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Research Article

Risk Factors for Ten-Year Risk of Osteoporosis in Type 2 DM Patients Attending Tikur Anbessa Specialized Hospital Diabetic Center Cross-sectional Study

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is a major contributing factor to osteoporotic fractures via different mechanisms. This study assessed the ten-year risk of osteoporosis and associated factors for osteoporotic fractures in T2DM patients. *Methods*: Data from 175 type diabetes mellites (T2DM) patients over 40 years attending a diabetes clinic at Tikur Anbessa Specialized Hospital (TASH) were collected. Demographic information, diabetic complications, blood sugar levels, and other medical illnesses were collected by a structured questionnaire and from an electronic medical record system. The 10-year fracture risk assessment (FRAX) tool was used without bone mineral density (BMD) measurement. multivariate logistic regression was used to analyze factors associated with fragility fractures. *Results*: Half the participants were female, with a median age of 60. Most were married, well-educated, and urban residents. The median duration of diabetes was 11 years. The median FRAX score indicated a moderate 10-year risk of hip fracture (≥3%) and a high risk of major osteoporotic fracture (≥20%). Overall, 30.9% of patients had a high 10-year risk of osteoporotic fracture. The majority (78.3%) had macrovascular complications, with neuropathy, retinopathy, and nephropathy being the common ones. Higher FBS, higher HbA1c, and the presence of macrovascular complications were significantly associated with a higher risk of fractures. *Conclusion*: This study found a high prevalence (30.9%) of a 10-year risk of osteoporotic fractures in T2 DM patients. Poor glycemic control (higher HbA1c and FBS) and the presence of macrovascular complications were significantly associated with an increased 10-year osteoporotic fracture risk.

Keywords

Osteoporosis, DM, Fragility Fracture, FRAX Tool, Diabetic Complication

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1. Introduction

Globally, an estimated 151 million people live with type 2 DM, and by 2030this number is expected to rise to 324 million—type 2 DM results in many harmful complications, cardiovascular and renal complications being the most common. Several factors increase the risk of falls in type 2 DM patients, which include diabetic foot ulcer, diabetic peripheral neuropathy, diabetic retinopathy, and autonomic disturbances like orthostatic hypotension [1].

A large-scale meta-analysis published in 2020 investigated the association between type 2 diabetes mellitus (T2DM) and fracture risk, encompassing over 17.5 million participants from cohort and case-control studies. The findings reinforce the link between T2DM and an increased risk of fractures, particularly hip fractures. The analysis revealed a significant increase in hip fracture risk for individuals with T2DM. Compared to controls, men with T2DM exhibited a 13% greater risk, while women with T2DM showed a 34% increase in hip fracture risk. The study also identified a 19% rise in the risk of nonvertebral fractures (e.g., spine or wrist) among individuals with T2DM compared to the non-diabetic group. Notably, the analysis suggests that the heightened fracture risk in T2DM patients might be influenced by specific T2DM-related risk factors, potentially explaining variations in risk across the entire T2DM population [2].

A well-established risk factor for fractures is low bone mineral density (BMD) [3]. However, individuals with type 2 diabetes (T2DM) often have higher than expected BMD, potentially due to insulin resistance. Despite this higher BMD, T2DM patients experience fractures at a greater rate compared to those without diabetes. This suggests alternative mechanisms contributing to bone fragility in this population [4].

The FRAX tool, a commonly used method for fracture risk assessment, might underestimate the elevated risk of osteoporotic fracture in T2DM patients. This highlights the need to incorporate additional factors into this group's fracture risk prediction [5, 6].

Elevated glycation of bone matrix proteins in type 2 diabetes mellitus patients might be a factor leading to their increased risk of fractures [6, 7].

Studies have also shown an association between fracture risk and diabetes treatment, such as insulin and thiazolidinedione use [8, 9]. However, due to the interactions among medication, glycemic control, and diabetes-associated comorbidities, the relative effects of each factor still need to be determined [10].

Diabetes-associated complications, including peripheral neuropathy and congestive heart failure, were found to play a significant role in fracture risk [11].

A U-shaped relationship exists between HbA1c and fracture risk; HbA1c levels between 6.5% and 6.9% are associated with the lowest risk of fragility fractures. Conversely, HbA1c levels equal to or exceeding 9% were linked to an increased risk of fragility fractures. Interestingly, this could potentially indicate infrequent patient-provider interaction, as patients with uncontrolled diabetes might be less likely to receive regular healthcare [12].

2. Methods

2.1. Study Design

An institution-based cross-sectional study assessed the risk of high-risk fractures and associated factors in type 2 DM patients at Tikur Anbessa specialized hospital diabetic center from February 2023 to February 2024. The study included type 2 DM patients above the age of 40. Patients with one or more of the following were excluded from the study. 1) Individuals with active malignancy, 2) Type1 DM, 3) individuals taking anticoagulation therapy, 4) individuals with ESRD other than diabetic nephropathy, and 5) those who are <40 years old.

2.2. Study Procedure

A structured questionnaire was used to collect socio-demographic data, smoking, alcohol use, Parental history of hip fracture, awareness about osteoporosis, usage of vitamin supplements and calcium supplements, a diet rich in vitamin D and calcium, frequency of fall-down accidents in the past year, bone pain use of glucocorticoids and other risk factors for osteoporosis.

Laboratory data and macrovascular and microvascular complications were obtained from the electronic record system.

2.3. Sampling Procedure

All eligible patients with complete data were involved in the study.

2.4. Statistical Analysis

The quality of their data was ensured by verifying its completeness and consistency through cross-checking. The Kobo toolbox was used to enter and manage data. After extraction, the data was analyzed using SPSS version 26 software. A p-value of less than 0.05 was considered statistically significant. First, binary regression was used to identify factors linked to osteoporosis. Subsequently, a multiple logistic regression model included variables with a p-value less than 0.25 in the initial analysis for further evaluation.

3. Results

3.1. Sociodemographic Characteristics

The study included a total of 175 patients. Out of this, 88 (50.3%) were females, and the median (IQR) age was 60 (52-66) years. 134 (76.6%) were Orthodox Christians and 20 (11.4%) were Muslims. Most patients (74.3%) were married, and 78 (44.6%) had attended college and above. Most patients (85.1%) were from Addis Ababa, and almost all (97.1) lived in an urban setup. 68 (38.9%) were government employees, and the median monthly income of the participants was 5000 (3000-8000) ETB. (Table 1)

Table 1. *Sociodemographic characteristics of patients.*

		N	%	Median (IQR)
Sex	Male	87	49.7	
	Female	88	50.3	
Age (years)				60 (52-66)
Educational level	Unable to read and write	4	2.3	
	Able to read and write	10	5.7	
	Primary education	30	17.1	
	High school	53	30.3	
	College and above	78	44.6	
Residence	Rural	5	2.9	
	Urban	170	97.1	
Address	Addis Ababa	149	85.1	
	SNNPR	2	1.1	
	Amhara	1	0.6	
	Harare	1	0.6	
	Oromia	22	12.6	
Occupation	Daily laborer	2	1.1	
	Farmer	2	1.1	
	Government employee	68	38.9	
	Housewife	50	28.6	
	Merchant	8	4.6	
	Self-employed	45	25.7	
Monthly income (ETB)				5000 (3000-8000)

3.2. Diabetes Profile of Patients

The median (IQR) duration of diabetes among participants was 11 (6-20) years. The median (IQR) levels of HgA1c and FBS were 8.0 (7.0-9.4) and 150 (125-192), respectively. Macrovascular complications occurred in 137 (78.3%) patients, while neuropathy, retinopathy, and nephropathy were seen in 143 (81.7%), 140 (80.0%), and 126 (72.0%) patients, respectively.

Table 2. Diabetes profile of patients.

		Median (IQR)	N	%
Duration of DM (years) - median (IQR)		11 (6-20)		
Degree of control HgA1c		8.0 (7.0-9.4)		
Degree of glycemic control /FBS		150 (125-192)		
Macrovascular complications	No		137	78.3
	Yes		38	21.7
Neuropathy	No		143	81.7
	Yes		32	18.3
Nephropathy	No		126	72.0
	Yes		49	28.0
Retinopathy	No		140	80.0
	Yes		35	20.0

3.3. Risk Factors for Ten Years Risk of Osteoporosis

The most common risk factors identified were drinking alcohol, personal history of fracture, family history of hip fracture, and cigarette smoking seen in 115 (65.7%), 113 (64.6%), 110 (62.9%) and 17 (9.7%) patients, respectively. 151 (86.3%) patients took milk, cheese, or yogurt, while 42 (24.0%) used vitamin supplements. The median (IQR) weight and height were 71 (63-80) kilograms and 1.65 (1.58-.70) meters, respectively.

3.4. Risk Factors for Fracture

124 (70.9%) patients had a history of fall accidents in the past year, whereas 74 (42.3%) complained of difficulty keeping their balance. 71 (40.6%) had trouble with their vision, and 18 (10.3%) thought the lighting condition in their living and bathrooms was poor. History of bone pain and arrhythmia was elicited in 57 (32.6%) and 5 (2.9%) patients, respectively.

Table 3. Risk factors for osteoporosis.

Variables		N	%	Median (IQR)
Alcohol intake≥3 units/day	No	60	34.3	
	Yes	115	65.7	
Active Cigarette smoking	No	158	90.3	
	Yes	17	9.7	
Vitamin supplement intake	No	133	76.0	
	Yes	42	24.0	
Calcium supplement intake	No	155	88.6	
	Yes	20	11.4	
Hormonal supplement intake	No	175	100.0	
	Yes	0	0.0	
Milk, cheese, or yogurt intake	No	24	13.7	

Variables		N	%	Median (IQR)
Family history of hip fracture (father or mother)	Yes	151	86.3	
	No	65	37.1	
Epilepsy	Yes	110	62.9	
	No	171	97.7	
Stroke	Yes	4	2.3	
	No	167	95.4	
RA	Yes	8	4.6	
	No	173	98.9	
SLE	Yes	2	1.1	
	No	175	100.0	
Spinal cord injury	Yes	0	0.0	
	No	175	100.0	
Malabsorption	Yes	0	0.0	
	No	174	99.4	
IBD	Yes	1	0.6	
	No	174	99.4	
Cirrhosis	Yes	1	0.6	
	No	173	98.9	
Glucocorticoid intake	Yes	2	1.1	
	No	172	98.3	
Previous history of fracture	Yes	3	1.7	
	No	62	35.4	
	Yes	113	64.6	
Weight (Kg)				71 (63-80)
Height (M)				1.65 (1.58-.70)

Table 4. *Risk factors for falls and fractures.*

Variables		N	%
Fall accident in the past year.	No	51	29.1
	Yes	124	70.9
Difficulty of keeping balance	No	101	57.7
	Yes	74	42.3
Difficult in vision	No	104	59.4
	Yes	71	40.6
Condition of lighting in living and bathrooms	Poor	18	10.3
	Good	157	89.7
History of arrhythmia	No	170	97.1

Variables		N	%
History of bone pain	Yes	5	2.9
	No	118	67.4
Multiple myeloma	Yes	57	32.6
	No	175	100.0
	Yes	0	0.0

3.5. Knowledge About Osteoporosis (Bone Thinning)

61 (34.9%) patients knew about bone thinning, and 40 (22.9%) patients knew that T2DM is related to bone thinning. Only 22 (12.6%) patients were screened for osteoporosis, out of which 12 (54.5%) received treatment. 77 (44%) patients knew the importance of osteoporosis screening.

Table 5. *Knowledge about osteoporosis.*

Variables		N	%
Know about osteoporosis (bone thinning)	No	114	65.1
	Yes	61	34.9
Screened for osteoporosis (bone thinning)	No	153	87.4
	Yes	22	12.6
Know the importance of osteoporosis (bone thinning) screening	No	98	56.0
	Yes	77	44.0
Know that T2DM is related to osteoporosis (bone thinning)	No	135	77.1
	Yes	40	22.9

3.6. Prevalence of 10-Year Risk of Osteoporosis

The median (IQR) FRAX score for the 10-year probability of a hip fracture ≥ 3% and a 10-year probability of a major osteoporosis-related fracture ≥ 20% were 1.5 (0.5-3.3) and 7.8 (3.0-10.0), respectively. Using the FRAX score for the 10-year probability of a hip fracture, 54 (30.9%) patients had a 10-year risk of osteoporosis. However, only 8 (4.8%) had an increased risk of 10-year risk of osteoporosis using the FRAX score for the 10-year probability of a major osteoporosis-related fracture, and all had a 10-year probability of a hip fracture of ≥3%. Accordingly, the overall prevalence of a 10-year risk of osteoporosis in this study is 30.9%.

3.7. Factors Associated with Ten-Year Risk of Osteoporosis

Upon binary regression, monthly income ≤5000 ETB, longer duration of DM, higher FBS, higher HgA1c, and the presence of macrovascular complications, diabetic nephropathy, diabetic neuropathy, and diabetic retinopathy were associated with using a P-value of 0.25 as a cutoff. These variables were then taken to multivariate logistic regression, after which only three variables were found to have a statistically significant association with increased risk of 10-year osteoporosis. These variables were higher FBS (AOR, 1.01; 95% CI, 1.00-1.02; P= 0.011), higher HgA1c (AOR, 1.45; 95% CI, 1.11-1.88; P= 0.006), and presence of macrovascular complications (AOR, 2.73; 95% CI, 1.12-6.66; P= 0.027).

Table 6. *Factors associated with ten-year risk of osteoporosis.*

Variables		Osteoporosis		COR (5% CI)	AOR (5% CI)	P value
		No	Yes			
Monthly income (ETB)	≤5K	69	36	1.00	1.00	
	>5K	52	18	0.66 (0.34-1.30)	0.54 (0.24-1.21)	0.134
Duration of DM (years) – median (IQR)		10 (5-18)	15 (9-21)	1.05 (1.01-1.09)	1.02 (0.98-1.07)	0.397
FBS (mg/dL) – median (IQR)		138 (118-160)	189 (155-240)	1.02 (1.01-1.03)	1.01 (1.00-1.02)	0.011*
HgA1c (%) – median (IQR)		7.6 (6.9-8.8)	9.3 (8.5-10.3)	1.78 (1.42-2.23)	1.45 (1.11-1.88)	0.006*
Nephropathy	No	91	35	1.00	1.00	
	Yes	30	19	1.65 (0.82-3.30)	0.86 (0.36-2.05)	0.730
Neuropathy	No	102	41	1.00	1.00	
	Yes	19	13	1.70 (0.77-3.76)	1.11 (0.42-2.91)	0.835
Retinopathy	No	101	39	1.00	1.00	
	Yes	20	15	1.94 (0.90-4.17)	1.55 (0.61-3.92)	0.353
Macrovascular complications	No	102	35	1.00	1.00	
	Yes	19	19	2.91 (1.39-6.13)	2.73 (1.12-6.66)	0.027*

*Statistically significant

4. Discussion

This study identified a 30.9% prevalence rate for a 10-year risk of osteoporosis.

The diagnosis of osteoporosis is based on BMD measurements or clinically by the presence of a fragility fracture; multiple studies showed an association between type 2 DM and the risk of osteoporotic fractures but showed mixed outcomes [13-16]. Some studies have shown a surprisingly lower prevalence of osteoporosis, as measured by bone mineral density (BMD), in patients with type 2 diabetes compared to healthy controls [17-19]. One potential explanation for this unexpected finding could be the presence of degenerative changes and diffuse idiopathic skeletal hyperostosis (DISH), which are frequently observed in patients with type 2 diabetes [20]. In contrast, a systematic review conducted in China found a greater prevalence of osteoporosis among individuals with type 2 diabetes mellitus (T2DM) [21].

Our study participants' median age (IQR) was 60 (52-66) years, consistent with different metanalysis. Our result showed no association between fragility fracture with age and sex, suggesting that type DM might play a vital role in both sexes and across different age groups; this finding is also seen in other meta-analyses [13].

Our study showed a strong association between the degree of glycemic control (HGA1C and fasting blood sugar) and increased risk of fragility fractures, FBS (AOR, 1.01; 95% CI, 1.00-1.02; P= 0.011), HgA1c (AOR, 1.45; 95% CI, 1.11-1.88; P= 0.006). This finding is consistent with different studies; Conway et al. revealed a complex relationship between HbA1c levels and the risk of osteoporosis-related fractures. This relationship was described as cubic, meaning that both very low and very high HbA1c levels were associated with increased fracture risk, as opposed to a simple linear relationship where only high HbA1c would be a risk factor [12].

A meta-analysis by Lin et al. found a strong link between HbA1c and osteoporosis risk. Individuals with HbA1c levels equal to or above 7 had a significantly increased risk of osteoporosis compared to those with HbA1c below 7. This translates to an adjusted hazard ratio (HR) of 1.49, with a 95% confidence interval (CI) ranging from 1.15 to 1.92 (p = 0.002) [15]. Krakauer JC et al. also found that poor glycemic control metabolic effects led to increased bone resorption and bone loss in young adults [22].

Li CI et al. found an increasing trend between the HbA1c level and hip fracture incidence in individuals with type 2 DM above 65 years. The risk of hip fracture was 24%–31% higher among patients with HbA1c levels ≥ 9% than among patients with HbA1c levels of 6%–7% after adjusting for numerous risk factors for fracture [23].

A study investigated bone mineral density (BMD) in 78 poorly controlled type 2 diabetes patients (T2DM) aged 28-73 with initial HbA1c exceeding 8%. The patients underwent BMD measurements before and after three weeks of improved glycemic control. The study found that better blood sugar

control decreased bone mineral loss within this short period. This suggests that managing blood sugar levels in T2DM patients might play a role in protecting against bone loss [24].

Macrovascular complications such as ischemic heart disease, peripheral arterial diseases, and cerebrovascular diseases were found to be significantly associated with increased fragility fractures and osteoporosis in our study.

Macrovascular complications occurred in 137 (78.3%) patients, while neuropathy, retinopathy, and nephropathy were seen in 143 (81.7%), 140 (80.0%), and 126 (72.0%) patients, respectively. A statistically significant association between macrovascular complications and risk of osteoporosis was seen (AOR, 2.73; 95% CI, 1.12-6.66; P= 0.027).

These findings agreed with findings from different studies. A retrospective study by Lee et al. examined the link between diabetes and fracture risk [11]. After accounting for various factors like age, ethnicity, and medical conditions, the study found that Individuals with diabetes had an approximately 22% increased risk of any clinical fracture compared to those without diabetes (adjusted risk ratio: 1.22, 95% CI: 1.21-1.23). Similarly, the risk of hip fracture was also about 21% higher in diabetic patients (adjusted risk ratio: 1.21, 95% CI: 1.19-1.23). Crucially, the study identified specific health conditions that might explain a significant portion of this increased fracture risk in diabetic patients. These mediating factors were Peripheral neuropathy, cardiovascular disease, and Congestive heart failure. These three conditions together accounted for 45.5% of the fracture risk associated with diabetes.

Although other studies indicated a correlation between microvascular complications and an increased risk of osteoporosis [11]. In this study, we did not find a significant association between microvascular complications and the risk of fragility fracture and osteoporosis. Diabetic retinopathy (AOR, 1.00; 1.55 (0.61-3.92, p=0.353), diabetic nephropathy (AOR, 1.00; 0.86 (0.36-2.05; p=0.730) and diabetic peripheral neuropathy (AOR, 1.00; 1.11 (0.42-2.91; p=0.835). This discrepancy might be explained by the effects of treatments to control microvascular complications, although further investigation is needed.

To our knowledge, this is the first study in our country focusing on the prevalence of osteoporosis in type 2 DM patients and associated risk factors. Despite the lack of materials to do BMD in our setup, the study tried to estimate the risk of fragility fracture.

Limitations of the study: Since the study was done in a single center and most participants were urban dwellers, it is challenging to generalize the result for the general population.

The unavailability of the DEXA scan in our center for BMD measurements limited our ability to exclude potential confounding factors. FRAX score without BMD risk calculation may underestimate the risk of osteoporosis and fragility fractures. Recall bias also might be a factor.

5. Conclusion

The prevalence of a 10-year risk of osteoporosis was 30.9% in this study. Levels of HGA1C, FBS, and macrovascular complications were significantly associated with the risk of fragility fractures and osteoporosis.

Abbreviations

AOR	Adjusted Odds Ratio
BMD	Bone Mineral Density
CD	Crohn's Disease
CHF	Congestive Heart Failure
CI	Confidence Interval
CVD	Cerebrovascular Disease
DISH	Diffuse Idiopathic Skeletal Hyperostosis
DM	Diabetes Mellitus
ETB	Ethiopian Birr
FBS	Fasting Blood Sugar
FRAX	Fracture Risk Assessment Tool
HbA1c	Hemoglobin A1c
HIV	Human Immunodeficiency Virus
IBD	Inflammatory Bowel Disease
IHD	Ischemic Heart Disease
IQR	Interquartile Range
MOF	Major Osteoporotic Fracture
PAD	Peripheral Arterial Disease
RA	Rheumatoid Arthritis
SLE	Systemic Lupus Erythematosus
T1DM	Type 1 DM
T2DM	Type 2 DM
UC	Ulcerative Colitis

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Author Contributions

Gebeyehu Azibte: Conceptualization, Methodology, Investigation, Analysis, and manuscript Writing.

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Institutional Review Board Statement

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Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Consent for Publication

Not applicable.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article.

Conflicts of Interest

The authors declare no conflicts of interest.

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