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Original Article

Internal Medicine Section

Bone Mineral Density among Lean Type II Diabetes Mellitus Patients-A Cross-sectional Comparative Study

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ABSTRACT

Introduction: In case of diabetes mellitus, the pathological process behind fragility of the bone are complex. This process is found to be mediated by various factors like hyperglycaemia, oxidative stress and the accumulation of products of glycation.

Aim: To study bone mineral density in lean diabetics and to compare with normal population.

Materials and Methods: The present study was undertaken as a cross-sectional comparative study among 60 participants (30 cases of lean diabetics and 30 normal controls). The convenient sampling technique was done to select study participants and the study was carried out during the period from January 2015 to December 2016. Patients who were already a known case of Type 2 diabetes mellitus or newly diagnosed to have Type 2 diabetes mellitus whose BMI was <18.5 kg/m^2 were considered as cases. Chi-square test was used for finding a statistically significant difference in proportions; Independent student t-test was used for finding the statistically significant difference between means; Pearson's correlation coefficient was estimated for finding linear association between two continuous variables; a p-value <0.05 was considered to be statistically significant.

Results: On comparison of cases with controls no statistically significant differences were observed between the two groups in terms of age, waist-hip ratio and BMI (p-value >0.05). Bone mineral density parameters were found to be significantly lower among lean diabetes mellitus patients. HbA1C was found to negatively correlate with that of bone mineral density.

Conclusion: Osteopenia and osteoporosis, characterised by low bone mineral density values were found to be highly prevalent among lean diabetics.

Keywords: Body mass index, Osteoporosis, Underweight

INTRODUCTION

Diabetes mellitus is a clinical disease characterised by hyperglycaemia caused by absolute or relative deficiency of insulin. Although various studies have reported different operational definitions for lean diabetics in different parts of the world, individuals with diabetes mellitus and BMI <18.5 Kg/m^2 was the most commonly accepted operational definition for lean diabetics in the tropics [1]. The prevalence of lean diabetic varied from 3.5% to 10% across different regions in India [2-6]. In the Indian subcontinent, the onset of Type 2 diabetes mellitus is at a younger age and the majority of patients with Type 2 diabetes mellitus are non-obese [7].

Among patients with diabetes mellitus the turnover rate of bone is decreased and the bone material properties and microstructure of bone are altered; the latter particularly so when microvascular complications are present. The pathological process, in diabetes mellitus, behind fragility of the bone is complex. This process is mediated by various factors like hyperglycaemia, oxidative stress and the accumulation of products of glycation, which are found to trade-off certain properties of collagen, rise the adiposity of bone marrow, inflammatory mediator release and adipokine release, and potentially affect the functioning of osteocytes. Other factors contributing to the reduced bone mineral density are iatrogenic hypoglycaemia and drugs which exert a direct effect on metabolism of bone and minerals (e.g., thiazolidinedione) [8,9]. Increased risk of osteoporosis among patients with diabetes mellitus was reported by various researchers among different studies carried out across India [10-14]. Authors from other countries have also reported similar observations [15-20]. However, there was limited research on bone mineral density among lean diabetic patients. The present study was carried out as an attempt to evaluate bone mineral density in lean patients with diabetes mellitus.

MATERIALS AND METHODS

The study was carried out in the Department of General Medicine in a Tertiary Care Hospital in New Delhi. The present study was undertaken as a cross-sectional comparative study among 60 participants (30 cases of lean diabetics and 30 normal controls). The minimum required sample size was calculated using the formula **Z2pq/d^2**, with an alpha error of 5% and considering the power of the study as 80%. The expected proportion of patients with diabetes mellitus who are lean was taken as 6.67% from a study by Mondal T et al., [5]. Absolute precision of 10% was used for sample size calculation. Convenient sampling technique was done to select study participants (cases and controls) from all the patients who sought medical care during the period from January 2015 to December 2016.

Patients who were already a known case of Type 2 diabetes mellitus or newly diagnosed to have Type 2 diabetes mellitus (based on ADA criteria) whose BMI was <18.5 kg/m^2 were considered as cases. Apparently healthy individuals who were not having diabetes mellitus (based on fasting and postprandial glucose level- done by Hexokinase mediated reaction-based method with semi-autoanalyser) having BMI <18.5 kg/m^2 were considered as eligible controls. Healthy controls were selected from the hospital who were reporting for some other minor short-term illness or the relatives of the patients. Relatives of the cases group patients were not included as controls so as to avoid confounding effect of weight among them since they may share a similar genetic make-up. Individuals with BMI >18.5 kg/m^2, with acute illnesses, who are critically ill, with chronic systemic diseases other than Type 2 diabetes mellitus (especially renal failure, liver failure, malignant disease, on steroids or anti-epileptic drugs, and other endocrinopathies), Pregnant/lactating and post-menopausal women were not included in the study.

Detailed history and examination were done in order to assess any patients' eligibility to participate in the study. When any of the patients were found to be eligible to participate based on the aforementioned predetermined criteria, the individual was explained in detail about the procedures involved and implication of the study in their native language. Institute Ethical Committee approval (vide letter no. 104/12/Mar/BH-2016 dated 30 Mar 2016) was sought and obtained before the study was started. Informed written consent was obtained from the patients before including them in the study. Subsequently, study specific examinations were done followed by biochemical investigations and radiographic analysis.

Predesigned semi-structured questionnaire was used for collection of socio-demographic information and detailed evaluation of subjects about family history, history of fracture, drug history, specifically steroid use, hepatic, renal disease, thyroid and parathyroid disease, inflammatory conditions like rheumatoid arthritis, malabsorption and menopausal status. The following anthropometric parameters were assessed for all the study participants: (i) Height (measured with a standard stadiometre; rounded off to the nearest centimetre); (ii) Weight (measured using a dial Type weighing scale; rounded off to the nearest 100 g); (iii) Waist circumference and Hip Circumference (measured using an inch tape; rounded off to the nearest centimetre). Bone mineral density was measured using QDR-4500 DOS Series bone densitometer.

STATISTICAL ANALYSIS

Means and proportions were calculated for continuous variables and categorical variables respectively; chi-square test was used for finding statistically significant difference in proportions; Independent student t-test was used for finding statistically significant difference between means; Pearson's correlation coefficient was estimated for finding linear association between two continuous variables; a p-value <0.05 was considered to be statistically significant. Data entry was done using MS Excel 2013 and IBM SPSS Version 23.0 was used for statistical analysis.

RESULTS

In comparison, of cases with controls, no statistically significant differences were observed between the two groups in terms of age, waist hip ratio and BMI (p-value >0.05). Also, it was noted that blood sugar values (fasting and postprandial) and HbA1c values were significantly higher among the cases as compared to that of controls (p-value <0.05) [Table/Fig-1].

Characteristic	Cases (n=30) n (%)/ μ±SE	Controls (n=30) n (%)/μ±SE	Total n (%)/ Difference in μ (95% CI)	p-value
Age (in years)				
18-30	1 (50.0)	1 (50.0)	2 (100.0)	
31-45	18 (51.4)	17 (48.6)	35 (100.0)	
46-60	8 (44.4)	10 (55.6)	18 (100.0)	
>60	3 (60.0)	2 (40.0)	5 (100.0)	
BMI (in kg/m²)	17.9±0.1	17.7±0.1	0.2 (0.0-0.04)	0.11
Waist hip ratio	0.87±0.003	0.85±0.005	0.02 (0.0-0.3)	0.028
Fasting blood sugar (in mg/dL)	170.2±12.2	87.6±1.3	82.6 (58-107)	<0.001
Postprandial blood sugar (in mg/dL)	231.9±15.3	119.3±2.1	112.6 (82-144)	<0.001
HbA1c	7.9±0.17	5.1±0.06	2.7 (2.3-3.0)	<0.001

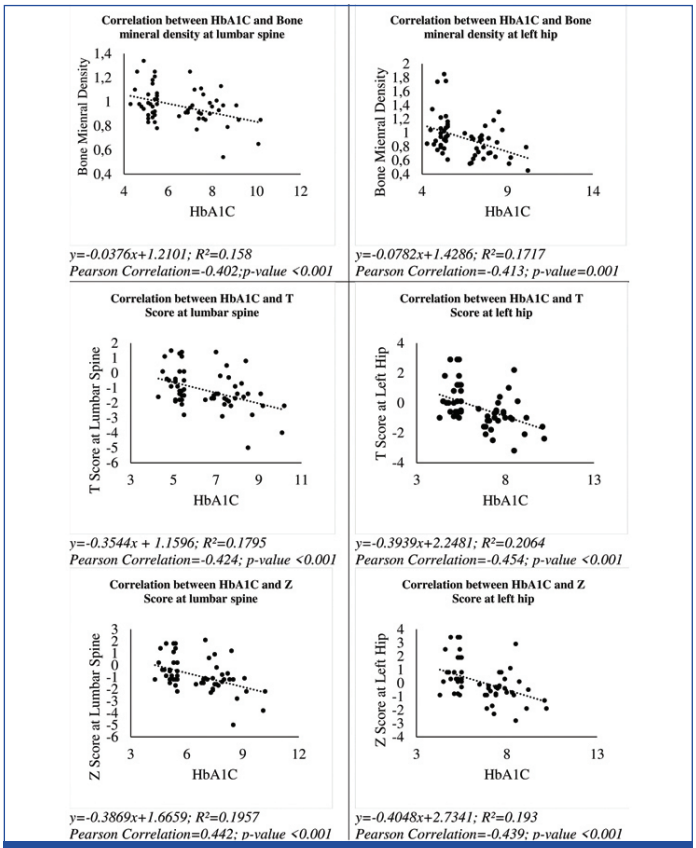
[Table/Fig-1]: Distribution of study participants based on demographic and baseline characteristics.

Bone mineral density at the lumbar spine had a mean value of 0.92 among cases, whereas among controls the mean value of bone mineral density was found to be 1.01 (p-value=0.013). The mean T score measured at the lumbar spine, of cases group patients, was -1.577 whereas among the controls the mean T score value was -0.72 (p-value=0.008). z score measured at lumbar spine had a mean value of -1.37 among cases, whereas among controls the z score value was found to be -0.39 (p-value=0.006). Bone mineral density measured at left hip had a mean value of 0.79 among cases, whereas among controls it was 1.04 (p-value=0.001). z score measure at left hip had a mean value of -0.567 among cases, whereas among controls the z score value was found to be 0.763 (p-value <0.001) [Table/Fig-2].

Characteristic	Cases (n=30) n (%)	Controls (n=30) n (%)	Total (n=60) n (%)	p-value
Bone mineral density at lumbar spine				
Normal	7 (29.2)	17 (70.8)	24 (100.0)	**0.023**
Osteopenia	19 (61.3)	12 (38.7)	31 (100.0)	
Osteoporosis	4 (80.0)	1 (20.0)	5 (100.0)	
Bone mineral density at left hip				
Normal	17 (36.2)	30 (63.8)	47 (100.0)	**<0.001**
Osteopenia	11 (100.0)	0 (0.0)	11 (100.0)	
Osteoporosis	2 (100.0)	0 (0.0)	2 (100.0)	
Characteristic	**Cases (n=30) μ±SE**	**Controls (n=30) μ±SE**	**Difference in μ (95% CI)**	**p-value**
Bone mineral density at lumbar spine	0.92±0.02	1.01±0.02	0.09 (0.01–0.1)	**0.013**
T score at lumbar spine	-1.577±0.23	-0.72±0.2	0.8 (0.2–1.4)	**0.008**
Z score at lumbar spine	-1.37±0.25	-0.39±0.2	0.9 (0.2–1.5)	**0.006**
Bone mineral density at left hip	0.79±0.04	1.04±0.05	0.24 (0.1–0.4)	**0.001**
T score at left hip	-0.977±0.19	0.343±.22	1.3 (1.9–0.7)	**<0.001**
Z score at left hip	-0.567±0.2	0.763±.24	1.33 (-1.9 – -0.6)	**<0.001**

[Table/Fig-2]: Bone mineral density parameters among cases and controls.

HbA1c was found to negatively correlate with that of bone mineral density measured at the lumbar spine (Pearson's correlation coefficient=-0.402, p-value <0.001) and at left hip (Pearson's correlation coefficient=-0.413, p-value=0.001). [Table/Fig-3].



[Table/Fig-3]: Correlation between bone mineral density parameters and HbA1c values.

DISCUSSION

The present study was an attempt to study bone mineral density in lean diabetics and to compare with lean controls without diabetes mellitus. Higher proportion of cases had osteoporosis and osteopenia at both lumbar spine and hip when compared to the controls in the present study.

To the best of literature search, there were limited research data on bone mineral density among lean diabetic patients though research studies were done among all patients with diabetes mellitus. Dutta M et al., evaluated bone mineral density in patients with Type 2 diabetes mellitus [11]. It was observed in the study that Bone mineral density was lower in diabetic patients as compared to controls, which was similar to the present study results. Mathen PG et al., in their research work carried out in southern India stated that bone mineral density was significantly lower in cases with diabetes mellitus as compared to controls [13]. Also, the femoral neck and lumbar spine T-score was significantly lower in cases compared to controls. Majima T et al., found in their study that Bone mineral density and z score at the distal radius were significantly lower in Type 2 diabetic patients than those in control group [21]. Also, a negative correlation was observed between HbA1c values and bone mineral density among patients with non-insulin-dependent diabetes mellitus. A similar negative correlation between HbA1c and Bone mineral density was observed in the present study also. Yaturu S et al., in their cross-sectional study among veterans reported that bone mineral density of hip was significantly lower and incidence of osteoporosis higher in non-insulin-dependent diabetes mellitus subjects compared with age and body mass index matched study participants without diabetes mellitus [17]. Identical observations were noted in the present study also. Komatsu Y and Majima T, reported in their research findings that bone mineral density was significantly lower in patients with Type 2 diabetes mellitus as compared to controls [19]. On Contrary, Chakrabarty N et al., reported no statistically significant correlation between bone mineral density and diabetes in their study conducted in Kolkata, eastern India [12]. Kamalanathan S et al., in their study among diabetic patients observed that 19.5% of the patients had low bone mineral density and bone mineral density in the diabetes group was significantly higher than the control group in both sexes at the hip and spine [10]. Dietary factors of the study population (Kolkata) could have influenced the study outcome, however, any clear explanation has not been given in the study.

Some of the strengths of the present study were that comparison with identical controls improves the validity of the study findings. The study is one of the nouvelle research work carried out in India among lean diabetic patients, based on the literature search of the authors. Relatively smaller sample size could be a possible limitation of the study.

LIMITATION

Effect of oral anti-diabetic drugs on the bone mineral density was not studied which is a limitation of the study.

CONCLUSION

Osteopenia and osteoporosis, characterised by low bone mineral density values were found to be highly prevalent among lean diabetics as compared to controls in the present study population. HbA1C values of the study participants were found to negatively correlate with that of bone mineral density.

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