# RANKL and osteoprotegerin serum levels in obese children and adolescents

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**The authors disclose any conflicts of interest**

## BACKGROUND

There is growing evidence of a correlation between fat and bone metabolism at both the clinical and molecular levels, although the systemic regulators have not been clearly identified. The receptor activator of nuclear factor kB ligand (RANKL) and its soluble decoy receptor, osteoprotegerin (OPG), are involved in bone resorption and vascular calcification. In particular, RANKL promotes differentiation and activates mature osteoclasts to reabsorb bone by binding to its specific receptor RANK. OPG competes with RANK in binding to RANKL, preventing its osteoclastogenic effect. Moreover, OPG levels has been related with insulin resistance in adult obese subjects.

## OBJECTIVE AND HYPOTHESES

We aimed: 1. to evaluate RANKL and OPG serum levels in obese children and adolescents and healthy lean controls; 2. to investigate correlation between metabolic alterations and OPG levels; 3. to correlate OPG and RANKL levels with bone status assessed by QUS.

## METHODS

Twenty-five subjects (16 males, median age 10.8 ± 2.6), with body mass index (BMI) >95th centile for age and sex, were enrolled. BMI standard deviation score (BMI-SDS) was derived from population standard. As control group were recruited 28 non-obese subjects (18 males, median age of 10.8 ± 2.6 years), age- and sex-matched. All subjects underwent anthropometric measurements, evaluation of lipid profile, glucose and insulin levels, and HOMA-IR. RANKL and OPG levels were measured in the sera from all obese subjects and controls. Bone status was assessed by QUS through BTT-Z-score and Ad-Sos-Z-score evaluation.

## RESULTS

RANKL and OPG serum levels in obese and in controls

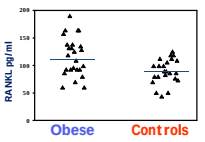


**Figure 1.** Obese children have higher RANKL (p=0.01) and lower OPG (p<0.006) serum levels compared with controls.

RANKL and cholesterol serum levels

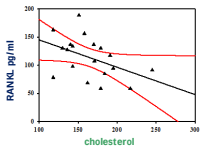


**Figure 2.** RANKL serum levels inversely correlated with serum cholesterol levels (p<0.05).

RANKL/OPG and HOMA-IR

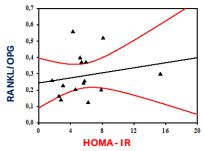


**Figure 3.** RANKL/OPG correlated with HOMA-IR (p<0.04).

OPG serum levels versus waist circumference and BMI

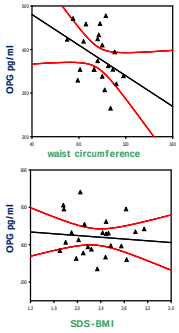


**Figure 4.** OPG serum concentrations inversely correlate with waist circumference (p<0.05), SDS-BMI (p<0.05).

OPG serum levels versus insulin and HOMA-IR

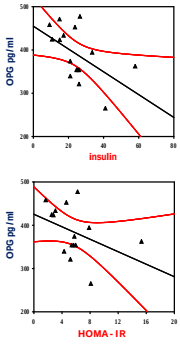


**Figure 5.** OPG serum concentrations inversely correlate with insulin levels and HOMA-IR (p<0.04).

Obese children have higher RANKL (p=0.01) and lower OPG (p<0.006) serum levels compared with controls (fig. 1); thus, RANKL to OPG ratio was significantly higher in patients than controls (p<0.001). However, these serum levels did not correlate with BTT-Z-score and Ad-Sos-Z-score, although obese patients had significantly reduced QUS parameters compared to the controls (p<0.01). Interestingly, in the patients BTT-Z-score and Ad-Sos-Z-score inversely correlated with serum LDL levels (p<0.04 and p<0.01 respectively), whereas RANKL inversely correlated with serum cholesterol levels (p<0.05) (fig. 2) and RANKL/OPG correlated with HOMA-IR (p<0.04) (fig. 3). Parallel results demonstrated that OPG serum concentrations significantly correlate with waist circumference (p<0.05), SDS-BMI (p<0.05), insulin levels and HOMA-IR (p<0.04) (fig. 4,5).

## CONCLUSIONS

Our results pointed out to a complex alteration in obese children involving adipose tissue, bone and glucose metabolism, which is orchestrated by RANKL/OPG/RANK axis.