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

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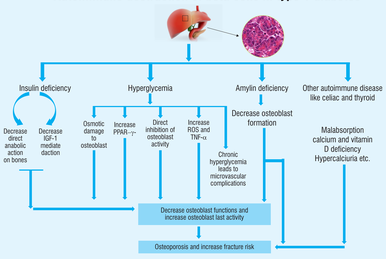
INTRODUCTION

- Various studies have reported that Bone Mineral Density (BMD) is reduced in patients with Type 1 Diabetes Mellitus (T1DM)[1]
- In fact, osteopenia has been described in T1DM patients long ago, even before the availability of modern techniques to measure BMD[1]
- However, the data is not consistent among all the reported studies [1]
- Potential mechanisms leading to osteoporosis in patients with T1DM [1]

Autoimmune destruction of beta cells in type 1 diabetes



OBJECTIVE

To perform a meta-analysis to estimate the difference in BMD between T1DM and non-diabetic populations

METHODOLOGY

- Eligibility Criteria

  Cases: T1DM patient (of any age group)

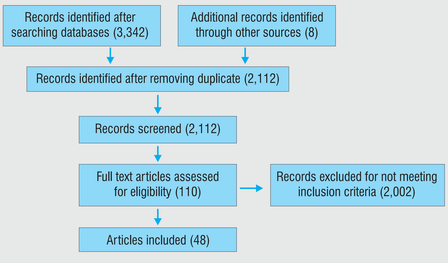
  Control: Healthy subject (non diabetic)

  BMD measurement:
  - BMD was measured by dual energy X-ray absorptiometry (DXA)
  - BMD measurements were expressed as an absolute value in g/cm [2]

  Study design: All observational studies were included (case controlled and cohort studies)
- Literature Search: Performed in PubMed and EMBASE for cross-sectional cohort and case-control studies pertaining to T1DM and osteoporosis
- Additional searches were conducted to include research abstracts, cross references and bibliography of individual articles
- Studies up to January 2014 were included
- Key Words:
  - Type 1 Diabetes Mellitus
  - Bone Mineral Density
  - Dual energy X-ray absorptiometry (DEXA)
  - Assessment of studies was performed by two independent researchers
- A random effects was used to pool data in case of substantial heterogeneity among studies
- Heterogeneity and publication bias were assessed

RESULTS

PRISMA Flow Diagram



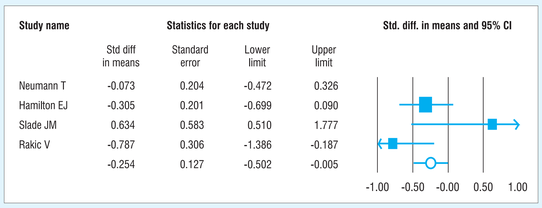
RESULTS

- Number of studies included: 48
- Number of patients involved:
  - Cases: 2,885
  - Controls: 4,814
- Meta-analysis showed that BMD in T1DM patients was significantly lower at many regions
- Pooled mean differences of BMD in patients with T1DM when compared with control:
  - 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)
  - Forearm region:
    - Women: -0.21 (95% CI: -0.43 to 0.00)
    - Femoral neck: No significant difference was found in BMD (in both men and women)

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

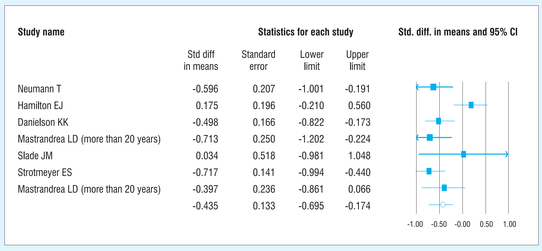
Site	Gender	Number of studies	Effect size (SMD)	95% CI	P value	I^2 value
Spine	**Male**	**9**	-0.308	**0.479 to -0.136**	**0.001***	**0 %**
	Female	17	0.101	0.292 to 0.104	0.353	69 %
Hip	**Male**	**4**	-0.254	**0.502 to -0.005**	**0.045***	**63 %**
	Female	**7**	-0.435	**0.695 to -0.174**	**0.001***	**51 %**
Femoral neck	Male	8	0.077	0.574 to 0.727	0.818	98 %
	Female	11	0.170	0.779 to 1.119	0.725	93 %
Forearm	Male	3	-0.069	0.332 to 0.195	0.609	0 %
	Female	4	-0.218	0.437 to 0.002	0.052	49 %

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



Fixed effect= SMD -0.254, 95% CI -0.502 to -0.005 (p value = 0.045), I^2=51 %

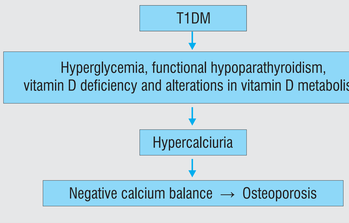
- Hip BMD in Female Subjects with Type 1 diabetes mellitus compared to healthy subjects



Random effect model = SMD -0.435, 95% CI -0.695 to -0.174 (P value= 0.001), I^2= 62.97

DISCUSSION

- Proposed pathogenic mechanisms behind reduced BMD in T1DM patients: [2]
  - Hyperglycemia
  - Autoimmune inflammation
  - Increased PPAR-γ→ activity increased marrow adiposity
  - Hypoinsulinemia and hypoamylinemia
  - Deficit of IGF-I and Vitamin D
  - Nonenzymatic glycosylation of type 1 collagen with subsequent formation of AGEs (advanced glycation end products)
- Factors influencing the bone in T1DM patients
- Age of onset
  - Prepubertal onset T1DM: decreased bone formation and inadequate accrual peak bone mass osteopenia [3]
- Gender
  - Men with T1DM are more prone to osteopenia than women [4]
  - Estrogen adequacy and/or use of estrogen-based oral contraceptive pills might be the reason for higher bone mass in women compared to men [4]
- BMI
  - Lower BMI is associated with higher incidence of osteoporosis [5]
  - Adipose tissue → adipocytokines → increase in BMD [5]
  - T1DM patients → lower BMI lower adipose tissues → more prone to develop OP [5]
- Poor glycemic control [6]
  - T1DM → poor glycemic control → microvascular complications (Retinopathy, Neuropathy, Nephropathy)
  - Retinopathy and neuropathy → fall → fractures
  - Nephropathy Hypercalciuria AND alter vitamin D metabolism vitamin D deficiency
- Endocrine factors [7]



CONCLUSIONS

- Both men and women with T1DM have preponderance to have lower BMD levels
- Multiple factors can influence BMD in individuals with T1DM:
  - Age
  - Gender
  - Menopausal status
  - Bone type
- Large prospective epidemiological studies are required to confirm our findings

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