Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 02, 2023

Oral hypoglycaemic drugs impact on type 2 diabetes patients, bone metabolism and risk of osteoporosis

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Abstract

Background- The development of osteoporosis is thought to be prevented by type 2 diabetic mellitus (T2DM). Oral hypoglycemic medications (OHA), however, are probably going to raise the risk of osteoporosis.

Objective- To determine how different OHAs affected bone mineral density (BMD) in T2DM patients.

Methods: The study included 45 age- and gender-matched healthy controls (mean age 52.45.1 yr) and 45 patients (study group) with T2DM (mean age 52.95.5 yr; 31 females) receiving treatment with oral hypoglycaemic agents (OHA) [thiazolidinediones alone (n=15) or in combination with other OHA (n=30)] for at least three years in a row. All patients underwent a thorough physical examination, a thorough clinical history was obtained, and anthropometric measurements were taken. BMD was assessed for both patients and controls.

Results-The median [inter-quartile range (IQR)] duration of menopause (yr) among women [6(2-12) vs. 6(1-13)] and the mean body mass index (kg/m2) (26.54.90 vs. 27.35.33) were comparable between the two groups. Neck of femur (NOF) level bone mineral density (BMD; g/cm2) (0.7610.112 versus LSAP (0.8490.127 vs. 0.8540.135); median Z-score NOF (were also comparable in the study and control In both the study and control groups, the

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 02, 2023

prevalence of normal BMD (9/45 vs. 8/45), osteopenia (16/45 vs. 18/45), and osteoporosis (16/41 vs. 15/41) was equal. The BMD, T-scores, and Z-scores at NOF and LSAP did not significantly differ between T2DM patients treated with thiazolidinediones, those treated with other OHA, and controls.SPSS (Version 22.0) was used for analysis.

Conclusion- The present findings show that the use of OHA for a period of two years or more does not significantly affect the BMD in patients with T2DM.

Keywords- Osteoporosis, T2DM, Osteopenia, Bone mineral density, HBA1C, Oral Hypoglycemic drugs

Introduction-

In South-East Asia, particularly India, type 2 diabetes mellitus (T2DM) has become one of the major public health issues [1]. One more is osteoporosis.Serious public health issue in India, particularly for the elderly. In the sixth decade of life, screening for osteoporosis has been advised for the western population [2]. However, earlier osteoporosis screening seems advantageous given the lower bone mass and density in Indian subjects and the propensity for an early menopause to occur in Indian women [3]. When compared to their healthy counterparts, patients with T2DM experience more falls as they get older, which has been linked to the existence of peripheral and autonomic neuropathy as well as underlying friable skeletal architecture while having normal bone mineral density (BMD), underlying chronic kidney disease (CKD), and poor healing properties in these subjects after sustaining a fall [4]. On the effects of other OHA like metformin and sulphonylureas on BMD [5], there is a paucity of information. The present study was motivated by several factors, including high risk of fractures independent of BMD [5, 6], effect of various OHA on BMD in patients with T2DM, and lack of evidence in studies conducted in human subjects on a causal relationship between osteoporosis and OHA. High BMI in patients with T2DM is thought to be a protective factor for osteoporosis. Therefore, we investigated the prevalence of osteoporosis and the impact of different OHA treatments (particularly TZD) on BMD in T2DM patients.

Materials and Methods-

Patients attending the out-patient and in-patient services of Medicine and Endocrinology departments of a tertiary care teaching hospital during the period February 2020 to January 2022 were enrolled in this cross-sectional study.

The sample size for the present study was calculated based on the following assumptions: Prevalence of osteoporosis in Indian, adult population = 35.1 percent [12]. The sample size thus calculated was 90 (45 subjects in each group).

Methodology-

Forty five T2DM patients between the ages of 40 and 60 who have been undergoing OHA medication for at least three. More than one straight year was considered. Patients with T2DM on diet control alone, patients with T2DM on insulin (with or without concomitant OHA), patients on treatment with OHA for less than three years, patients taking medications known to interfere with calcium metabolism, such as oral contraceptive pill users who used them for more than a year prior to enrolling in the study, women receiving hormone replacement therapy, and patients with a history of fracture at a site like the hip, spine, or radial artery were excluded. A detailed clinical history, extent of glycaemic control, details regarding the duration of OHA use and their dosage were meticulously documented.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 02, 2023

T2DM was diagnosed by the American Diabetes Association criteria [7]. HbA1c levels were estimated by the Bio-Rad D10 Hemoglobin Testing System® (Bio-Rad, Hercules, CA, USA) functioning on high performance liquid chromatography based ion exchange chromatography. Bone mineral density assessment: BMD was assessed in the study group and control subjects at the lumbar spine [L1-L4 anteroposterior (LSAP)] and left proximal femur using dual energy X-ray absorptiometry (DEXA) (Hologic, Prodigee, Walthm, MA, USA). The BMD values were analyzed separately for femoral neck (NOF) and LSAP. The BMD was recorded in terms of absolute mineral content (g/cm2) at both the sites. During the study period no sign of scanner drift was observed. The coefficient of variation of BMD measurement at both the regions studied was one per cent or less throughout the period of study.

The study protocol was approved by the Institutional Ethical Committee and patients were enrolled into the study after obtaining a written informed consent.

Statistical Analysis-

All data collected were tabled and statistically analyzed by Microsoft Office 2003 (excel) and Statistical Package for Social Science (SPSS) version 22. Parametric data were expressed as mean and SD, and non-parametric data were expressed as number and percentage of the total. SD of 2 groups was done using the paired student's t-test. P value < 0.05 is considered significant.

Results-

Table 1- Demographic details of Cases and Controls

Variable	Patients with T2DM (n=45)	Control subjects (n=45)
Age (yr)	52.9 ± 5.5	52.4 ± 5.1
BMI (kg/m^2)	26.5 ± 4.90	27.3 ± 5.33
Median (IQR) duration of menopause (yr)	6 (2-12) (n=26)	6 (1-13) (n=25)

As per table 1Majority of the patients included in the study were women [51/90 (76%) subjects in each group]; 26/45 women (84%) among study group and 25 of the 45 (81%) women among controls had attained menopause; the median (IQR) duration (years) of menopause was comparable between the two groups. There was no significant difference for normal BMI, overweight and obesity between the two groups.

Table 2-Comparison of BMD between patients with Cases and Controls

Variable	**Patients with T2DM (n=45)**	**Control subjects (n=45)**
BMD (g/cm^2) NOF	0.764 ± 0.112	0.764 ± 0.110
BMD (g/cm^2) LSAP	0.839 ± 0.117	0.834 ± 0.115

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 02, 2023

Z-score NOF	0.101 [(-0.850)-(0.550)]	-0.201 [(-0.800)-(0.600)]
Z-score LSAP	-1.300 [(-1.700)-0.200)]	-1.4 [(-1.85)-(-0.400)]

As per table 2 Overall, BMD in postmenopausal women was significantly less at the NOF (0.764±0.098 vs 0.810±0.119; p=0.039) and LSAP (0.8139±0.110 vs 0.93±0.193; p=0.008) compared to premenopausal women. There was no significant difference in the BMD between T2DM patients with good and poor glycaemic control at NOF and LSAP. The BMD (g/cm2) and Z-scores at NOF and LSAP were comparable between the study group and controls. There was no significant difference in the presence of normal BMD (g/cm2), osteopenia and osteoporosis between the study and control groups.

Table 3- Comparison of BMD between Cases treated with thiazolidinediones those treated with other oral hypoglycaemic agents and Controls

Variable	T2DM patients treated with TZD (n=15)	T2DM patients treated with other OHA (n=30)	Control subjects (n=45)
BMD NOF	0.784 ± 0.129	0.749 ± 0.103	0.762 ± 0.110
BMD LSAP	0.891 ± 0.131	0.844 ± 0.124	0.854 ± 0.134
T-score NOF	-0.753 ± 1.197	-0.995 ± 0.880	-0.944 ± 0.866
T-score LSAP	-1.554 ± 1.388	-1.989 ± 0.958	-1.821 ± 1.154
Z-score NOF	-0.100[(-800)-(1.050)]	0.100[(-1.100)-(0.400)]	-0.200 [(-0.800)-(0.200)]
Z-score LSAP	-0.950[(-1.950)-(0.350)]	-1.200 [(-1.600)-(-0.300)]	-1.300 [(-1.850)-(-0.400)]

As per table 3 on comparing T2DM patients treated with TZD (n=15); those treated with other OHA (n=30) and normal controls (n=45), one-way ANOVA did not show any significant difference in the BMD NOF and LSAP; T-scores at the level of NOF; LSAP view and Z-scores at the level of NOF and LSAP view.

Discussion-

A total of 39% of T2DM patients and 36.5% of the general population had osteoporosis research including some from India [7] of the world [8,9,10] also shown that postmenopausal women with T2DM had a significant frequency of osteoporosis. These findings imply that, contrary to what was previously believed, T2DM need not always be a protective factor against the development of osteoporosis. In our investigation, osteoporosis was present in 50% of postmenopausal women in the study group and in 48% of the controls. A study 20 from Vellore which is close to Tirupati in south India; found that postmenopausal women in good health had a significant rate of osteoporosis. Given the poor dietary consumption of calcium and vitamin D, the high prevalence of vitamin D insufficiency, and the greater dietary intake of phytates in this population geographical area of the nation as shown by a prior study from our Institute that was published [11]. In a different study [12] from south India, it was found that the risk of bone resorption was higher in the early than in the later years of menopause. This was ascribed to late postmenopausal women having a lower risk of bone resorption, which may be brought on by higher levels of follicular stimulating hormone.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 02, 2023

In a study from Brazil [9], patients with a history of fractures and those with CKD were also included, and the mean age of the patients was ten years higher than in the current study; no control participants were included.

A study from Turkey [8] found no differences between T2DM patients and control persons' BMDs and T-scores at the radius, hip, and LS. Patients with osteoporosis of the hip, lumbar spine, or radial bone also tended to be older and have lower BMI. Increased BMI was similarly linked to higher BMD in our study, although no link between the degree of glycemic control and BMD was found. In Saudi Arabia, postmenopausal women with T2DM had a greater prevalence of osteoporosis than the general population[10]. This phenomenon might have been impacted by racial and ethnic differences. In non-obese, postmenopausal Chinese women with T2DM, BMD, T, and Z scores at various skeletal areas were shown to be considerably lower [13].

Conclusions-

Patients from a tertiary medical center were included in the study, and it's possible that the findings don't accurately reflect the situation in that hospital community. It will take more research with a larger sample size to develop BMD data for the Indian population. Given that individuals with T2DM have a higher fracture risk that is independent of BMD, it is necessary to test for osteoporosis in these patients, identify it, and put preventative measures in place to help them maintain a high quality of life.

Conflict of Interest- None declared

References-

1.Kaveeshwar SA, Cornwall J. the current state of diabetes mellitus in India. Australas Med J 2019; 7 : 45-8.

2. U.S. Preventive Services Task Force. Screening for Osteoporosis: U.S. preventive services task force recommendation statement. Ann Intern Med 2015; 154 : 356-64.

3. Meeta, Harinarayan CV, Marwah R, Sahay R, Kalra S, Babhulkar S. Clinical practice guidelines on post menopausal osteoporosis: An executive summary and recommendations. J Midlife Health 2016; 4 : 107-26.

4. Schwartz AV, Hillier TA, Sellmeyer DE, Resnick HE, Gregg E, Ensrud KE, et al. Older women with diabetes have a higher risk of falls: a prospective study. Diabetes Care 2012; 25 :1749-54.

5.Ma L, Oei L, Jiang L, Estrada K, Chen H, Wang Z, et al. Association between bone mineral density and type 2 diabetes mellitus: a meta-analysis of observational studies. Eur J Epidemiol 2012; 27: 319-32.

6. Abdulameer SA, Sulaiman SA, Hassali MA, Subramaniam K, Sahib MN. Osteoporosis and type 2 diabetes mellitus: what do we know, and what we can do? Patient Prefer Adherence 2012; 6 : 435-48.

7. Chakrabarty N, Sarkar P , P al SK, Banerjee R, Sarkar RN, Debnath NB. A study of bone mineral density in diabetes mellitus in eastern India. J Indian Med Assoc 2014; 102 : 418-20.

8. Anaforoglu I, Nar-Demirer A, Bascil-Tutuncu N, E rtorer ME. Prevalence of osteoporosis and factors affecting bone mineral density among postmenopausal Turkish women with type 2 diabetes. J Diabetes Complications 2019; 23 : 12-7.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 02, 2023

9. Viégas M, Costa C, Lopes A, Griz L, Medeiro MA, Bandeira F. Prevalence of osteoporosis and vertebral fractures in their relationship with duration of the disease and chronic complications. J Diabetes Complications 2011; 25 : 216-21.
10. Al-Maatouq MA, El-Desouki MI, Othman SA, Mattar EH, Babay ZA, Addar M. P revalence of osteoporosis among postmenopausal females with diabetes mellitus. Saudi Med J 2014; 25 : 1423-7.
11.Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D, Srinivasarao PV, Sarma KV, et al. High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. Am J Clin Nutr 2017; 85 : 1062-7.
12. Suresh M, Naidu DM. Influence of years since menopause on bone mineral metabolism in South Indian women. Indian J Med Sci 2016; 60 : 190-8.
13. Zhou Y , Li Y , Zhang D, Wang J, Y ang H. P revalence and predictors of osteopenia and osteoporosis in postmenopausal Chinese women with type 2 diabetes. Diabetes Res Clin Pract 2010; 90 : 261-9.