Lower Bone Mineral Density in type 1 Diabetes Mellitus(T1DM) is probably associated with Wnt/β-catenin pathway downregulation through increased Dickkopf-1 levels

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Background: Disruption of many bone metabolic pathways and reduced bone mass are associated with Diabetes Mellitus. Increased fracture risk and elevated Dickkopf-1 and sclerostin levels, which are inhibitors of Wnt/β-catenin pathway, have been found in adult T2DM patients but no relevant data exist on childhood T1DM.

Aims and objective: We aimed at studying plasma Dickkopf-1 and sclerostin concentration in children and adolescents with T1DM and controls. We subsequently correlated Dickkopf-1 and sclerostin levels with metabolic bone markers and bone mineral density (BMD).

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

Results: BMD was found lower and Dickkopf-1 levels were found higher (13.56±5.34 vs 11.35±3.76 pmol/L, p=0.0194) in T1DM patients (Fig. 1).

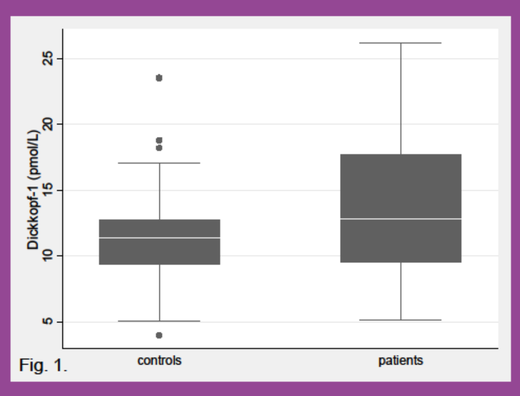

Fig. 1.

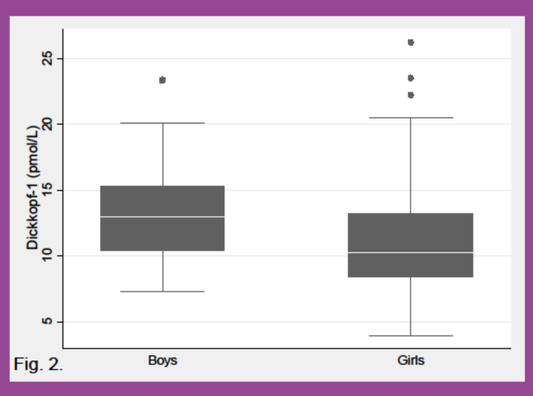

Fig. 2.

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

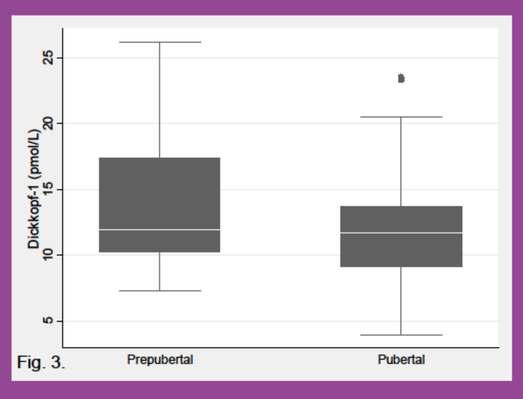

Fig. 3.

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‡
OPG	0.28* / 0.25*	0.33* / 0.34*	0.18 / 0.07
√ALP	0.38‡ / 0.31†	0.49‡ / 0.39*	0.40* / 0.39*
i-Phosphorus	0.31† / 0.24*	0.47† / 0.42*	0.34* / 0.14
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†
iu ins/kg/day	--	0.32* / 0.35*	--

*p<0.05, †p<0.01, ‡p<0.001

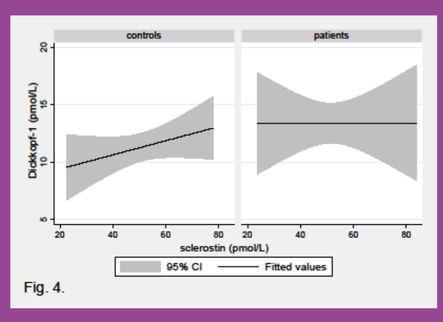

Fig. 4.

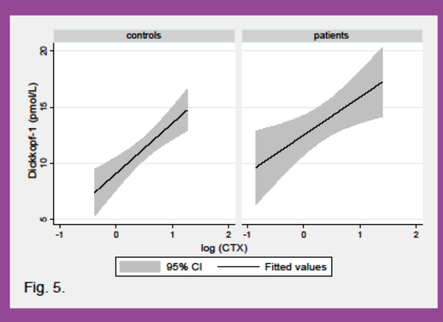

Fig. 5.

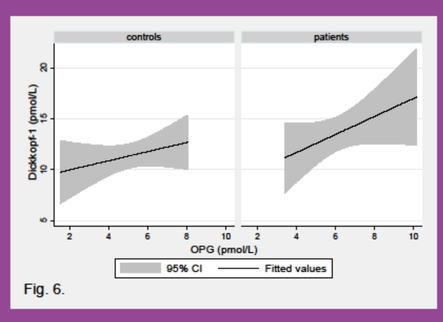

Fig. 6.

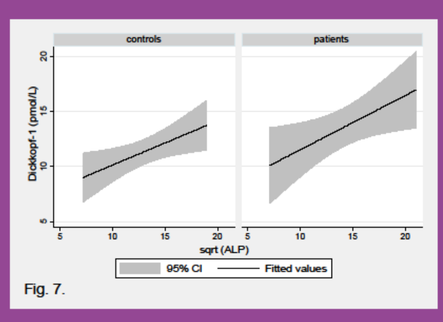

Fig. 7.

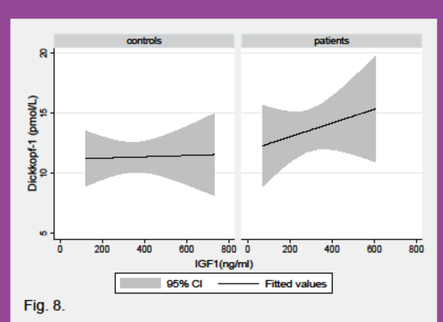

Fig. 8.

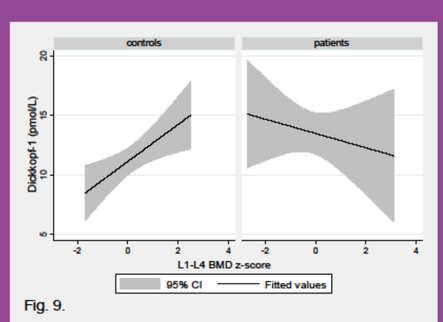

Fig. 9.

Dickkopf-1 correlated with Sclerostin (Fig. 4.) and L1-L4 BMD z-score (Fig. 9.) only in controls and with OPG(Fig. 6.) and i-Phosphorus only in patients, while in both groups a significant correlation with log(CTX) (Fig. 5.) and √ALP (Fig. 7.) was documented

A significant correlation of Dickkopf-1 with IGF-1 (Fig.8) and insulin dose was also shown in patients.

Conclusions: Higher levels of Dickkopf-1 were found in T1DM children and adolescents, indicating a downregulated Wnt signaling system and possible lower osteoblast activation that could be associated with T1DM osteopathy.

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