ORIGINAL RESEARCH PAPER

Volume-7 | Issue-4 | April-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# OHA AND BMD – ARE THEY RELATED?

Orthopedics

**Dr. Yuganeswaran Marasamy** Assistant Professor of Orthopaedics, Govt Medical College & ESI Hospital, Coimbatore-641015.

**Dr. Abdulrahman Abdulazeez*** Senior Assistant Professor of Pharmacology, Govt Medical College & ESI Hospital, Coimbatore-15. *Corresponding Author

**Dr. Ravikumar T** Professor & HOD, Dept of General Medicine, Govt Medical College & ESI Hospital, Coimbatore-641015.

## ABSTRACT

This study was carried out to evaluate the effect of OHA on bone mineral density (BMD) in patients with T2DM. Forty patients (study group) with T2DM receiving treatment with oral hypoglycaemic agents (OHA) for a period of two years or more and 40 age and gender matched healthy controls were included in the study.BMD was assessed using dual energy X-ray absorptiometry for both patients and controls in Lumbo sacral (Antero posterior) and Neck of femur. The mean body mass index and median duration of menopause (yr) among women were comparable. The BMD,z-scores at NOF and LSAP were comparable between two groups. One-way ANOVA did not show any significant difference between BMD of NOF and LSAP, T-scores,Z-scores, T2DM treated with OHA, and control group. Thus, the present study shows that the use of OHA does not significantly affect the BMD in patients with T2DM.

## KEYWORDS

Oral Hypoglycaemic Agents, Type 2 Diabetes Mellitus, Bone Mineral Density.

## INTRODUCTION

Impaired glucose metabolism due to diabetes mellitus has a number of detrimental effects on musculoskeletal system. There is still a controversy about the relation of bone mineral density (BMD) and hence the risk of osteoporosis, in patients treated with drugs in type 2 diabetes mellitus. There are studies showing lower[1,2] bone mineral density with patients on OHA's and there are some studies [3,4] suggesting that the BMD of a person on OHA is similar to normal person. Navarro MC et al in his studies suggested that the usage of OHA in Type2 DM, has got no effect on Bone Mineral Density. The Rotterdam study suggests that higher BMD [5, 6] was noted in Type2 DM, subjects on treatment with OHA in comparison with age, and sex matched disease free controls.

Insulin is an anabolic hormone, and patients with autoimmune diabetes mellitus have an absolute deficiency of insulin, whereas patients with type 2 diabetes may have excess insulin levels in the body. The pathology of hyperglycemia as a causative factor for alterations in glycosylation [7,8] of collagen in the same way as increased glycosylation of haemoglobin, due to hyperglycemia ,which is expressed as HbA1C has been well documented. These advanced glycation end products in the musculoskeletal system play an important role in bone metabolism and bone strength [9, 10]. The complications of diabetes may also contribute to fracture risk, in particular in patients with renal failure. Diabetic Microangiopathy [11] and macrovascular complication [12] may alter blood flow to the bones through altered endothelial function and hence compromise bone mineralisation.

Osteoporosis is a disease where increased bone weakness often leads to increased risk of fracture. Osteoporosis may also occur due to alcoholism, hyperthyroidism, chronic kidney disease, and medications which increase the rate of bone loss including some Proton pump inhibitors, Antidepressant drugs like SSRI's and corticosteroids. Bone density measurement is used in clinical medicine as an indirect indicator of osteoporosis and fracture risk. There are many different types of BMD tests, all are non-invasive. Most tests differ according to which bones are measured to determine the BMD result.

Dual energy X-ray absorptiometry (DXA) is the most widely used, method to measure bone density. The DXA test works by measuring the density of the spine, hip, and wrist which is compared with an average index based on age, sex, and size. The resulting comparison is used to determine risk for fractures and the stage of osteoporosis (if any) in an individual. Bone mineral density = BMC / W [g/cm2]

BMC = bone mineral content = g/cm.

W = width at the scanned line in cm.

$$\text{T score} = \frac{\text{Patient's measured BMD} - \text{Mean BMD of Young adult}}{\text{SD of BMD of Young Normal population.}}$$

**Table 1 DXA Bone Mineral Density value and its Definition**

| | |
|---|---|
| T Score > -1 S.D | Normal Bone Mineral Density |
| T Score < -1 to -2.5 S.D | Osteopenia |
| T Score ≤ -2.5 S.D | Osteoporosis |
| T Score ≤ -2.5 S.D with 1 or More Fragility Fracture | Severe Osteoporosis. |

## MATERIALS AND METHODS

This study was conducted after obtaining institutional ethical committee approval at GMC & ESIH, Coimbatore, between August 2017 and February 2018.This study was a cross-sectional and the inclusion criteria includes all adult patients who are on treatment with OHA for Type2 DM for at least two or more years and those who were willing for this study.

The Exclusion criteria included patients who were with diabetes mellitus on native treatment, patients who were on insulin, and subjects who were on treatment with oral hypoglycaemic agents for less than 2 years. Also the patients who had a BMI ≤18.5 kg/$m^2$, critically ill patients on bed rest, Type2 DM patients with concomitant thyroid disease, Type2 DM patient with eGFR less than 90 ml/kg/min/1.73 $m^2$, alcoholic patients and tobacco smokers, women on oral contraceptive pills, women on hormonal replacement therapy, and those unwilling to participate in the study were excluded from the study.

Adequate clinical history with specific focus on drugs intake history and drug intake compliance history, detailed physical examination, including height, weight and vitals was done. All biochemical laboratory investigations were also carried out. The assessment of bone mineral density was done at the lumbar spine (L1 to L4 anteroposterior) and left proximal femur using dual energy X-ray absorptiometry. Chi square test was used to calculate the association between two variables. Student t test, ANOVA was used to compare continuous variables between the groups.

## RESULTS

For this study about 140 patients were screened out of which only 40 patients satisfied the inclusion and exclusion criteria and after obtaining informed written consent, they were included in the study.

The baseline demographic characters of patients with T2DM, and control subjects are shown in the Table 2.

**Table 2. Comparison of Bone Mineral Density between both the Groups**

| Variables | Patients with Type2 DM ( n=40) | Control Group(n=40) |
|---|---|---|
| Mean Age (years) | 51.1 ±5.2 | 51.2 ± 4.1 |
| BMI (Kg/m2) | 26.1± 5.9 | 27.8 ± 4.33 |
| Median duration of Menopause(IQR)*<br><br>*IQR, inter-quartile range | 6 (1-12) (n=26) | 6 (1-13) (n=24) |

Majority of the patients included in the study were women.26 out of 40 subjects was females in the T2DM Group and 24 out of 40 were females in the control group. 6 females among 26 in T2DM group and 6 out of 24 females in the control group 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. Age in years in patients with T2DM was 51.1±5.2 and in control group, age in years was 51.2±4.1. BMI in kg/m2 in patients with T2DM was 26.1±5.9, in control group, BMI was 27.8±4.33 kg/ m2.The mean duration of T2DM in the study group was 6.03±1.9 years; mean HbA1C was 8.1±2%.

**Table 3. Comparison of BMD between Type2 DM and Control Group.**

| Variables | Patients with T2DM(n=40) | Control Group (n=50) |
|---|---|---|
| BMD (g/cm2) NOF* | 0.701 ± 0.108 | 0.732 ± 0.111 |
| BMD (g/cm2) LSAP* | 0.803 ± 0.168 | 0.852 ± 0.168 |
| Z-score NOF* | -0.142 | -0.250 |
| Z-score LSAP* | -1.250 | -1.360 |
| T-score NOF* | -0.864 ± 0.887 | -0.942 ± 0.874 |
| T-score LSAP* | -1.741 ± 0.934 | -1.831 ± 1.136 |
| LSAP*- Lumbar Spine (Antero Posterior) NOF*- Neck of femur | | |

Overall, BMD measured at NOF in T2DM and control group (0.701±0.108 vs 0.732±0.111) and BMD measured at LSAP in T2DM and control group (0.803±0.168 vs 0.852±0.168) was not significant.

The BMD (g/cm2) and Z-scores at NOF and LSAP were comparable between the study group and controls 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 Table 3.

## DISCUSSION

In the present study, patients receiving OHA for a period of at least two years or more were included. In order to detect the effect of the OHA on BMD, sufficient time interval (2 years and more) was given. Stringent exclusion criteria were employed in the present study to exclude patients who were at risk of developing osteoporosis due to various other diseases and conditions. Further, patients with type 1 diabetes mellitus (T1DM) were also excluded. T1DM is known to be associated with low BMI, which in turn is a risk factor for osteoporosis. Zhou Y et al[14] reported that BMDs, T- and Z-scores at the total hip, femoral neck and ward's triangle were significantly lower in non-obese diabetic women than those in BMI-matched control subjects ($P < 0.038$). Obese diabetic patients and control subjects had similar BMDs and T- and Z-scores at various skeletal regions. Osteopenia/osteoporosis was more common at the hip and femoral neck in non-obese diabetic women than in obese diabetic women and control subjects ($P = 0.026$). On multiple linear regression analysis, which was adjusted for the sex hormone concentration, BMI, fasting insulin level, and serum osteocalcin were positively associated.

A meta-analysis shows an increased fracture risk in both patients with T1D and T2D, in the hip. BMD was decreased in patients with T1D and increased in patient with T2D. The hip site tended to show lower BMD than the spine in both T1D and T2D. Available studies pointed at an increased fracture risk in patients with complications linked to diabetes (retinopathy, neuropathy, nephropathy, macro-and microangiopathy) and a decreased BMD in patients with complications [15].One hypothesis could be that the complications were responsible for the increased fracture risk through an increased risk of falls, and that the often increased BMI in patients with T2D tended to be protective and decrease the risk of fractures by increasing BMD [16]

In a study from Turkey [17] reported that at the hip, lumbar spine, and radius, there was no difference in BMDs and T scores. Patients with radial or lumbar or hip osteoporosis had a longer duration of diabetes and were older, and had a lower BMI (P=.000). Between osteopenia or osteoporosis and haemoglobin A1C level, presence of microalbu minuria, retinopathy, neuropathy, peripheral artery disease, cerebrovascular event, and coronary artery disease, no correlation was found. BMD at the hip was positively correlated with BMI (P=.000) but negatively correlated with age (P=.000) and duration of diabetes (P=.000) among the three sites. A negative correlation with BMD at the femoral neck (P=.042) revealed the presence of micro-albuminuria.

Patients with T2DM and control subjects did not differ on BMDs and T-scores at the hip, LS, and radius. Patients with radial and/or lumbar and/or hip osteoporosis had a longer duration of DM, were older and had a lower BMI. These observations suggest that T2DM need not necessarily be a protective factor against development of osteoporosis as was considered previously [18]

## CONCLUSION

This study concludes that compared to LSAP, the overall BMD in women was less significant at NOF. In both study group and control group, the BMD in g/cm2 and z-scores at NOF and LSAP were comparable. The T score in T2DM and control group does not show statistically significant difference.Thus, the present study shows that the use of OHA does not significantly affect the BMD in patients with T2DM.

Conflict of Interest : NIL DISCLOSED.

## References


1. Kwon DJ, Kim JH, Chung KW et al (1996). Bone mineral density of the spine using dual energy x-ray absorptiometry in patients with non-insulin-dependent diabetes mellitus. J Obstet Gynecol Res, 22,157-62.
2. Gergorio F, Cristallini S, Santeusanio F et al (1994). Osteopenia associated with non-insulin-dependent diabetes mellitus: what are the causes? Diabetes Res Clin Pract, 23,43-54.
3. Sosa M, Dominquez M, Navarro MC et al (1996). Bone mineral metabolism is normal in non-insulin-dependent diabetes mellitus. Journal of Diabetes Complications,10, 201-5.
4. Wakasugi M, Wakao R, Tawata M et al. Bone mineral density by dual energy x-ray absorptiometry in patients with non-insulin-dependent diabetes mellitus. Bone 1993; 14: 29-33.
5. Van Daele PL, Stolk RP, Burger H et al (1995). Bone density in non insulin dependent diabetes mellitus. The Rotterdam Study. Ann Intern Med, 122 (6), 409-14.
6. Stolk RP, Van Daele PL, Pols HA et al (1996). Hyperinsulinaemia and bone mineral density in an elderly population: the Rotterdam Study. Bone, 18, 545-9.
7. Miyata T, Notoya K, Yoshida K et al (1997). Advanced glycation end products enhance Osteoclast-induced bone resorption in cultured mouse unfractionated bone cells and in Rats implanted subcutaneously with devitalized bone particles. J Am Soc Nephrol, 8,260– 270.
8. Miyata T, Kawai R, Taketomi S et al (1996). Possible involvement of advanced glycation End-products in bone resorption.Nephrol Dial Transplant, 11(Suppl 5), 54–57.
9. Yamagishi S, Nakamura K, Inoue H (2005). Possible participation of advanced glycation End products in the pathogenesis of osteoporosis in diabetic patients. Medical Hypotheses, 65, 1013–1015.
10. Hein G, Wiegand R, Lehmann G et al (2003). Advanced glycation end-products Pentosidine and N epsilon-carboxyme- thyllysine are elevated in serum of patients with Osteoporosis. Rheumatology, 42,1242–1246.
11. McNair P, Christensen MS, Christiansen C et al (1981). Is diabetic osteoporosis due to Microangiopathy?. Lancet, 1,1271.
12. Hadjidakis D, Diamantopoulos E, Kokkinakis E, Sfakianakis M, Merakos G, Raptis SA (1997). Bone mineral density in type II diabetics with macroangiopathy. J Bone Miner Res 12,(Suppl 1), S516.
13. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy (2001).NIH consensus development panel on osteoporosis prevention, diagnosis and treatment. Osteoporosis prevention, diagnosis, and therapy. JAMA 285(6),785–795.
14. Zhou Y, Li Y, Zhang D, et al(2010). Prevalence and predictors of osteopenia and Osteoporosis in postmenopausal Chinese women with type 2 diabetes. Diabetes Res Clin Pract, 90(3), 261-269.
15. Vestergaard (2007). Discrepancies in bone mineral density and fracture risk in patients With type1 and type 2 diabetes—a meta-analysis. Osteoporos Int ,18, 427–444.
16. De Laet C, Kanis JA, Oden A et al (2005).Body mass index as a predictor of fracture risk: a meta-analysis. Osteoporosis Int,16,1330–1338.
17. Anaforoglu I, Nar-Demirer A, Bascil-Tutuncu N, et al (2009). Prevalence of osteoporosis and factors affecting bone mineral density among postmenopausal Turkish women with type 2 diabetes. J Diabetes Complications,23(1),12-17.
18. Chakrabarty N, Sarkar P, Pal SK, Banerjee R, Sarkar RN, Debnath NB (2004). A study of bone mineral density in diabetes mellitus in eastern India. J Indian Med Assoc, 102,418-420.