TRACE ELEMENTS, HIGH-SENSITIVITY C-REACTIVE PROTEIN AND BONE MINERAL DENSITY IN EGYPTIAN ELDERLY DIABETICS

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ABSTRACT

Aims: To study the levels of magnesium (Mg), zinc (Zn), copper (Cu) and high-sensitivity C-reactive protein (hs-CRP) in elderly diabetics versus controls and their influence upon the relationship between Bone Mineral Density (BMD) and type 2 diabetes mellitus (DM).

Materials and methods: A case control study (50 diabetic patients and 50 non-diabetic participants) was conducted among elderly, aged ≥ 60 years, recruited from geriatric outpatient clinic in Ain Shams University Hospital. Patients were subjected to comprehensive geriatric evaluation followed by assessment of BMD by dual energy x-ray absorptiometry in femoral neck and lumbar spine, and T score recording. Zn, Cu, Mg and hs-CRP blood levels were measured for all participants.

Results: Diabetic patients had significantly lower values of Zn and Mg and higher values of Cu and hs-CRP than non diabetics (P < 0.001 for all parameters). In the studied group, type 2 DM is not alone a risk factor for osteoporosis and low Mg level is a significant predictor of the lumbar spine T score (P = 0.023) rather than the femoral neck one (P = 0.51), after adjusting for other covariates.

Conclusion: Diabetics have lower Zn and Mg and higher Cu and hs-CRP levels than non diabetics. In elderly low Mg is a significant predictor of low BMD only in the lumbar spine, and standalone type 2 DM can't be considered as a risk factor for osteoporosis.

Key words: Osteoporosis, elderly, magnesium, trace elements, CRP, diabetes mellitus.

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Introduction

There is an increased risk for low bone mineral density (BMD) and for bone fractures in patients with type 1 and to a lesser extent type 2 diabetes mellitus (DM)⁹. On the other hand, Gerdhem et al. found that BMD values in patients with type 2 DM were 11% higher compared with healthy controls⁵. Magnesium (Mg), zinc (Zn) and copper (Cu) are essential cofactors for enzymes, involved in synthesis of various bone matrix constituents, so their deficiencies may lead to bone density loss and osteoporosis⁶. On the other hand, there are conflicting results about Cu and Zn levels link to bone turnover and bone density⁴. Elderly with DM appear to be at high risk for mineral deficiency including Zn and Mg⁵.

Pro-inflammatory cytokines could have been involved in the pathogenesis of osteoporosis⁷. Osteoporotic hip and spine fracture is a major public health problem associated with high human and economic costs⁸. The trabecular bone is a metabolically active bone that is preferentially lost at the time of menopause, so it is important in assessing osteoporotic risk⁶. Therefore, authors suggest measurement of lumbar spine (as representation of trabecular bone) and femoral neck (as representation of cortical bone) T scores to study bone density⁹. The role of association among trace elements (Mg, Zn and Cu) and high-sensitivity C-reactive protein (hs-CRP) with both DM and BMD in trabecular and cortical bone density separately, in elderly, is
considered an important issue, but the available literature about this point is deficient. Therefore, we aimed at studying the difference between elderly with and without type 2 DM focusing on trace elements (Mg, Zn and Cu), hs-CRP and BMD, and the impact of trace elements (Mg, Zn and Cu) and hs-CRP upon the association between DM and BMD. BMD was assessed in two body sites; the lumbar spine (as representation of trabecular bone) and the femoral neck (as representation of cortical bone). T score was calculated for each site.

Materials and methods

A case control study (50 diabetic and 50 non-diabetic participants) was conducted among elderly, aged ≥ 60 years, recruited from geriatric outpatient clinic in Ain Shams University Hospital. Informed consent was obtained from all participants and the study was approved by the ethical committee of the faculty of medicine Ain Shams University.

All participants underwent clinical examination, nutritional screening using the Mini-Nutritional Assessment form to exclude malnourished subjects\(^{(11)}\) and basic activities of daily living (ADL) evaluation\(^{(12)}\).

In the osteoporosis unit in the geriatrics and gerontology department in Ain Shams University using DPX-L densitometer (Lunar) instrument, BMD by dual energy x-ray absorptiometry (DEXA) was assessed in two body regions: femoral neck (as cortical bone) and lumbar spine (as trabecular bone). T score was calculated for both sites. Serum levels of Zn, Cu, Mg and hs-CRP were measured in all participants. Venous blood samples were collected, centrifuged and stored at -70°C till assayed.

Exclusion criteria: patients currently receiving trace elements as food supplementation, patients with acute inflammatory disorders, secondary osteoporosis (except DM), current smokers or malnourished (patients with a score of less than 17 in mini nutritional assessment scale) were excluded. Then data analysis was performed in the following pattern: qualitative data are presented in frequency tables (numbers and percentages). Quantitative data are presented in the form of mean ± SD (table 1).

P value was set at 0.05 and all data manipulation and analysis were performed using the 16th version of statistical package for the social sciences (SPSS).

Normality distribution of the variables was tested using one sample Kolmogorov Smirnov test. Non-parametric data were log transformed into parametric data. Two independent t-test was used to compare quantitative data. Chi square or Fisher’s Exact test was used to compare qualitative data.

Linear logistic regression analysis was used to detect if Mg, Zn, Cu or hs-CRP could impact the association between DM and BMD in elderly and if any of them was a predictor of femoral neck or lumbar spine T score, with adjustment for other covariates.

Results

The mean age of the study group was 65.85 +/− 5.98 and 45% were males. Diabetic patients have significantly lower value of the lumbar spine and femoral neck T-scores (P= 0.001 and 0.021 respectively) (table 1).

Using linear regression analysis, DM was a significant predictor of both femoral neck and lumbar spine T scores. This significant result was maintained even after adjustment for other factors, age, gender, low trauma fracture, body mass index (BMI), the parental history of low trauma fracture and ADL.

The significance of the factors used in adjustment was based upon the risk factors incorporated into Fracture Risk Assessment Tool\(^{(13)}\), and risk factors of primary osteoporosis as defined by WHO\(^{(14)}\).

Our results demonstrated that DM is not considered as a predictor for T score after additional adjust-

<table>
<thead>
<tr>
<th>variables</th>
<th>Whole sample n= 100</th>
<th>Cases (diabetic) n=50</th>
<th>Controls (non-diabetic) n=50</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65.85+/-5.98</td>
<td>65.40+/-5.9</td>
<td>66.30+/-6.1</td>
<td>0.45</td>
</tr>
<tr>
<td>Gender: males</td>
<td>45 (45%)</td>
<td>21 (42.0%)</td>
<td>24 (48%)</td>
<td>0.55</td>
</tr>
<tr>
<td>History of low trauma fracture</td>
<td>8 (8%)</td>
<td>6 (12.0%)</td>
<td>2 (4%)</td>
<td>0.27</td>
</tr>
<tr>
<td>Body mass index</td>
<td>31.23+/-7.5</td>
<td>31.59+/-6.9</td>
<td>30.85+/-8.1</td>
<td>0.63</td>
</tr>
<tr>
<td>ADL (low)</td>
<td>74 (74%)</td>
<td>39 (78%)</td>
<td>35 (70%)</td>
<td>0.36</td>
</tr>
<tr>
<td>T-score of lumbar spine</td>
<td>-1.4+/-1.5</td>
<td>-1.94+/-1.5</td>
<td>-0.91+/-1.3</td>
<td>0.001</td>
</tr>
<tr>
<td>T-score of neck of femur</td>
<td>-1.94+/-1.3</td>
<td>-1.49+/-1.32</td>
<td>-0.89+/-1.22</td>
<td>0.021</td>
</tr>
<tr>
<td>Mg (mg/dl)</td>
<td>1.75+/-0.5</td>
<td>1.34+/-0.38</td>
<td>2.17+/-0.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Zn (ug/dl)</td>
<td>72.52+/-22.5</td>
<td>54.4+/-15.73</td>
<td>90.64+/-10.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cu (ug/dl)</td>
<td>110.41+/-3.2</td>
<td>127.9+/-16.85</td>
<td>92.92+/-13.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>hs-CRP (ug/ml)</td>
<td>3.93+/-2.9</td>
<td>6.28+/-2.28</td>
<td>1.58+/-0.73</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 1: Socio-demographic and clinical characteristics, T score and laboratory data in the whole sample and in cases versus controls.
ment for trace elements and hs-CRP. The Mg is the only significant predictor, among with the studied laboratory variables, of T score; the lower the Mg is, the worse the T score in the lumbar region is (P=0.023), while it is not significant in the neck of femur (P=0.51) (table 2).

**Table 2:** Regression analysis to study the impact of DM upon T score of both femoral neck and lumbar spine.

<table>
<thead>
<tr>
<th>Variables in regression</th>
<th>Femoral neck</th>
<th>Lumbar spine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P value</td>
<td>Odd ratio</td>
</tr>
<tr>
<td>DM only</td>
<td>0.003</td>
<td>0.55</td>
</tr>
<tr>
<td>DM*</td>
<td>0.001</td>
<td>0.52</td>
</tr>
<tr>
<td>DM**</td>
<td>0.02</td>
<td>0.62</td>
</tr>
<tr>
<td>DM***</td>
<td>0.95</td>
<td>1.05</td>
</tr>
<tr>
<td>Mg***</td>
<td>0.51</td>
<td>1.9</td>
</tr>
</tbody>
</table>

*Adjusted for age and gender.
**Adjusted for age, gender, BMI, ADL, history of parenta low trauma fracture and history of low trauma fracture.
*** as the previous plus including Mg, Zn, Cu and hs-CRP in regression.

**Discussion**

In this study, serum Zn and Mg levels were significantly lower among diabetic patients than non diabetics and this agreed with Abou-Seif and Youssef(19). Higher Cu and hs-CRP levels in diabetics were reported by Walter et al.(18) and Adole et al.(17) consecutively, which is in accordance with the current results. Additionally, Pizent et al. found positive association between Cu and CRP(18). There is a lack of data on osteoporosis in patients with type 2 DM(19). Furthermore, there are controversies, regarding the BMD in diabetics as unchanged, increased(20,21) or decreased(22,23).

The current study revealed that after adjusting for age, gender, BMI, ADL, history of low trauma fracture, parental history of low trauma fracture, Mg, Zn, Cu and hs-CRP, type 2 DM per se cannot be considered as a risk factor for osteoporosis. It is also worth mentioning that Chen et al.(22) and Al-Maetoouq et al.(23) concluded that the mean BMD was lower in the diabetic group compared with the non diabetic control group.

However, adjusted regression and hs-CRP and trace elements measurements were not done. Furthermore, separate analysis of the impact upon trabecular and cortical bone was not evaluated. On the other hand, our results are in accordance with the conclusion of Sharifi et al. Initially, they found higher femoral BMD in diabetics. This could be attributed to a difference in patients’ history of low trauma fracture or sedentary lifestyle; these factors were not discussed although they excluded bedridden subjects.

Sharifi et al. concluded that DM is no longer a risk for osteoporosis in postmenopausal women, after adjustment for other covariates, as age and BMI(19).

In the current data, the absence of the significant prediction of DM for BMD, after adjustment for Mg, Zn, Cu and hs-CRP, might explain the controversies between the studies discussing BMD in diabetics versus controls, as lower BMD in diabetics could be attributed to other minerals deficiency as Mg. Mg deficiency could exaggerate osteoporosis in type 2 diabetics rather than DM itself.

The absence of the significant prediction of type 2 DM upon worse BMD could be attributed to the suspected increase of sex hormone and the decrease of sex hormone binding protein with insulin resistance(20).

Current data revealed that the lower the Mg is, the worse the bone density is, only in the lumbar spine. The prediction of low Mg for worse BMD could be explained by Bellucci et al who found that low extracellular Mg diminishes osteoblast growth and increases the number of osteoclasts generation from bone marrow precursors(20).

However, the impact of Mg deficiency only upon lumbar spine rather than neck of femur could be explained by Gruber et al. who demonstrated Mg depletion marked effect on the trabecular bone, due to its greater surface area and turnover, so it was more quickly responsive to Mg depletion rather than the cortical bone in the skeleton of the mouse(20). Therefore, Mg supplementation can be recommended for elderly diabetics, as it could improve BMD especially in the lumbar spine.

**Conclusions**

Diabetics have lower Zn and Mg and higher Cu and hs-CRP than non diabetics. In elderly, low Mg is a significant predictor of low BMD, only in the lumbar spine. Type 2 DM alone can’t be considered as a risk factor for osteoporosis in elderly subjects.

**References**

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Manganese, and magnesium status and complications.


