Association of Vitamin B12 with Bone Mineral Density in Postmenopausal Women in Bangladesh

Muhammad Saiedullah1,**, Shahnaj Begum1, SM Muraduzzaman3

1Dept of Applied Laboratory Sciences, Bangladesh University of Health Sciences (BUHS)
2Dept of Biochemistry and Cell Biology, Bangladesh University of Health Sciences (BUHS)
3Dept of Biomedical Engineering & Medical Physics, Bangladesh University of Health Sciences (BUHS)

DOI: 10.36348/sjbr.2021.v06i09.002 | Received: 15.08.2021 | Accepted: 21.09.2021 | Published: 25.09.2021

*Corresponding author: Muhammad Saiedullah

Abstract

The risk of osteoporosis is higher in postmenopausal women. In this cross-sectional study, BMD and blood samples from 77 postmenopausal women (age > 45 years) were studied. BMD and T-scores of the study subjects were determined at the femoral neck and lumbar spines by Dual Energy X-ray Absorptiometry (DEXA). Serum VitB12 was measured by enzyme-linked immunoabsorbent assay. The mean±SD age of the postmenopausal women was 56.4±7.9 years. Bone mineral densities (g/cm²) were 0.80±0.16, 0.76±0.18, 0.74±0.14 and T-scores were -2.21±1.45, -1.41±1.22, -1.53±1.20 respectively at the lumbar spine, right femoral neck and left femoral neck. The mean±SD of vitB12 was 245.9±274.3 pg/mL. On multiple regression analysis, β values for log(VitB12) with BMD were 0.119 (p = 0.140), 0.015 (p = 0.012) at the lumbar spine and right femoral neck and left femoral neck respectively. In conclusion, vitamin B12 is found to be positively associated with bone mineral density. Patients with osteoporosis experienced long-term morbidity including chronic pain, deformity, and disability, which indirectly give rise to loss of normal function. It is considered one of the most important health problems that pose a negative impact on society.

Keywords: Bone Mineral Density, Vitamin B12, Osteoporosis.
murine genetic model, decreases liver taurine and oral supplementation of taurine enhanced osteoblast functions and subsequently reduced osteoporosis (Roman-Garcia et al., 2014). Another 2-year follow-up study demonstrated that osteoporosis associated with pernicious anemia was markedly improved by vitamin B₁₂ supplement therapy (Melton et al., 1994). The formation of collagen or alteration to the metabolism of osteoblasts was found to be modulated by Vitamin B₁₂ in a dose-dependent manner (Kim et al., 1996; Bailey et al., 2015). The deficiency of vitamin B₁₂ was found to increase the risk of low BMD and fractures (Clarke et al., 2015). Osteocalcin secreted by osteoblast, one of the markers of bone formation (Marrone et al., 2012; Wheater et al., 2013), was found to be higher in premenopausal women with low BMD compared to normal BMD (Jeong et al., 2014). In a cross-sectional observational study in Turkish postmenopausal women with low BMD in the femoral neck and in the vertebrae was found to have significantly lower serum levels of vitamin B₁₂ (Bozkurt et al., 2009). On the other hand, a study consisting of 328 British postmenopausal women, found no significant association between BMD and vitamin B₁₂ (Baines et al., 2007). In another cross-sectional observational study consisting of 131 Croatian women also revealed a lack of association between BMD and vitamin B₁₂ (Rumbak et al., 2012). Thus, the relationship between vitamin B₁₂ and BMD was found to be varied in different populations. In our population, it remains to be evaluated. By considering the worldwide rise in fracture due to osteoporosis and population exposed in developing countries, particularly in postmenopausal women in Bangladesh (Jabin et al., 2017), this study aimed to evaluate the role of vitamin B₁₂ on bone mineral density.

**MATERIALS AND METHODS**

**Study design and sample**

Seventy-seven (77) postmenopausal women (age> 35 years) without a history of known comorbid diseases, were included in this cross-sectional study and was conducted in the Dept. of Applied Laboratory Sciences, Bangladesh University of Health Sciences (BUHS), Dhaka, Bangladesh, referred for screening for osteopenia or osteoporosis to the National Institute of Nuclear Medicine & Allied Sciences, Bangladesh Atomic Energy Commission. Volunteers were informed in detail about the purpose and nature of the study and written consent was obtained from willing subjects. History of diabetes mellitus and hypertension and the Body mass index (BMI) of the study subjects were recorded.

**Determination of Bone mineral density and serum VitB₁₂**

Bone mineral density was scanned at the lumbar spine (L₂ to L₄) and proximal femur by dual-energy X-ray absorptiometry (DEXA) (Muraduzzaman et al., 2021) using a GE Lunar DPX-NT PRO (Lunar Corp, Adison, WI, USA) in the National Institute of Nuclear Medicine & Allied Sciences, Bangladesh Atomic Energy Commission, Dhaka, Bangladesh following standard protocols and expressed in g/cm² and as peak bone mass percentage (T-score) against the normal subjects. Levels of serum Vit B₁₂ were measured by enzyme-linked immunosorbent assay (Assaypro, USA).

**STATISTICAL ANALYSIS**

The distribution and skewness of the data for continuous variables were tested, and were presented as mean ± standard deviation. Data that rejected normal distribution were logtransformed for correlation and multiple regression analysis using MedCalc version 11.4 and a p-value < 0.05 was considered as significant.

**RESULTS**

**Characteristics of the study subjects**

The age range of the study subjects was 35 to 75 years. Characteristics of the study subjects are shown in Table 1. Of the 77 subjects, 42 (54.5%) were hypertensive and 35 (45.5%) were normotensive; 21 (27.3%) were diabetic, 56 (72.7%) were nondiabetic, 29 (37.7%) were overweight (BMI: 25-30 kg/m²) and 11 (14.3%) were obese (BMI>30 kg/m²). The age distributions followed a normal distribution (p = 0.196) (Fig 2).

<table>
<thead>
<tr>
<th>Table-1: Characteristics of the study subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
</tbody>
</table>

Results were expressed as mean±SD%; BMI, Body mass index

© 2021 | Published by Scholars Middle East Publishers, Dubai, United Arab Emirates 227
Fig-2: Age distribution of the study subjects

Bone mineral density in the study subjects

Bone mineral density BMD at the lumbar spine was significantly higher than right femoral neck ($p = 0.006$) and left femoral neck ($p < 0.001$) but similar at the right and the left femoral neck ($p = 0.246$). Similarly, T-score was higher at the lumbar spine than the femoral neck ($p < 0.001$) and similar in the femoral necks ($p = 0.243$) (Table 2).

Table-2: BMD in the lumbar spine and the femoral neck

<table>
<thead>
<tr>
<th>Location</th>
<th>BMD (g/cm$^2$)</th>
<th>T-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar spine</td>
<td>0.80±0.16</td>
<td>-2.21±1.45</td>
</tr>
<tr>
<td>Right femoral neck</td>
<td>0.76±0.18</td>
<td>-1.41±1.22</td>
</tr>
<tr>
<td>Left femoral neck</td>
<td>0.74±0.14</td>
<td>-1.53±1.20</td>
</tr>
</tbody>
</table>

Vitamin $B_{12}$ status of the study subjects

The mean±SD of vit$B_{12}$ was 245.9±274.3 pg/mL. The distribution rejects normality ($p<0.001$). The range of vit$B_{12}$ was 47.1 to 1846.3 pg/mL. Fig 3 represented the Box-and-Whisker plot of Vit$B_{12}$ values after logarithmic transformation.

Fig-3: Box-and-Whisker plot of vit$B_{12}$

Relationship of BMD and T-score with Vit$B_{12}$ in postmenopausal women

The correlation coefficients of BMD and T-score at the lumbar spine, right femoral neck and left femoral neck are presented in Fig 4 and Fig 5. BMD and T-scores at the lumbar spine and left femoral neck was significantly related to log(vit$B_{12}$) (Fig 4A, Fig 4C and Fig 5A, Fig 5C). The correlation coefficients of BMD and T-score with log(vit$B_{12}$) were not statistically significant (Fig 4B and Fig 5B).
Multiple regression analysis

The coefficient of BMD at the lumbar spine, right femoral neck or left femoral neck in multiple regression analysis considering age, BMI, Log(vitB₁₂), hypertension and diabetes, as independent variables presented in Table 3. BMD and T-scores at the lumbar spine and left femoral neck showed a significant positive association with log(vitB₁₂) (Table 3) but BMD and T-score at right femoral neck showed no such association with log(vitB₁₂) on adjusting confounding variables (Table 3).

Table 3: Coefficient of BMD in multiple regression analysis

<table>
<thead>
<tr>
<th></th>
<th>Lumbar spine</th>
<th>Right femoral neck</th>
<th>Left femoral neck</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMD (g/cm²)</td>
<td>β</td>
<td>p-value</td>
<td>β</td>
</tr>
<tr>
<td>Age</td>
<td>-0.003</td>
<td>0.195</td>
<td>-0.006</td>
</tr>
<tr>
<td>BMI</td>
<td>0.012</td>
<td>0.006</td>
<td>0.009</td>
</tr>
<tr>
<td>LogB₁₂</td>
<td>0.119</td>
<td>0.018</td>
<td>0.085</td>
</tr>
<tr>
<td>HTN</td>
<td>-0.059</td>
<td>0.129</td>
<td>-0.061</td>
</tr>
<tr>
<td>DM</td>
<td>-0.005</td>
<td>0.903</td>
<td>0.014</td>
</tr>
<tr>
<td>T-score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.028</td>
<td>0.176</td>
<td>-0.031</td>
</tr>
<tr>
<td>BMI</td>
<td>0.107</td>
<td>0.007</td>
<td>0.083</td>
</tr>
<tr>
<td>LogB₁₂</td>
<td>1.028</td>
<td><strong>0.022</strong></td>
<td>0.698</td>
</tr>
<tr>
<td>HTN</td>
<td>-0.535</td>
<td>0.121</td>
<td>-0.504</td>
</tr>
<tr>
<td>DM</td>
<td>-0.062</td>
<td>0.864</td>
<td>-0.064</td>
</tr>
</tbody>
</table>

BMI, body mass index; HTN, hypertension and DM, diabetes mellitus
DISCUSSION

Osteoporosis is a major health problem among postmenopausal women (Bock et al., 2008; Ahmed et al., 2019). Though estrogen (Riggs et al., 1998) and Vitamin D (Sahota, 2000; Lips and van Schoor, 2011); deficiency play key roles, Vitamin B12 (vitB12) deficiency may also facilitate the process (Kim et al., 1996; Bailey et al., 2015; Dai et al., 2015). In this cross-sectional study, the relationship between osteoporosis and vitB12 was evaluated in a group of postmenopausal women of Bangladeshi Nationality.

In this study, a positive relationship was found between serum vitB12 levels and bone mineral density (BMD) and T-score at the lumbar spine and left femoral neck. On multiple regression analysis, an independent positive association was found between vitB12 and BMD and T-score measured at the lumbar spine and left femoral neck but not with BMD and T-score measured at the right femoral neck after adjusting the confounding variables. This finding is consistent with findings of the Framingham osteoporosis study done on the American population (Tucker et al., 2005) where decreased vitB12 was shown to be associated with low bone mass in hip and lumbar spine, and suggested that vitB12 may be a controllable risk factor for prevention of osteoporosis. In another study done on the American population, Morris et al. reported that indicators of vitB12 status (serum vitB12 level and methyl malonic acid) were positively associated with BMD in elderly (Morris et al., 2005). McLean et al., in a study found that BMD is lower in people with decreased vitB12 (McLean et al., 2008) which increases the risk of fracture. In another study done by Bozcurt et al found a significant association of low BMD and low level of vitB12 in postmenopausal women at the femoral neck and lumbar spine which is consistent with our findings (Bozcurt et al., 2009).

On the other hand, Rejnmark et al. found no association between BMD and vitB12 in a cross-sectional study but found a positive association between BMD and dietary Folate (Rejnmark et al., 2008). In another study performed by Holstein et al. found no significant association of trabecular bone mass with serum level of vitB12 on the patient with osteoarthritis (Holstein et al., 2009). Rumbak et al. also found no significant association between BMD and serum level of vit B12 (Rumbak et al., 2012). A study performed to find an association between vit B12 (Dietary and serum levels) and BMD in patient with celiac disease found a positive association BMD and Vit B12 among men but not in women (Clarke et al., 2015). Bailey et al. found no direct association of vit B12 with BMD but the main indicator of this vitamin, and methyl malonic acid (MMA) and serum Homocysteine (Hcy) levels were associated significantly with BMD (Bailey et al., 2015). A similar result was observed by Cagnacci et al. (2003, 2008) and Gjesdal et al. (2006). Yazdanpanah et al. (2007), Rejnmark et al. (2008) or Dai et al. (2013) found no significant association between dietary intake of vit B12 and BMD. These contradictory findings may be due to differences in methods used to measure vitB12 such as investigation of dietary intake of vit B12, plasma or serum level of vit B12, analysis of MMA. Also the population which took part in these studies are from different regions that may also be a cause of contradictory findings. The limitation of our study was that due to its limited sample size, the study does not reflect the result of the general population in Bangladesh. We did not measure the Hcy level and MMA to confirm functional deficiency of vit B12. Also the cross-sectional nature of the study does not help to establish the causal relationship between vitB12 and BMD. But to our knowledge, this study is the first to be performed to investigate the relationship between BMD and vit B12 in postmenopausal women of Bangladesh. As osteoporosis and age-related bone disorders are now a day’s becoming a public health burden in the aging Bangladeshi population, we hope our study will help to start additional research for better understanding the role of vitamin B12 in bone health in older women in Bangladesh.

CONCLUSION

Vitamin B12 is positively associated with bone mineral density and T-score at the lumbar spine and left femoral neck but not at the right femoral neck in postmenopausal women.

REFERENCE


