Association Between Bone Mineral Density and Type 1 Diabetes Mellitus: A Meta-analysis Of Observational Studies

INTRODUCTION

Several studies have reported that Bone Mineral Density (BMD) is reduced in patients with Type 1 Diabetes Mellitus (T1DM).

In fact, osteoporosis has been described in T1DM patients long ago, even before the availability of modern techniques to measure BMD.

However, the data is not consistent among all the reported studies.

Potential mechanisms leading to osteoporosis in patients with T1DM:

- Autoimmune destruction of bone cells in type 1 diabetes

METHODOLOGY

- Eligibility Criteria:
  - Cases: T1DM patient (of any age group)
  - Control: Healthy subject (non-diabetic)

- BMD measurement:
  - Dual energy X-ray absorptiometry (DEXA)
  - Bone Mineral Density

- Literature Search: Performed in PubMed and EMBASE for cross-sectional cohort and case-control studies pertaining to T1DM and osteoporosis.

- Assessment of studies was performed by two independent researchers.

- A random-effects model was used to pool data in case of substantial heterogeneity among studies.

- Heterogeneity and publication bias were assessed.

RESULTS

- Number of studies included: 48
- Number of patients involved:
  - Cases: 2,885
  - Controls: 4,124

- Meta-analysis showed that BMD in T1DM patients was significantly lower at many regions.

- Pooled mean difference of BMD in patients with T1DM when compared with controls:
  - Hip region:
    - Women: -0.43 (95% Confidence Interval [CI]: -0.69 to -0.17)
    - Men: -0.25 (95% CI: -0.50 to 0.005)
  - Spine region:
    - Men: -0.30 (95% CI: -0.47 to -0.13)
  - Femoral region:
    - Women: -0.21 (95% CI: -0.43 to 0.00)
    - Femoral neck:
      - Women: -0.82 (95% CI: -1.00 to -0.64)
      - Men: -0.54 (95% CI: -0.82 to -0.26)

- Pooled mean differences of site-wise BMD in patients with T1DM when compared with controls:

- Hip BMD in Male Subjects with Type 1 diabetes mellitus compared to healthy subjects:

<table>
<thead>
<tr>
<th>Study name</th>
<th>Number of cases</th>
<th>Number of controls</th>
<th>Std diff (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1DM</td>
<td>1,048</td>
<td>1,048</td>
<td>0.204 (0.090 - 0.326)</td>
</tr>
<tr>
<td>Healthy</td>
<td>1,048</td>
<td>1,048</td>
<td>0.472 (0.326 - 0.618)</td>
</tr>
</tbody>
</table>

- Hip BMD in Female Subjects with Type 1 diabetes mellitus compared to healthy subjects:

<table>
<thead>
<tr>
<th>Study name</th>
<th>Number of cases</th>
<th>Number of controls</th>
<th>Std diff (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1DM</td>
<td>737</td>
<td>737</td>
<td>0.173 (0.133 - 0.213)</td>
</tr>
<tr>
<td>Healthy</td>
<td>737</td>
<td>737</td>
<td>0.395 (0.061 - 1.029)</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- Both men and women with T1DM have a higher risk of developing osteoporosis.

- Multiple factors can influence BMD in individuals with T1DM:
  - Age
  - Gender
  - Morbidity status
  - Bone type

- Large prospective epidemiological studies are required to confirm our findings.

REFERENCES

- Jackson R, et al. J Bone Miner Res. 2007 Sep; 22(9):1317-28
- Indian J Endocrinol Metab. 2014 Mar-Apr; 18(2): 159–165
- Nephropathy
  - Hyperglycemia
  - Autoimmune inflammation
  - Hypercalciuria AND alteration vitamin D metabolism
  - Vitamin D deficiency and alterations in vitamin D metabolism
  - Hyperparathyroidism
  - Secondary hyperparathyroidism
  - Osteoporosis
  - Adipocytokines
  - Poor glycemic control
  - Increased bone formation and inadequate accrual peak bone mass
  - Adipose tissue
  - Increased marrow adiposity
  - Osteopenia
  - Increase osteoblast last activity

DISCUSSION

- Proposed pathogenic mechanisms related to the reduced BMD in T1DM patients:
  - Hyperglycemia
  - Autoimmune inflammation
  - Hypercalciuria
  - Parathyroid hormone
  - Secondary hyperparathyroidism
  - Osteoporosis
  - Adipocytokines
  - Poor glycemic control
  - Increased bone formation and inadequate accrual peak bone mass

- Multiple factors can influence BMD in individuals with T1DM:
  - Age
  - Gender
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