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Original Research Article

Estimation of bone mineral density among type 2 diabetes mellitus patients in western Odisha

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ABSTRACT

Background: Diabetes Mellitus is one of the most common chronic non-communicable diseases in the world. The relationship between type 2 diabetes mellitus (T2DM) and bone mineral density (BMD) has been controversial. Early identification of reduction in bone mass in a diabetic patient may be helpful in preventing the bone loss and future fracture risks. Objective: The aim is to study the effect of T2DM on BMD among patients in western Odisha.
Methods: A cross-sectional study was conducted on 120 patients between 40 and 65 years of age which included 60 diabetic and 60 nondiabetic subjects. BMD was measured using qualitative ultrasound and the data were compared among age-matched subjects of both the groups. Statistical analysis was performed using unpaired Student's t-test and test of equality of proportions.
Results: No significant difference was observed in bone density of both the groups. On further analyzing the data, incidence of osteoporosis was higher among diabetic subjects, whereas incidence of osteopenia was higher among nondiabetic subjects.
Conclusions: Although significant difference in bone mineral density was not observed in both the 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.

Keywords: Bone mineral density, Osteoporosis, Qualitative ultrasound, Type 2 diabetes

INTRODUCTION

Diabetes mellitus is a metabolic disorder resulting from a defect in insulin secretion, insulin action, or both. A consequence of this is chronic hyperglycemia with disturbances in carbohydrate, fat, and protein metabolism. Diabetes mellitus (DM) is a common disorder of carbohydrate, fat, and protein metabolism reflected by inappropriate high fasting and postprandial glucose levels (hyperglycemia). This ailment results from the absence or scantiness of insulin secretion with or without concurrent impairment of insulin action. Consequently, the disease was classified into two types known as type I (insulin dependent, IDDM) and II (non-insulin dependent, NIDDM) according to the degree of pancreatic defect.

According to World Health Organization (WHO) at least 366 million people worldwide have diabetes in 2011. This figure will rise to 552 million by 2030.The number of people with type 2 DM is increasing in every country.

DM is not confined to abnormal blood glucose levels but progresses to affect other body systems. This fact has been confirmed by several epidemiological studies and clinical trials that have linked hyperglycemia to several complications at the macrovascular (coronary artery disease and cerebrovascular disease) and microvascular

levels (renal failure, blindness, limb amputation, neurological complications and premature death.[1]

Endocrine and metabolic alterations in diabetes mellitus can trigger disorders of calcium homeostasis, skeletal metabolism, and bone mass.

It is reported that more than of 50% type 1 diabetes patients have osteoporosis (OP), which is called diabetic osteoporosis (DO), a reduced bone mass and an increased fracture risk shown to occur in type 1 diabetes mellitus.[2] On the other hand, in type 2 diabetes, several but not all cross-sectional studies have found normal or elevated bone mass, and these results are surprising given the increased fracture risk associated with type 2 diabetes.[3-5] In type 2 DM patients complicated with OP, there is a larger decrease in bone formation than bone resorption in compared with the case of postmenopausol OP, and this mainly influences the indexes of bone formation and may be a lower turnover ratio type.

Most studies indicate less bone mineral density (BMD) with insulin dependent diabetes mellitus.[6] But with type 2 diabetes some authors report increased some report decreased and some others report unaltered.[7-9] BMD Metabolic bone disease is underestimated in our country due to unawareness of the same, both among patients as well as health providers. Early identification of reduction in bone mass in a diabetic patient may be helpful in preventing the bone loss and future fracture risk.

Interpretation of fracture data as a measure for bone health is particularly difficult in patients with long-standing diabetes. Visual and neurologic complications can predispose patients to accidents resulting in an increased fracture risk not necessarily dependent on bone density alone. Other factors that make studies difficult to interpret include the presence of diabetic renal disease, autonomic, and neuropathic changes that could contribute to a loss of BMD and a low level of physical activity related to diabetic complications.[6]

Diabetes could influence bone through several mechanisms, some of which may have contradictory effects. Obesity, widespread in type 2 diabetes mellitus (T2DM), is strongly associated with higher BMD, probably through mechanical loading and hormonal factors, including insulin, estrogen, and leptin.[10] Hyperinsulinemia may promote bone formation.[11] However, low levels of insulin and the progression of T2DM may cause reductions in BMD.

Higher glucose levels in the blood interact with several proteins to generate a higher concentration of advanced glycation end-products (AGEs). Yamagishi et al. hypothesized that AGEs in collagen may interact with bone to reduce bone strength, resulting in osteoporosis in patients with diabetes.[11] Accumulated AGEs in the body may stimulate apoptosis of osteoblasts, thereby contributing to the defective bone formation.[12]

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.[13] Some studies have shown low levels of Vitamin D with altered Vitamin D metabolism in patients with diabetic osteopenia.[14] In addition, microvascular complications of diabetes lead to reduced blood flow to bone and may contribute to bone loss and fragility.[15]

Diabetic osteopathy may need attention as one of the common disease complications. Recently, BMD has been identified as a key determinant of future fracture risks. Each standard deviation of a decrease in BMD yields three-fold increases in fracture risk.[16]

Therefore, we decided to assess BMD of type 2 diabetic patients with more than 5 years of diabetes using QUS. The results from the diabetic patients were compared with nondiabetic age-matched control subjects, recruited from the same geographical region.

We investigated whether there is any difference among DM patients and a control group in terms of lumbar and femur BMD (bone mineral density) and standard deviation scores (Z score and T score).

METHODS

This randomized, prospective, controlled study was conducted in VIMSAR BURLA. Patients with type 2 diabetes mellitus were included in the patient groups. Healthy individuals were included in the control group. In addition to their demographic characteristics (age, gender, weight, height, body mass index [BMI]), used medicines were obtained. The patients included in this study were between the ages of 40 and 65. The control group in this study consisted of healthy individuals.

All the recruited subjects signed informed consent forms before participating in the study, and approval of a local ethics committee was obtained.

The exclusion characteristics were known cases of malabsorption syndromes, malignant diseases, chronic pancreatitis or pancreatotomy, primary hyperparathyroidism, thyroid function abnormalities, paget's disease, and inflammatory disorders such as rheumatoid arthritis, systemic lupus erythematosus, postmenopausal women or those with history of hysterectomy and patients treated with steroids, gonadotropin-releasing hormone agonists, gonadal hormones, immunosuppressants, anticonvulsants and calcium and Vitamin D supplements, thiazolidinediones and bed-ridden patients were excluded from the study.

The medicines taken by the patients, and their disease durations were recorded. Data about the presence of diabetic complications (retinopathy, ischemic cardiac disease, hypertension, neuropathy, nephropathy) were

regularly recorded in during follow-up. The whole blood count, fasting blood glucose, urea, creatine, C-reactive protein, HbA1c (glycolysed hemoglobin), alkaline phosphatase (ALP), calcium (Ca), phosphor (P) levels, and erythrocyte sedimentation rate (ESR) were examined.

BMD was measured in the distal end of radius using QUS and the data were analyzed on the basis of t-score and Z-score using the WHO criteria. T scores between −1 and -2.5 were considered to indicate osteopenia, and those equal or below -2.5 were considered to indicate osteoporosis (WHO Study Group, 1994).

The calculations were performed using the Statistical Package for Social Sciences for Windows software version 20.0. BMD data of type 2 diabetic subjects were compared with those without diabetes matched for age using unpaired Student's t-test. In patients with abnormal BMD, test of equality of proportions was used to compare osteopenia and osteoporosis. Statistical significance was based on a value of $p < 0.05$ with a 95% confidence interval.

RESULTS

Characteristics of the study populations with and without diabetes are given in Table 1.

Table 1: Demographic features of case and control group.

	DM (N=60)	Control (N=60)	T	P
Age (yr)	58.3±8.5	54.6±7.4	1.13	0.92 (NS)
Sex (male)	34	30		
BMI (kg/m^2)	34.2±5.1	26.8±6.5	1.85	0.062 (NS)

DM: diabetes mellitus; SD: standard deviation. $p < 0.05$ is significant.

The mean age for diabetics was 56 years and nondiabetics was 54 years. Basic characteristics when compared, both groups had a similar body mass index (BMI). 34 diabetic patients are male and 30 healthy subjects are male.

In Table 2 clinical parameters of the case and control groups were compared. FBS, HbA1C were significantly high in diabetic patients. Serum creatinine values also were higher in diabetic subjects. Other metabolic parameters such as serum calcium, phosphorous, and alkaline phosphate levels were similar in both the groups. BMD values were similar, and no significant difference was found in both the groups.

This Table 3 depicts the BMD distribution among the study population. The majority of the participants (56.6%) in the study had abnormal BMD. Among them, 54% were diabetics and 60% were nondiabetics. The rest with normal BMD, 46% were diabetics and 40% were nondiabetics. No significant difference was found in the groups with regard to BMD.

Table 2: Clinical parameters of patient and control groups (mean ± SD or n, %).

	DM(N=60)	Control (N=60)	t	p
Ca(mg/dl)	8.7± 0.2	8.4± 0.3	1.12	0.72 (NS)
P(mg/dl)	4.3± 0.7	4.1± 0.5	1.5	0.133 (NS)
ALP(U/L)	84.4± 32.3	82.3± 30.4	0.1	0.26 (NS)
FBS(mg/dl)	179± 48.9	97.6± 14.3	7.3	0.005 (HS)
HbA1C	8.45± 1.2	5.45± 0.3	6.9	0.002 (HS)
Urea	48± 11.2	42± 8.2	1.03	0.35 (NS)
Creatine	0.9± 0.3	0.7± 0.2	6.22	0.00 (HS)
CRP	0.2± 0.4	0.12± 0.05	1.02	0.24 (NS)
ESR	16.5± 7.8	14.3± 6.5	1.06	0.32 (NS)
BMD T score (femur)	-0.45± 1.03	-0.34± 1.2	0.082	0.95 (NS)
BMD Z score	-0.89± 1.08	-0.87± 1.06	0.122	0.89 (NS)

DM: diabetes mellitus; SD: standard deviation. $p < 0.05$ is significant NS: Not significant. HS: Highly significant.

Table 3: Value of BMD in case and control group.

	DM (N=60)	Control (N=60)	Total (N=120)
Normal BMD	28(46%)	24(40%)	52(43.3%)
Abnormal BMD	32(54%)	36(60%)	68(56.6%)

Table 4: Risk of osteopenia and osteoporosis in case and control group.

	DM(N=60)	Control(N=60)
Normal BMD	28	24
Osteopenia	21	32(88%)
Osteoporosis	11(34%)	4

Table 4 illustrates the distribution of osteopenia and osteoporosis among the study population Sub-analysis of abnormal BMD was performed as osteopenia and osteoporosis, and on further studying the data, osteoporosis was found to be higher in diabetics (34%) and osteopenia was found higher in nondiabetics (88%).

In Table 5 a negative correlation was found among people with abnormal BMD and HbA1C with P<0.05. A

positive correlation was found among people with abnormal BMD and FBS with P<0.05. Duration of diabetes is also high in patient with abnormal BMD.

Table 5: Correlation of BMD with biochemical parameters.

Dibetic	With normal BMD=28(46%)	With abnormal BMD =32(54%)	P
HbA1C	8.9	6.8	0.00
FBS	124	183	0.03
Duration (YR)	6.8	8.4	0.02

p < 0.05 is significant

DISCUSSION

The most important aim of our study was to compare the bone mineral densities of type 2 diabetes mellitus patients with those of a normal, healthy population. Although osteoporosis is one of the complications of type 1 diabetes, the effect of type 2 DM on bone mineral density is controversial. In different studies, the BMD values in type 2 DM have increased, decreased, or stayed normal.[17,18] In general, the type 2 DM patients with low BMD values have been observed to have long-term diabetes and menopause, to have poor glucose control, and to have disordered renal functions. Furthermore, in some studies, it has been concluded that diabetic women are protected from osteopenia. This can be explained in type 2 DM, unlike the case of type 1 DM, by the frequent observation of obesity due to increased insulin resistance and the higher of osteoarthritis in DM patients.

Osteoporosis is a prevalent metabolic bone disease, and its occurrence in diabetic patients further increases their burden of disease. BMD is used as an indicator for assessing susceptibility to osteoporosis.[19,20] The mean duration of diabetes among cases was 8 years.

In this study, no significant difference was observed in BMD among both the groups. These findings were supported by studies carried out by Wakasugi et al and Athulya G. Asokan et al.[21,22] When further analysis of abnormal BMD was performed as osteopenia and osteoporosis, the incidence of osteopenia was found higher among diabetics.

Many mechanisms have been asserted to contribute to diabetic osteopenia. One of them is that it can lead to diabetic osteopenia due to deficiency in anabolic activation of insulin.[23] Another mechanism asserted in diabetic osteopenia is suppression of osteoblastic bone formation.[24] In previous studies, it has been shown that decreases in osteoblastic functions occurred in diabetic ostopenia. Previous studies have also shown that the bone cycle speed in type 2 DM is much slower than that in healthy postmenopausal patients.[25] In another study on type 1 and type 2 diabetes patients, it has been underlined that the decrease in bone mass can be related with decrease in bone formation and microangiopathy in bone tissue.[26] In histopathologic examination of type 2 DM patients, the osteoblast surface, cortical thickness, osteoid thickness, osteoid volume, and bone volume have been found to be lower in diabetic patients. It has been concluded that the mechanism laying behind the diabetic osteopenia can be the decrease of quantitative osteoid, the decrease of osteoblasts, and finally the decrease of bone cycle. In DM patients, chronic hyperglycaemia decreases estradiol synthesis by causing ovarian damage. Estradiol has a direct stimulatory effect on osteoblasts, and this may contribute to osteoporosis.

These findings were Same As the observations seen in few studies. Ishida et al. in their study assessed the degree of diabetic osteopenia and serum Vitamin D metabolic level in type 2 diabetics and found decreased bone mass in diabetic subjects.[27] Gregorio et al observed reduced bone mineral content in poorly controlled diabetic subjects.[8] Interestingly, some other studies had shown diabetes as a promoter for bone health. Barrett-Connor and Holbrook found that women with T2DM had a significantly higher BMD level than women with normal glucose tolerance.[7] Meema and Meema postulated in 1967 that diabetes was an anti-osteoporotic condition.[28]

In this study, no significant difference was observed in the BMI of two groups and the study did not signify BMI as a predictor for BMD. In diabetic subjects who had normal BMD, mean BMI was 25.3 kg/m2 and in those with abnormal BMD, mean BMI was 24.1 kg/m^2. This was against a meta-analysis that had demonstrated BMI as an important predictor of BMD and that low BMI is associated with decreased BMD, increased risk of osteoporosis and increased risk of fracture.[29]

In this study, a negative association was observed between the duration of diabetes and BMD. These results were consistent with findings of Wakasugi et al and Kao et al.[21,15] They demonstrated duration of diabetes as a risk factor for decreased BMD in T2DM subjects. This study also demonstrated a negative association between glycemic control and BMD. Those with abnormal BMD had a mean HbAIc of 8.9% and normal BMD had a mean HbAIc of 6.8% which was statistically significant. The mean fasting blood sugar among diabetics with normal BMD was 124 mg/dl and abnormal BMD was 183 mg/dl, the differences were statistically significant. These findings were supported by studies carried out by Okazaki et al. who found that metabolic improvements in poorly controlled T2DM decreased bone loss within a short period.[30] However, these findings were against the observation of Weinstock et al. who found no significant relationship between BMD, duration of diabetes or HbAIc.[31]

Although, in this study diabetic subjects had no significant difference in BMD when compared to nondiabetic counterparts, the incidence of osteoporosis was higher among them. The study revealed a negative

association between glycemic control, duration of diabetes and BMD. The study also observed an increasing creatinine values among those with abnormal BMD. Henceforth, all diabetics should be evaluated for the risk of osteoporosis and appropriate preventive measures may be offered.

CONCLUSION

BMD scores had negative correlation with duration of diabetes and glycemic control and duration of diabetes. Although diabetic subjects had no significant difference in BMD as compared to the nondiabetic counterparts, prevalence of osteoporosis was higher among them as compared to control group. However, additional studies are required to determine whether osteoporosis is aggravated by T2DM and whether it should be considered as one of the long-term complications of diabetes. Further studies with Vitamin D levels and assessment of BMD using DEXA scan may be required. Thus, identifying and evaluating populations at increased risk of developing osteoporosis is critical in disease prevention and management. It will help diabetic patients to lead a better life.

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