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±3.53 years, T1DM duration: 5.15±3.33 years), along with 40 healthy matched controls (age 12.99±3.3 years). 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).

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 \( \Delta \)ALP (Fig. 7.) was documented.

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.).

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.