable bone loss with TZD use [3,4]. Mechanistically, peroxisome-proliferator–activated receptor-γ activation promotes adipogenesis at the expense of osteoblastogenesis, suppressing bone formation and potentially accelerating postmenopausal bone loss. Given that many postmenopausal women with T2DM also carry cardiovascular and hepatic comorbidities, characterizing TZD-associated changes in BMD provides clinically actionable information for risk stratification.Sodium–glucose cotransporter-2 (SGLT2)

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inhibitors initially raised concern after a canagliflozin safety signal in CANVAS suggested higher fracture rates; however, pooled evidence across the class now indicates a largely neutral effect on fracture risk, with heterogeneity by molecule and population [5]. Dedicated analyses of canagliflozin have not consistently shown clinically meaningful BMD deterioration, though careful attention to volume depletion and fall risk remains prudent in older women [6]. By contrast, dipeptidyl peptidase-4 (DPP-4) inhibitors appear skeletal-neutral in meta-analyses, neither increasing fractures nor showing a strong effect on BMD, suggesting suitability in patients where bone safety is a priority [7]. The evidence for glucagon-like peptide-1 receptor agonists (GLP-1 RAs) is likewise generally neutral concerning fracture risk; some comparative analyses report no significant increase versus other agents, and any direct effects on BMD remain small or inconsistent in randomized data [8]. Insulin therapy presents a more complex picture. Although insulin has anabolic effects on bone in experimental systems, clinical studies indicate a modestly increased fracture risk among insulin users—likely mediated by hypoglycaemia-related falls, comorbidity burden, and confounding by indication—rather than a direct detrimental impact on bone mass [9]. For postmenopausal women, this underscores the importance of fall-prevention strategies and cautious titration where fracture risk is high. Metformin, the anchor first-line agent for T2DM, has been associated with osteoblast-supportive pathways in preclinical models; however, contemporary meta-analyses of clinical studies do not demonstrate a robust protective effect on fracture risk, and effects on BMD appear minimal overall [10].

METHODS AND MATERIALS

This cross-sectional study was carried out in the Department of Medicine of Sir Salimullah Medical College and Mitford Hospital, over 12 months from July 2023 to June 2024, involving 120 postmenopausal women—60 with type 2 diabetes mellitus (case group) and 60 age-matched non-diabetic women (control group). Postmenopause was defined as the absence of menstruation for at least 12 consecutive months, and type 2 diabetes mellitus was diagnosed according to the American Diabetes Association (ADA) criteria, with diabetic participants receiving either oral antidiabetic drugs (OAD) alone or OAD in combination with insulin for at least one year. Women with secondary causes of osteoporosis (e.g., endocrine disorders, chronic kidney disease), those on medications affecting bone metabolism (such as corticosteroids, bisphosphonates, or hormone replacement therapy), with surgical or premature menopause (<40 years), chronic inflammatory diseases, or malignancies were excluded. Data were collected using a structured proforma, recording socio-demographic information, age at menarche, age at menopause, duration since menopause, and for the diabetic group, duration of diabetes, glycemic control (assessed by HbA1c), and treatment modality. Anthropometric measurements were obtained to calculate body mass index (BMI). Bone mineral density (BMD) at the femoral neck and lumbar spine was measured for all participants using dual-energy X-ray absorptiometry (DXA), and T-scores and Z-scores were recorded. Statistical analyses were performed using appropriate software, with continuous variables expressed as mean ± standard deviation and categorical variables as frequency and percentage; comparisons between groups were made using unpaired t-tests and chi-square tests, and a p-value <0.05 was considered statistically significant.

RESULTS

The table shows the demographic profile of the study subjects. Mean age of the patients was 65.83 ± 8.75 years and 62.17 ± 7.67 years in diabetic and non diabetic post menopausal patients. There was no significant difference in the age of menarche and age at menopause. But the duration since menopause was significantly higher in diabetic patients than in non-diabetic patients. There was also no significant difference in BMI between the groups. [Table I].

Table – I: Demographic profile of the study subjects (*n*=120)

	Diabetic (n=60) n (%)	Non diabetic (n=60) n (%)	p-value
Age (years)			
50 – 59	8 (13.3)	19 (31.7)	
60 – 69	32 (53.3)	32 (53.3)	
≥70	20 (33.3)	9 (15.0)	
Mean ± SD	65.83 ± 8.75	62.17 ± 7.67	0.016
Age of menarche (years)	14.78 ± 0.69	14.63 ± 0.64	0.219
Age at menopause (years)	46.90 ± 3.39	46.95 ± 3.04	0.932
Duration since menopause (years)	19.70 ± 7.82	15.15 ± 8.27	0.002
Body Mass Index (kg/m^2)	24.60 ± 4.87	25.26 ± 3.40	0.397

Data were expressed as frequency, percentage, and mean (± Standard Deviation).
An unpaired t-test was done to measure the level of significance.

In the case group (n=60), the mean duration of diabetes mellitus was 10.53 ± 5.09 years, with the highest proportion (38.3%) having diabetes for 6–10 years, followed by 26.7% for 11–15 years, 20.0% for 1–5 years, and 15.0% for more than 15 years. Regarding glycemic control, 58.3% had suboptimal control (HbA1c > 7), while 41.7% maintained HbA1c ≤ 7. In terms of treatment, slightly more than half (51.7%) were on oral antidiabetic drugs (OAD) alone, whereas 48.3% were receiving a combination of OAD and insulin therapy. [Table II]

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Table – II: Diabetic variables of the case group (*n*=60)

	Frequency (n)	Percentage (%)
Duration of DM (years)		
1 – 5	12	20.0
6 – 10	23	38.3
11 – 15	16	26.7
>15	9	15.0
Mean±SD	10.53 ± 5.09	
Glycemic status		
HbA1c ≤ 7	25	41.7
HbA1c > 7	36	58.3
Type of treatment		
OAD	31	51.7
OAD + insulin	29	48.3

Data were expressed as frequency, percentage, and mean (± Standard Deviation).

Nearly half of both diabetic and non-diabetic participants (46.7% in each group) had been menopausal for 11–20 years. A shorter postmenopausal duration of 1–10 years was significantly more common in the non-diabetic group (33.3%) compared to the diabetic group (11.7%) (p = 0.008). Conversely, longer durations since menopause (21–30 years and >30 years) were more frequent among diabetic subjects (31.7% and 10.0%, respectively) than among non-diabetics (18.3% and 1.7%, respectively). [Table III]

Table – III: Duration since menopause of the study subjects (*n*=60)

Duration since menopause (years)	Diabetic (n=60)	Non diabetic (n=60)	p-value
1 – 10	7 (11.7)	20 (33.3)	0.008
11 – 20	28 (46.7)	28 (46.7)	
21 – 30	19 (31.7)	11 (18.3)	
>30	6 (10.0)	1 (1.7)	

Data were expressed as frequency and percentage.
An unpaired t-test was done to measure the level of significance

The table shows osteoporosis in diabetic and non diabetic post menopause patients. Osteoporosis was found to be significantly higher in diabetic patients than in non-diabetic patients. [Table IV]

Table – IV: Osteoporosis in Diabetic and Non diabetic patients (*n*=120)

	Diabetic (n=60) n (%)	Non diabetic (n=60) n (%)	p-value
Osteoporosis	38 (63.3)	24 (40.0)	0.033
Osteopenia	20 (33.3)	31 (51.7)	
Normal	2 (3.3)	5 (8.3)	

Data were expressed as frequency and percentage.
A chi-square test was done to measure the level of significance

Table V shows the association of drugs with bone mineral density in postmenopausal women with diabetes mellitus. There was no association of bone mineral density with the drug in postmenopausal women with diabetes mellitus. [Table V]

Table – V: Association of use of drug with bone mineral density in postmenopausal women with diabetes mellitus (*n*=60)

	Drug		p-value
	OAD (n=31) [Mean±SD]	OAD+insulin (n=29) [Mean±SD]	
T-score			
Femoral neck	-2.51 ± 0.96	-2.94 ± 1.17	0.129
Lumbar spine	-3.12 ± 1.50	-3.54 ± 1.52	0.287
Z-Score			
Femoral neck	-0.96 ± 0.81	-1.37 ± 1.16	0.116
Lumbar spine	-1.53 ± 1.06	-1.70 ± 1.45	0.594

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DISCUSSION

In this case–control study of postmenopausal women, osteoporosis was significantly more prevalent among participants with diabetes than among non-diabetic peers (63.3% vs 40.0%), and the diabetic group had a longer time since menopause. These observations are biologically and epidemiologically plausible. Bone loss accelerates across the menopausal transition and continues thereafter; thus, a greater duration since menopause—as seen in the diabetic cohort—would be expected to correspond with lower BMD and higher odds of osteoporosis, even after accounting for similar ages at menopause between groups [10,11]. Population studies likewise show that fracture risk is elevated in diabetes, and this excess risk is imperfectly captured by BMD alone—people with type 2 diabetes (T2D) often fracture at higher T-scores than non-diabetic individuals, reflecting diabetes-related deterioration in bone material properties and increased propensity to falls [1,2]. Our finding of a higher proportion of osteoporosis among women with diabetes, therefore, aligns with meta-analytic evidence indicating a substantial burden of osteoporosis in T2D globally [12]. At the same time, literature on BMD levels in T2D is mixed, with several cohorts (particularly those with higher BMI) reporting normal or even higher areal BMD in T2D despite greater fracture risk, the so-called "diabetic bone paradox" [2]. Recent syntheses continue to underscore this heterogeneity across skeletal sites and populations [13]. In our sample, diabetics showed more osteoporosis by DXA classification at the femoral neck and lumbar spine. Differences from studies reporting preserved or higher BMD may relate to our cohort's longer postmenopausal duration, the relatively older age structure of the diabetic group, and the high proportion with suboptimal glycemic status (58.3% with HbA1c >7%), all factors that have been linked to accelerated cortical loss, deficits in bone quality, and increased falls risk [1,2,10]. Ethnic and body-composition differences, skeletal site, and DXA measurement artifacts (e.g., spinal degenerative changes) may also contribute to between-study variability [1,2]. With respect to antihyperglycemic therapy, we observed no significant differences in T- or Z-scores between women treated with oral agents alone and those receiving a combination of oral agents plus insulin. This "null" association at the level of BMD is consistent with several lines of evidence. First, initiation of insulin in mid- to late-life diabetes has been associated with hip BMD decline in some longitudinal cohorts, but the magnitude is modest and may be confounded by disease severity and weight change; importantly, fracture excess with insulin appears to be driven at least partly by hypoglycemia and falls rather than large BMD decrements [14]. Second, for many contemporary non-TZD agents, randomized and real-world meta-analyses have generally shown neutral effects on fractures and BMD: DPP-4 inhibitors do not increase fracture risk, GLP-1 receptor agonists appear overall neutral with a possible signal for hip-fracture reduction in some analyses, and SGLT2 inhibitors have not shown clinically meaningful adverse effects on BMD [8,10,15]. In contrast, thiazolidinediones (TZDs) reliably increase fracture risk—particularly in postmenopausal women—through effects on osteoblastogenesis and bone resorption [10].

Limitations of The Study:

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

This study demonstrates that postmenopausal women with diabetes mellitus have a significantly higher prevalence of osteoporosis compared to their non-diabetic counterparts, a difference likely influenced by longer duration since menopause and suboptimal glycemic control. However, no significant association was observed between bone mineral density and the type of antidiabetic treatment (oral agents alone vs. oral agents plus insulin).

RECOMMENDATION

It is recommended that postmenopausal women with diabetes undergo routine bone health assessment, including timely BMD measurement, and be offered targeted osteoporosis prevention and management strategies—such as lifestyle modification, adequate calcium and vitamin D intake, and pharmacological therapy when indicated—regardless of their antidiabetic treatment regimen.

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