Fractures in Children with Type 1 Diabetes are associated with Poorer Bone Mineral Status and Glycaemic Control

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Background & Objective

Young people with Type 1 diabetes (T1D) have a higher risk of fractures. This study was designed to understand the effects of T1D on bone health in children.

Methods

Total body (TB) and lumbar spine (LS) BMC were measured, in T1D children aged 10-18 years, by DXA, size-corrected for bone area, and converted to SDS (BMC-for-BA-SDS) using local normative data. Fat mass, and lean mass for height, were also similarly converted to SDS. BAP, CTX and IGF1 were measured. Information on growth puberty, diabetes control (inc HbA1c for the previous 12 months), Vitamin D and physical activity scores (1=least, 5=most active) were recorded. Fracture history was corroborated with radiological evidence. All data are presented as median (ranges), with $p<0.05$.

Results

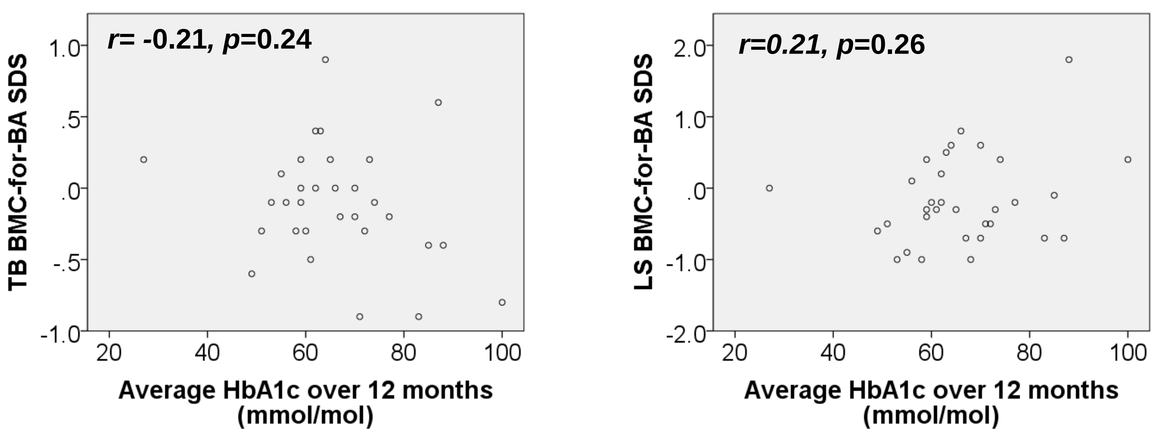
Parameters	T1DM (n=32)	*p*
Age (years)	13.7 (10.4,16.7)	
Gender (M/F)	16/16	
Height SDS	0.3 (-1.5,2.5)	<0.01
Weight SDS	0.8 (-1.3,3.2)	<0.01
BMI SDS	0.5 (-0.6,2.9)	<0.01
Tanner stage 1/2/3/4/5 (n)	3/7/10/11/1	
Disease duration (yr)	7.2 (3.1,12.4)	
Age at diagnosis (yr)	5.9 (1.3,10.8)	
HbA1c average in last 12m (mmol/mol)	65 (27,100)	
HbA1c at diagnosis (mmol/mol)	93 (56,164)	
Severity at diagnosis		
• **Not DKA/ DKA/ Unknown (n)**	21/11/1	
Fractured since diagnosis (n)	10	
Insulin dose (unit/kg/day)	1.0 (0.6,1.8)	
Insulin pump/injections	10/23	

Table 1: Clinical characteristics of the children with T1DM.
Children with T1D are taller and heavier with higher BMI

Parameters	T1DM (n=32)	*p*
TB BMC for BA SDS	-0.1 (-1.1,0.9)	0.02
LS BMC for BA SDS	-0.3 (-1.0,1.8)	0.01
Fat mass (%)	29.5 (15.2,54.5)	
Fat-mass/Height SDS	0.1 (-0.9,3.7)	0.25
Lean-mass/Height SDS	-0.5 (-3.4,1.2)	0.25
BAP SDS	-0.57 (-2.5,2.1)	<0.01
CTX SDS	-1.05 (-2.49,0.51)	<0.01
IGF1 SDS	-0.24 (-3.64,1.48)	0.36
Vitamin D (nmol/L), *n=25*	48 (18,75)	
PTH (mmol/L), *n=30*	3.6 (1.5,6.6)	
ALP (mmol/L), *n=31*	214 (79,438)	

Table 2: Bone mineral content and turnover markers in T1D.
Total body (TB) and lumbar spine (LS) BMDs are reduced in children with T1D with biochemical evidence of a low bone turnover state.

Fig 1: Correlation between TB and LS BMD with glycaemic control

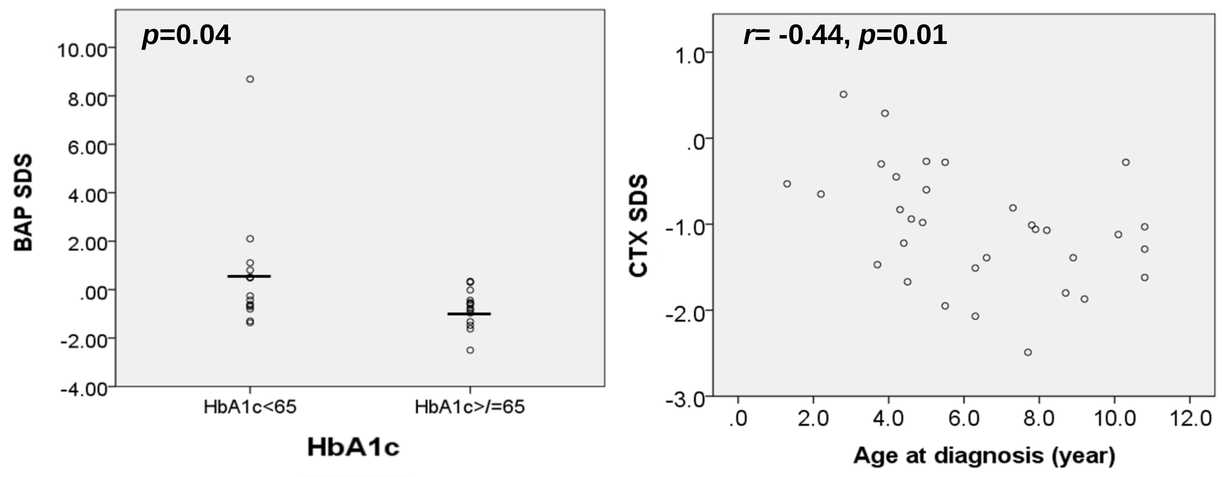


TB and LS BMD parameters did not show any correlation to HbA1c (Fig 1), age of diagnosis (p=0.24,p=0.90), or disease duration (p=0.96,p=0.76).

Results

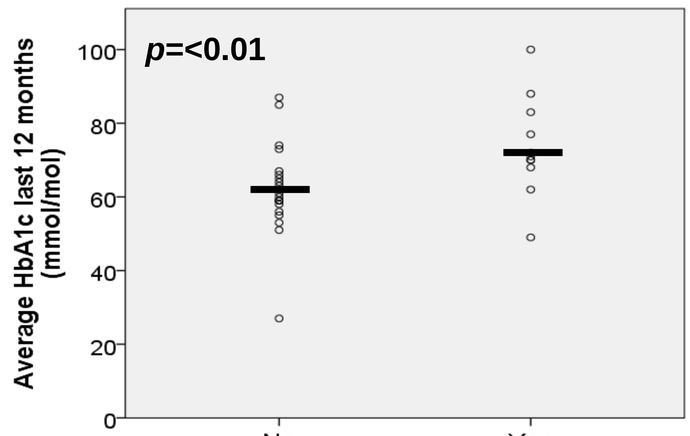
Interestingly, lower vitamin D levels were significantly associated with reduced LS BMD (p=0.03), but not TB BMD (p=0.46). A lower BAP was more likely in those with a HbA1c of ≥65mmol/mol (p=0.04) (Fig 2). CTX was inversely related to TB BMC SDS (r=-0.5, p<0.01) and age at diagnosis (r=-0.44, p=0.01) (Fig 2).

Fig 2: Relationship between BAP and CTX with disease characteristics



However, poorer glycaemic control was significantly associated with radiologically confirmed clinical fracture(s) (Fig 3), which were independent of age of diagnosis, disease duration or Vitamin D levels.

Fig 3: Glycaemic control in T1D with and without fractures post-diagnosis



Parameters	No fracture (n=22)	Fracture (n=10)	*p*
Age (year)	13.5 (10.7,16.7)	13.8 (10.4,16.4)	0.92
Gender (M/F)	9M:13F	7M:3F	
Height SDS	0.3 (-1.5,2.5)	0.4 (-1.4,2.1)	0.80
Weight SDS	0.8 (-0.4,2.4)	0.5 (-1.3,3.2)	0.37
BMI SDS	0.6 (-0.6,2.9)	0.5 (-0.6,2.4)	0.41
Puberty (Pre/Early/Late)	2:10:9	1:0:0	
Age at diagnosis (year)	6.5 (3.8,10.8)	4.4 (1.3,10.8)	0.08
Duration of disease (year)	7.0 (3.1,10.9)	8.6 (3.1,12.4)	0.20
HbA1c ave. in 12m (mmol/mol)	62 (27,87)	72 (49,100)	0.01
Vitamin D level (nmol/L)	48 (18,70)	47 (25,75)	0.88
TB BMC for BA SDS	0.0 (-0.5,0.9)	-0.5 (-1.1,0.0)	0.00
LS BMC for BA SDS	-0.3 (-1.0,0.8)	-0.5 (-1.0,1.8)	0.62
FM/Ht SDS	0.25 (-0.9,3.7)	0.04 (-0.8,2.5)	0.37
CTX SDS	-1.17(-2.49,0.29)	-0.73(-1.67,0.51)	0.05
Physical activity score	2.2 (1.3,3.7)	2.8 (1.7,4.1)	0.04

Table 3: Characteristics of T1D children with and without fracture(s) .
Children who have fractured had poorer glycaemic control and lower TB BMD

Conclusion

1) **Children with T1D display a low bone turnover state and have marginally reduced bone mineral status**
2) **Those who fracture have worse bone mineralisation and glycaemic control**
3) **Alteration of bone health in this population from such a young age, and especially in those with poor control, needs further study**

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