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Comparative Study of BMD in Type 2 Diabetic and Non-diabetic Male Patients

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Abstract

Introduction: Osteoporosis and diabetes are both common human diseases. The prevalence of both is increasing individually and in combination, due to better detection methods and changing definitions. Due to the different pathogenesis of Type 1 and Type 2 diabetes mellitus (T2DM), one of which is a predominant autoimmune process while the other mainly a metabolic disorder, it is not surprising that there is no uniform entity of diabetic bone disease as such, although such term has been proposed in the past but never gained momentum. Paradoxically, an increased risk of osteoporotic fracture in T2DM has been repeatedly demonstrated and this was independent of bone mineral density (BMD). This association with fracture adds uncertainty around the actual association between diabetes mellitus and BMD.

This study aims to study the population of diabetes at tertiary care center when they are compared with non-diabetics in terms of BMD.

Aims of Study: The aim of this study was to determine the prevalence of osteopenia and osteoporosis in T2DM and non-diabetic male patients using Dual Energy X-ray absorptiometry (DEXA scan).

Materials and Methods: Patients for the study included male patients between 40 and 60 years of age group attending outpatient department, health checkup, and admitted in the ward of Saifee Hospital, Department of Medicine. In 200 (100 type 2 diabetic males and 100 non-diabetic males), DEXA Scan was performed in the Department of Imaging, Saifee Hospital from June 2017 to April 2019.

Results: Type 2 diabetics were significantly associated with the presence of osteoporosis compared to non-diabetics (P = 0.001). Type 2 diabetics were significantly associated with body mass index (BMI) >25 (P = 0.0) and diabetics had a significantly higher BMI compared to non-diabetics (P = 0.0001). Type 2 diabetics above 50 years of age were significantly associated with osteoporosis (P = 0.000) and diabetics with osteoporosis were significantly older compared to diabetics without osteoporosis (P = 0.0018).

Conclusion: The study concluded that there is a correlation between T2DM, increasing age, glycemic control, increased BMI, increased calcium levels, and decreased BMD. Thus, physician treating diabetes must anticipate decreased BMD and rule out or correct all of these factors in patients of diabetes to prevent the complications of decreased BMD in these groups of patients. Therefore, early detection and treatment of osteoporosis/osteopenia by estimation of BMD in Type 2 diabetic males, strict diabetic control with target hemoglobin A1c <6.5, weight control with target BMI <25, supplementation with Vitamin D3 should be advocated.

Keywords: Diabetes, osteoporosis, dual-energy X-ray absorptiometry scan.

Introduction

Osteoporosis and diabetes are both common human diseases. The prevalence of both is increasing individually and in combination, due to better detection methods and changing definitions. Albright and Reifenstein reported their coexistence as early as in 1948 in a population that was not confined by age limits, but hitherto the association between them remains unclear despite indirect evidence although more associative rather than causal. Due to the different pathogenesis

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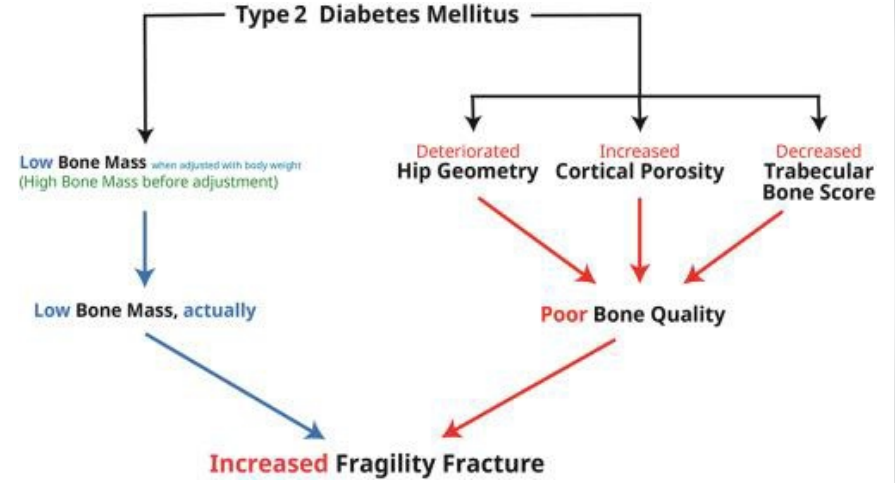

Figure 1: Pathophysiology of increased fracture fragility in Type 2 diabetes mellitus.

of Type 1 and Type 2 diabetes mellitus (T2DM), one of which is a predominant autoimmune process while the other mainly a metabolic disorder, it is not surprising that there is no uniform entity of diabetic bone disease as such, although such term has been proposed in the past but never gained momentum. While decreased bone mineral density (BMD) has consistently been observed in Type 1 diabetes mellitus patients, studies on BMD investigated in T2DM showed contradictory results with higher, lower or similar values in comparison with healthy control subjects, that is, the results were contradictory and not conclusive toward a definite conclusion. These inconsistent findings may be related to vast differences in study design, BMD measurement technology, differences in site of BMD examination, selection of patients, and presence or absence of complications. It may also be due to the different geographic location, the different ethnic background of the patients, and different food and lifestyle habits prevalent over different backgrounds. Barrett-Connor found that older women with T2DM had higher BMD levels at all sites compared to those with normal glucose tolerance, but this effect was not observed in men. It has also been suggested that obesity and hyperinsulinemia can lead to lower bone turnover in diabetic women so that the adverse effects of estrogen deficiency on bone mass are attenuated and delayed after menopause. This study aims to study the population of diabetics at tertiary care center when they are compared with non-diabetics in terms of BMD.

Background

Metabolic bone disease is underestimated in our country due to unawareness of the same, both among patients as well as health providers. It is like a silent epidemic, affecting many and turning out to be debilitating, with a substantial financial and economic loss to the patient, society, and nation. There is evidence that vitamin D (vit D) insufficiency is an independent risk factor for both Type 1 (T1D) and Type 2 (T2D) diabetes in adults with a history of diabetes, ultimately presents with problems related to Vitamin D deficiency which manifests as bone mineral disorders in the form of bone pain, muscle pain, and pathological fractures. Diabetes is often associated with changes in bone health and the term "Diabetic osteopathy" needs to be defined.

People with Type 2 diabetes have high rates of bone resorption and turnover and decreased BMD, compared with non-diabetic control subjects. This has been found to be both an independent effect as well as promoted by various factors. The end result of this is bone pain, weakness, and fractures on trivial trauma.

Various research by various workers has given conflicting reports and findings. The effect of non-insulin-dependent diabetes mellitus on bone mass has been controversial (Bouillon, 1991). There are reports of a decrease in bone mass (Levin et al., 1976; Lshida et al., 1985; Lsaia et al., 1987), normal findings (Giacca et al., 1988; Weinstock et al., 1989), and even an increase in bone mass (Meema and Meema, 1967; De Leeuw and Abs, 1977; Johnston et al., 1985). However, recently, both Type 1 and Type 2 diabetes have been shown to be associated with an increased risk of osteoporotic bone fractures of the hip after adjustment for confounders. This indicates that there is a need to further evaluate type two diabetes patients for bone disorders. Obesity, widespread in T2DM, is strongly associated with higher BMD, probably through mechanical loading and hormonal factors, including insulin, estrogen, and leptin. However, low levels of insulin and the progression of T2DM may cause reductions in BMD.

The pathological role of the non-enzymatic modification of proteins by reducing sugars, a process that is known as glycation (also called the "Maillard reaction"), has become increasingly evident in various types of diseases. The most common disease for this is diabetes mellitus due to the long duration of persistence of these products; these products can affect any organ system leading to the dysfunction, an effect that is cumulative over time.

It is now well established that early glycation products undergo progressive modification over time in vivo to the formation of irreversible cross-links, after which these molecules are termed "advanced glycation end-products (AGEs)." Once this process happens, it is very difficult to get rid of these products, and they start to affect the various organ systems, leading to end-organ complications of diabetes that ultimately

	Number of patients	Percentage
Normal	25	25
Osteopenia		
1 site	27	27
2 sites	13	13
3 sites	3	3
Osteoporosis		
1 site	15	15
2 sites	10	10
3 sites	7	7
Total	100	100
BMD: Bone mineral density		

Table 1: BMD data in diabetic patients.

	Number of patients	Percentage
Normal	55	55
Osteopenia		
1 site	17	8.5
2 sites	14	4
3 sites	1	0.5
Osteoporosis		
1 site	10	5
2 sites	2	1
3 sites	1	0.5
Total	100	100
BMD: Bone mineral density		

Table 2: BMD data in normal patients.

translates into morbidity and mortality. The formation and accumulation of AGEs in various tissues are known to progress during normal aging, and at an extremely accelerated rate in diabetes mellitus, thus being implicated in the development of atherosclerosis and diabetic microangiopathy. There are a couple of reports to show that AGEs may be involved in the pathogenesis of osteoporotic bone diseases. In vitro, AGEs enhance osteoclast-induced bone resorption in cultured mouse unfractionated bone cells. The similar response in mouse cell can be translated for the human body in the form of osteopenia and osteoporosis. In vivo, serum levels of AGEs are elevated in patients with osteoporosis. AGEs may directly contribute to osteoporosis, or it may be by stimulation of some other pathway that is yet not clear and the subject of speculation and research.

Another indirect effect of hyperglycemia is glycosuria, which causes hypercalciuria, leading to decreased levels of calcium in the body and poor bone quality, thus hastening bone loss. Hastening bone loss due to hypercalciuria can be detected early and effectively stopped if recognized and suspected on time. Some studies have shown low levels of Vitamin D with altered Vitamin D metabolism in patients with diabetic osteopenia.

Asokan et al. studied 150 patients between 40 and 70 years. A cross-sectional study was conducted at the tertiary care center from December 2010 to July 2012. Seventy-five diabetic subjects with at least 5 years of diabetes and 75 non-diabetic subjects were included in the study. The researchers concluded that although the significant difference in BMD was not observed in both groups; the incidence of osteoporosis was higher among Type 2 diabetics. Hence, all Type 2 diabetics should be evaluated for the risk of osteoporosis and should be offered appropriate preventive measures.

Oei et al. published in 2013, the Rotterdam study linking reduced BMD with inadequate glycemic control in diabetes. The Rotterdam study is a prospective, population-based cohort studying the determinants of chronic diseases and disability in Dutch men and women. Femoral neck and lumbar spine BMD was measured by dual-energy X-ray absorptiometry (DEXA) using a Lunar DPX-L densitometer. The researchers concluded that poor glycemic control in Type 2 diabetes is associated with fracture risk, high BMD, and thicker femoral cortices in narrower bones. They postulate that fragility in apparently "strong" bones in implantable cardioverter-defibrillator can result from microcrack accumulation and/or cortical porosity, reflecting impaired bone repair.

Dutta et al., published in 2012, the association between BMD and Type 2 diabetes. A total of 200 patients with T2DM were screened initially for the study. Finally, 67 patients (M:34, F:33) who satisfied the requirement of having been on 1 year of prescribed therapy were included for analysis. The researchers concluded that men and women with T2DM have lower BMD. BMD did not have a correlation to glycemic control. Glitazones, metformin, and insulin are associated with a decrease in BMD at the spine, and hip, while sulphonylureas are associated with an increase in BMD.

Lacunae in published literature

From an extensive review of published literature, it is not sure whether there is any link between diabetes and decreased BMD, and if there is then what are the other risk factors at play.

Aims of study

The aim of this study was to determine the prevalence of osteopenia and osteoporosis in T2DM and non-diabetic male patients using DEXA scan.

Materials and Methods

DEXA scan was performed on patients with T2DM and non-diabetic patients referred to the Department of Imaging, Saifee Hospital for DEXA scan during my data collection period (June 2017–April 2019). Hologic Horizon a QDR Series X-ray bone densitometer machine was used. The DEXA scan results were evaluated and interpreted to provide useful information on the BMD and found out the incidence of osteoporosis and osteopenia based on the T score and Z score in patients with T2DM and non-diabetics. BMD was measured in the distal end of the radius, LS spine, and neck of the femur, and the data were analyzed on the basis of T-score and Z-score using the World Health Organization criteria. Osteopenia and

	Diabetic	Non-diabetic	P-value
Normal	25	55	0
Reduced	75	45	
Diabetics were significantly associated with reduced BMD compared to non-diabetics (P = 0.0).			

Table 3: Normal bone mineral density.

	Diabetic	Non-diabetic	P-value
Present	43	32	0.108
Absent	57	68	
There was no significant relationship between the groups in the existence of only osteopenia			

Table 4: Osteopenia.

osteoporosis were taken as abnormal BMD.

Study site

This study was conducted at SAIFEE HOSPITAL, MUMBAI.

Study population

Patients for the study were included male patients between 40 and 60 years of age group attending the outpatient department, health checkup and admitted in the ward of Saifee Hospital, Department of Medicine.

study design

This was a observational study.

Sample size

The sample size was 200 (100 types 2 diabetic males and 100 non-diabetics).

Inclusioncriteria

Male patients in the age group of 40–60 years were included in the study.

Male patients with T2DM (fasting blood sugar [FBS] >126 mg/dL, postprandial blood sugar [PPBS] >200 mg/dL, hemoglobin A1c [HbA1C] >6.5% with insulin resistance/relative insulin deficiency).

Exclusion criteria

1. Male patients with T2DM with age <40 years and >60 years
2. Female patients
3. Patients had comorbidities affecting BMD like: Renal disease. Inflammatory diseases like rheumatoid arthritis. Chronic Liver disorders. Malabsorption syndrome. Malignancy
4. Patients taking drugs like: Steroids Antiepileptics
5. Patients having endocrinopathies. Hypo and Hyperthyroidism Parathyroid disease.

Results

This study was performed at Saifee Hospital, Mumbai, Department of Medicine. One hundred male patients each, Type 2 diabetics and non-diabetics were enrolled after satisfying inclusion and exclusion criteria. The patients were not matched, and neither was there blinding due to logistic reasons.

The study took into account 50% diabetics and 50% non-diabetics and the results were observed as follows: Table 1

One-fourth of the patients had a normal BMD in diabetics, whereas 43% were only osteopenic and 32% osteoporotic. Table 2.

About 55% of the patients had a normal BMD in non-diabetics, whereas 32% were only osteopenic and 13% osteoporotic.

Comparison of BMD: Non-diabetic versus diabetic males Table 3.

Diabetics were significantly associated with reduced BMD compared to non-diabetics (P = 0.0). Table 4.

There was no significant relationship between the groups in the existence of only osteopenia. Table 5.

Diabetics were significantly associated with the presence of osteoporosis compared to non-diabetics (P = 0.001).

Discussion

This study was performed at the Department of Medicine, Saifee Hospital, Mumbai. Saifee Hospital Mumbai caters to patients of diabetes mellitus, from nearby areas, the whole of Mumbai, an entire state, neighboring states, and even abroad. There are round the clock facilities for the care of diabetes patients including routine care, emergencies, and end-organ damage management.

Out of a total of 200 male patients, there were 100 patients who were non-diabetic and 100 who had T2DM. Due to logistic reasons blinding was not possible, however, every patient was male and thus gender matched.

One-fourth of the patients had a normal BMD in diabetics, whereas 43% were only osteopenic and 32% osteoporotic. This correlates with the study by Wakasugi et al. [10] the reason for 75% having a reduced BMD may be due to undergoing chronic inflammation or end-organ damage due to advanced glycation.

About 55% of the patients had a normal BMD in non-diabetics, whereas 32% were only osteopenic and 13% osteoporotic. This correlated with the findings by Meema and Meema [24] it is to be noted that, even in non-diabetics, 45% had reduced BMD, this may be due to the aging process.

Type 2 diabetics were significantly associated with reduced BMD compared to non-diabetics (P = 0.0). This correlated with the findings by Athulya et al. [4] Diabetics due to the longer duration of metabolic derangements,

	Diabetic	Non-diabetic	P-value
Present	32	13	0.001
Absent	68	87	
Diabetics were significantly associated with the presence of osteoporosis compared to non-diabetics (P = 0.001).			

Table 5: Osteoporosis.

develop permanent glycation products leading to significantly reduced BMD.

There was no significant relationship between the groups in the existence of only osteopenia. This correlates with Tuominen et al. [26] It is thus understood that diabetes predisposes to decreased BMD, but there are some other factors leading to either osteoporosis or osteopenia.

Type 2 diabetics were significantly associated with the presence of osteoporosis compared to non-diabetics (P = 0.001). This correlates with Wakasugi et al., [10] Oei et al. [27] Osteoporosis contributes to bone pain which may often be mistaken in diabetics due to neuropathy, go undetected, and ultimately lead to pathological fracture after trivial trauma.

Type 2 diabetics were significantly associated to be older compared to non-diabetics (P = 0.0011). This correlates with the findings of Meema and Meema [24] and Dutta et al. [28] this again stresses the point often believed by many, that there is a component of aging in diabetes pathogenesis.

Although not significant, patients with reduced BMD were older compared to patients with normal BMD (P = 0.088). This correlates with the findings of Wakasugi et al., [10] Athulya et al. [4] Thus decreased BMD has a component of aging compared to patients of normal BMD.

Type 2 diabetics above 50 years of age were significantly associated with osteoporosis (P = 0.000) and diabetics with osteoporosis were significantly older compared to diabetics without osteoporosis (P = 0.0018). This correlates with the findings of Meema and Meema [24] Tuominen et al. [26] this again underlines the importance of aging along with diabetes in the pathogenesis of decreased BMD.

These two factors may be associated with weakness in the calcium metabolism system leading to ultimately reduced BMD.

Type 2 diabetics were significantly associated with body mass index (BMI) >25 (P = 0.0) and diabetics had a significantly higher BMI compared to non-diabetics (P = 0.0001). This correlated with the findings of Athulya et al., [4] Oei et al. [27] A higher BMI is associated with obesity, and obesity has been linked with reduced BMD.

Patients with reduced BMD had significantly higher mean BMI compared to patients with normal BMD (P = 0.03). This has been correlated by Tuominen et al., [26] Dutta et al. [28] Higher mean BMI has been associated with pressure on the skeleton, and impaired metabolism of bone ultimately leading to decreased BMD.

Type 2 diabetics with osteoporosis had significantly higher mean BMI compared to non-osteoporosis subjects (P = 0.018). This correlates with the findings of Wakasugi et al., [10] Oei et al., [27] Meema and Meema [24] Thus diabetes, osteoporosis, and increased BMI all were interlinked to each other.

Diabetics had significantly raised FBS, PPBS, and HbA1c compared to non-diabetics, and significantly raised calcium compared to non-diabetics. The TSH, Vitamin D3, and creatinine levels were comparable between the groups.

Thus it is seen that there is a relationship between decreased BMD, T2DM, increased age, increased BMI, impaired diabetes control, and raised calcium levels. All or any of these components create interplay in the body which ultimately leads to decreased BMD which may translate into devastating osteoporosis.

Thus health-care providers must keep these interrelated factors in mind whenever tackling a patient of diabetes, that is, check the age of the patient, check the level of glycemic control, check the BMI, and check the calcium levels. These will help a physician detect decreased BMD early and correct for the same, to ultimately improve the outcome and reduce the morbidity of patients of T2DM.

Summary and Conclusion

This study performed at the Department of Medicine, Saifee Hospital Mumbai had the following salient findings:

1. Type 2 diabetics were significantly associated with reduced BMD compared to non-diabetics (P = 0.0)
2. There was no significant relationship between the groups in the existence of only osteopenia
3. Type 2 diabetics were significantly associated with the presence of osteoporosis compared to non-diabetics (P = 0.001)
4. Type 2 diabetics were significantly associated to be older compared to non-diabetics (P = 0.0011)
5. Although not significant, patients with reduced BMD were older compared to patients with normal BMD (P = 0.088)
6. Type 2 diabetics above 50 years of age were significantly associated with osteoporosis (P = 0.000) and diabetics with osteoporosis were significantly

older compared to diabetics without osteoporosis (P = 0.0018)

7. The TSH, Vitamin D3, and creatinine levels were comparable between the groups.

From the above findings, it is understood that there is a correlation between diabetes, increasing age, glycemic control, increased BMI, increased calcium levels, and decreased BMD. Thus physician treating diabetes must anticipate decreased BMD and rule out or correct all of these factors in patients of diabetes to prevent the complications of decreased BMD in these groups of patients.

Recommendations

1. Every Type 2 diabetic males should be screened for osteoporosis/osteopenia by BMD estimation as early as possible and if present should be treated
2. Serum Ca, Vitamin D3 level should be checked in Type 2 diabetic males and if needed should be corrected
3. Strict weight control should be done in Type 2 diabetic males (target BMI <25)
4. Strict blood sugar control should be done in Type 2 diabetic males (target HbA1c <6).

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the Journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Conflict of Interest: NIL; **Source of Support:** NIL

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