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Bone mineral density is increased in 276 Danish children and adolescents with Type-1-Diabetes.

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Introduction:

Bone health is affected by Type-1-diabetes (T1D) and higher risk of fractures, prolonged fracture healing, reduced bone mineral density (BMD) and impaired bone metabolism have all been demonstrated in adults with T1D. Studies of bone health in children and adolescents with T1D have been few, limited in size and have presented conflicting results.

The **T1D BACKBONE STUDY** from the **CPH T1D Research Clinic** at Herlev — comprises two arms intending to investigate the status of bone health in pediatric T1D in both patients in the remission phase and in fully insulin dependent patients (defined as disease duration > 1 year). The current study aims at assessing BMD in a large cohort of growing children and adolescents with T1D in the "fully insulin dependent" phase. Further we examine which factors affects the bone health ie. metabolic control (HbA1c), vitamin D, PTH, disease duration, activity level and treatment regimen.

276 children and adolescents in the "fully insulin dependent" state of T1D have been included into the T1D backbone study. Out of these, 246 had their bone mineral density examined and were included in the present study.

Methods:

Participants had Total-BMD and TBLH-BMD (total body less head) evaluated by a Dual-energy X-ray absorptiometry (DXA) scan and had blood tests drawn as well as capillary measurements of fasting blood glucose and HbA1c. Further, a mean of all HbA1c measurements registered (excluding the first year of T1D) was used a marker of the metabolic history. Height was measured by stadiometer to the nearest mm and weight was examined using a traditional digital scale to the nearest 0.1 kg. BMI was calculated as (weight in kg / (height in meter x height in meter)).
The current insulin treatment was registered, both regarding treatment regimen (CSII/MDI), numbers of boluses used and the total daily insulin dose divided by the weight of the patient (TDD/Kg). Finally physical activity was assessed by a simple questionnaire about days with 1 hour activity the past week.

Statistics:

Total-BMD and TBLH-BMD is presented as Z-scores made available by the DXA software and height, weight and BMI is converted to standard deviation scores (sds) using a large Danish reference material. T-tests were used to test if Z-scores and sds-scores were significantly different from the population mean (Z-score/sds = 0) and to make comparisons between boys and girls. Pearsons correlation coefficients were used to investigate correlations. Finally multiple regression analyses were used to investigate the relationship between BMD (both Total-BMD and TBLH-BMD) and variables of interest such as HbA1c, time since onset of T1D (duration), gender and height. Results are presented as mean (Standard deviation). All analyses were done using SAS Enterprise Guide version 7.11.

Results:

Participants had a mean age of 13.9 years (±3.5), a mean disease duration of 4.9 years (±3.5) and a mean HbA1c of 62.6 mmol/mol (±14.2) Patients with T1D had significantly higher weight- and BMI-sds compared to the background population and both higher Total-BMD Z-score and TBLH-BMD Z-score (**Table 1**). Sub-analysis by gender show that only girls had higher weight and BMI compared to the background population. Further, girls had higher HbA1c, longer T1D duration and were less active compared to boys. Both genders had a mean Total-BMD Z-score significantly higher than the reference population but only girls had significantly higher mean TBLH-BMD Z-score (**Figure 1**).

Correlation analyses between TBLH-BMD Z-score and both HbA1c and HbA1c history indicated negative correlations for both, however, neither were significant. Significant correlations to TBLH-BMD Z-scores were seen in weight-, height- and BMI-sds, and further age, phosphate, PTH, calcium and magnesium showed consistent patterns between analysis (**Figure 2**).

In multiple linear regression analyses the negative effect of HbA1c on TBLH-BMD Z-score was significant. Also calcium and PTH negatively affected TBLH-BMD Z-score while age, height-sds, BMI-sds and physical activity all had positive influence. BMI- and weight-sds were the most influential factors explaining up to 34% of the variability in the model.

Table 1

	All patients	Boys	Girls	P (♂ vs ♀)
	246	134	112	
Age (yr)	13.9 (3.5)	13.6 (3.3)	14.2 (3.6)	*NS*
Disease duration (yr)	4.9 (3.5)	4.3 (3.2)	5.6 (3.8)	*P=0.05*
HbA1c (mmol/mol)	62.6 (14.2)	60.7 (14.0)	64.9 (14.2)	*P=0.019*
HbA1c history (mmol/mol)	60.0 (11.1)	58.6 (10.6)	61.6 (11.4)	*P=0.03*
TDD/Kg (IE/kg)	0.84 (0.26)	0.83 (0.27)	0.84 (0.26)	*NS*
Height SDS	0.03 (1.00)	0.04 (1.00)	0.01 (0.98)	*NS*
Weight SDS	0.27 (1.07)*	0.03 (0.97)	0.56 (1.11)*	*P<0.0001*
BMI SDS	0.34 (1.05)*	0.03 (0.97)	0.71 (1.03)*	*P<0.0001*
Physical Activity (days/week)	3.9 (2.1)	4.4 (2.1)	3.3 (2.0)	*P<0.0001*
Total-BMD Z-score	0.73 (0.96)*	0.65 (0.93)*	0.85 (1.02)*	*NS*
TBLH-BMD Z-score	0.22 (0.96)*	0.12 (0.84)	0.36 (1.08)*	*NS*
Regimen (%CSII)	64.2%	59.0%	70.5%	*NS*

* Significant different from the reference population

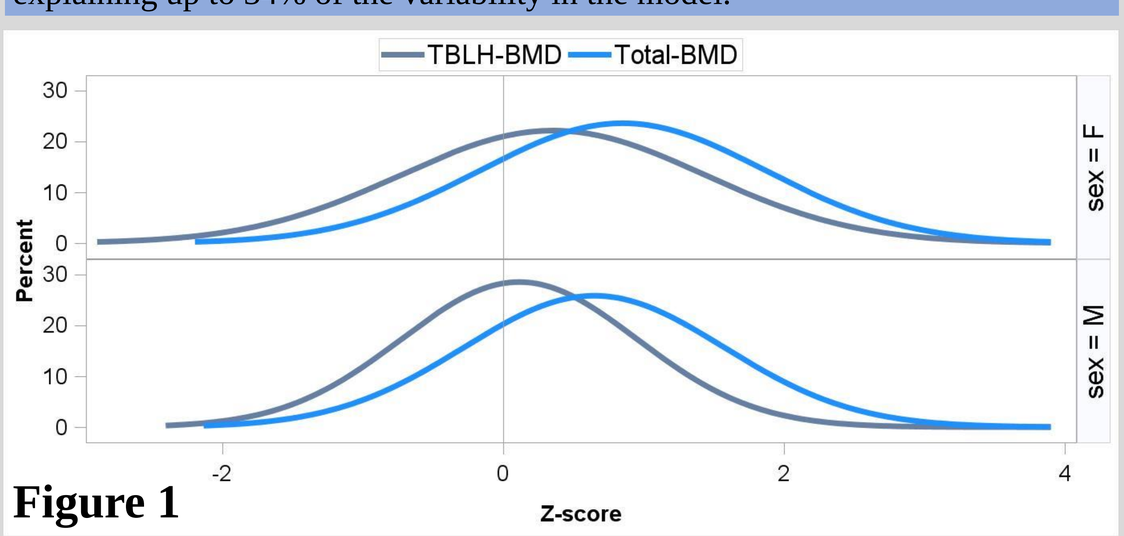

Figure 1

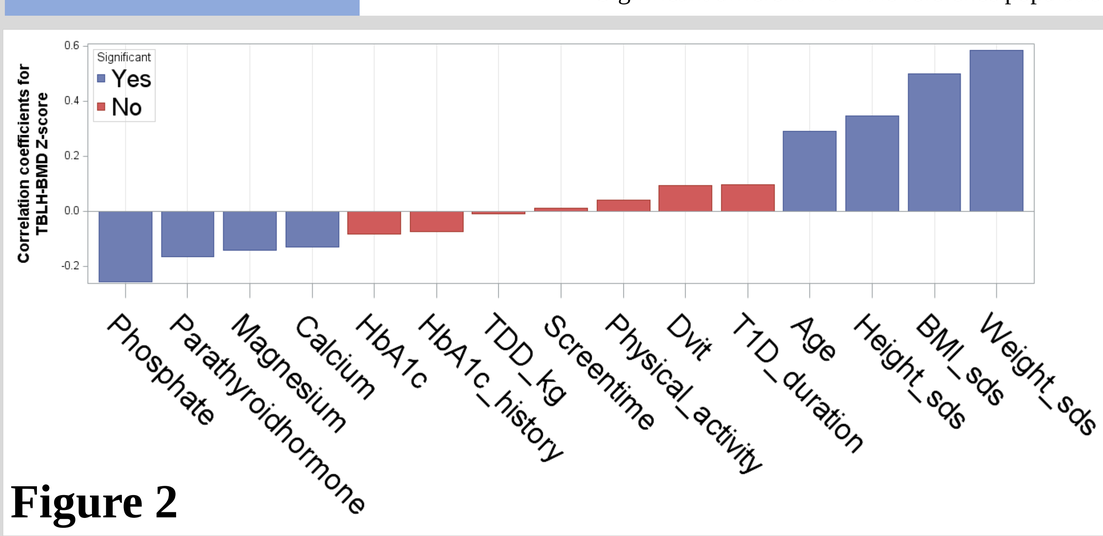

Figure 2

Conclusion:

There is no sign of reduced BMD in children and adolescents with T1D however girls tend to be heavier than the reference population. In fact Total-BMD Z-scores are increased in both boys and girls compared to the background population and TBLH-BMD Z-scores are increased in girls. HbA1c negatively affect TBLH-BMD however the stronger positive effects of other factors including weight and BMI may be the cause of our results. Though no sign of reduced BMD in children and adolescents with T1D, investigation of markers of bone metabolism would be of utmost interest to further elucidate the status of bone health and the potential development of the changes in bone health seen in adults with T1D.