Increased levels of Dickkopf-1 may indicate lower osteoblast signaling, predisposing to lower Bone Mineral Density in children and adolescents with type 1 Diabetes Mellitus (T1DM).

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Introduction: T1DM is a risk factor for reduced bone mass, disrupting several bone metabolic pathways. Dickkopf-1 is an inhibitor of the Wnt/b-catenin bone metabolic pathway. Increased fracture risk and elevated Dickkopf-1 levels have been documented in adult patients with T2DM. No relevant data exist on childhood T1DM. Our aim was to study plasma Dickkopf-1 concentration in children and adolescents with T1DM and controls and to correlate Dickkopf-1 levels with metabolic bone markers and bone mineral density (BMD)

Methods: Forty children and adolescents with T1DM were evaluated (mean±SD age:13.04±3.53years, T1DM duration:5.15±3.33years), along with 40 healthy matched controls (mean±SD age 12.99±3.3years). Dickkopf-1, Sclerostin, Osteocalcin, C-telopeptide crosslinks-CTX, electrolytes, PTH, total 25(OH) D were measured, while lumbar spine and total body BMD were evaluated.

Results: BMD was significantly lower in T1DM patients than controls. Dickkopf-1 levels demonstrated a Gaussian distribution, with higher levels in T1DM patients (13.56±5.34 vs 11.35±3.76 pmol/L, p=0.0194) (Figure 1.).

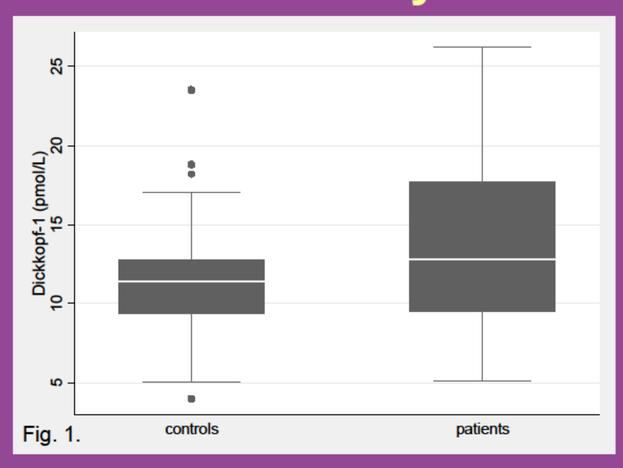

Fig. 1.

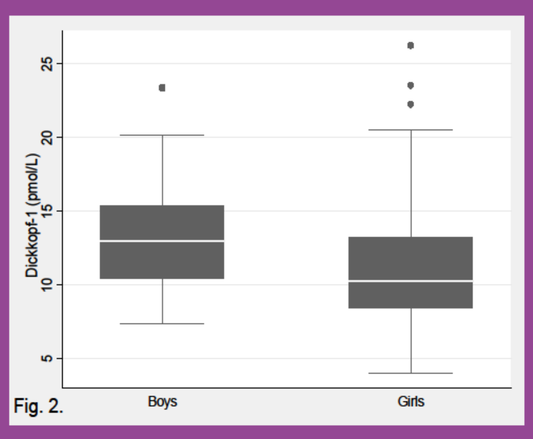

Fig. 2.

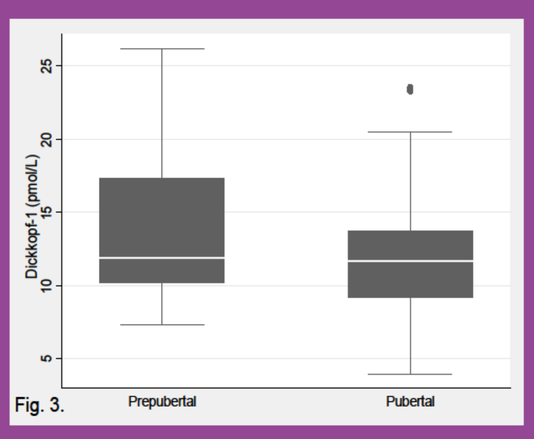

Fig. 3.

A trend for lower values was found in girls (13.36±4.04 vs 11.72±5.14 pmol/L, p=0.06) (Figure 2.) and in pubertal children (13.61±4.87 vs 11.83±4.56 pmol/L, p=0.054) (Figure 3.).

Dickkopf-1 correlated with Sclerostin and L1-L4 BMD z-score only in controls and with Osteoprotegerin and i-Phosphorus only in patients, while in both groups a significant correlation with log(CTX) and √ALP was documented (Table 1.).

A significant correlation of Dickkopf-1 with IGF-1 and insulin dose was also shown in patients.

Conclusions: T1DM children and adolescents had higher levels of Dickkopf-1 than controls, indicating a downregulated Wnt signaling system and possible lower osteoblast activation that could be associated with T1DM osteopathy.

Table 1. Pearson correlation coefficient and partial correlation coefficient, after adjusting for the effect of gender and Tanner stage, of Dickkopf-1 and bone metabolic markers, BMD estimators and glycaemic control.

	overall (n=80)	diabetes (n=40)	controls (n=40)
Sclerostin	0.06 / 0.08	-0.01 / 0.02	0.32* / 0.32*
log(CTX)	0.41‡ / 0.35‡	0.41* / 0.36†	0.58‡ / 0.52‡
logOsteocalcin	0.19 / 0.10	0.25 / 0.16	0.28 / 0.16
log(s-RANKL)	0.13 / 0.15	0.04 / 0.08	0.12 / 0.12
OPG	0.28* / 0.25*	0.33* / 0.34*	0.18 / 0.07
log(PTH)	0.04 / 0.03	0.17 / 0.17	-0.08 / -0.11
√ALP	0.38‡ / 0.31†	0.49‡ / 0.39*	0.40* / 0.39*
25(OH)D	-0.004 / -0.02	-0.03 / -0.04	0.05 / 0.04
Calcium	0.04 / 0.02	0.08 / 0.05	0.03 / 0.02
i-Phosphorus	0.31† / 0.24*	0.47† / 0.42*	0.34* / 0.14
Magnesium	0.05 / 0.01	0.20 / 0.19	0.15 / 0.06
IGF-1	0.03 / 0.20	0.14 / 0.35*	0.08 / 0.30
L1-L4 BMD z-score	0.05 / 0.05	-0.12 / -0.11	0.44† / 0.44†
TB BMD z-score	-0.005 / -0.04	-0.08 / -0.14	0.30 / 0.26
diabetes duration	--	-0.02 / 0.06	--
HbA1c	--	-0.07 / -0.02	--
HbA1c 6m	--	0.006 / 0.03	--
HbA1c 12m	--	0.01 / 0.03	--
iu ins/kg/day	--	0.32* / 0.35*	--

*p<0.05, †p<0.01, ‡p<0.001

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