SERUM CALPROTECTIN LEVEL IN CHILDREN: MARKER OF OBESITY AND ITS METABOLIC COMPLICATIONS.

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Aim of the study

Elevated calprotectin levels in plasma have been reported for a variety of chronic inflammatory conditions including rheumatoid arthritis, allograft rejections, inflammatory bowel disease, cancer, and lung diseases. In adults, increased circulating levels of calprotectin have been reported in obesity-related chronic low-grade inflammation. To our knowledge, this association has never been evaluated in the pediatric age group.
The aim of the present study was to investigate serum calprotectin levels in overweight and obese children and to detect the association of calprotectin with metabolic complications related to obesity in the pediatric population.

Patients and methods

We enrolled 131 Caucasian children and adolescents aged 11.7±4.1 years (67 females and 64 males) referred to our outpatients' clinic for auxological evaluation or obesity by their general practitioner or primary care pediatrician between May and October 2017.
According to the Italian Society for Pediatric Endocrinology and Diabetology (ISPED) criteria, the subjects were divided into three groups:
-subjects with obesity (group 1) BMI that exceeded the 95th percentile for the age and sex
-subjects with overweight (group 2): BMI 75th–95th percentile;
-subjects with normal weight (group 3): BMI < 75th percentile .

Exclusion criteria were: specific intestinal symptoms and intestinal diseases, known secondary obesity conditions, use of any medications, and concomitant chronic or acute illnesses.

Patients were classified as having Metabolic Syndrome (MetS) if they met three or more of the following criteria for age and sex: BMI>97th percentile, triglycerides >95th percentile, HDL cholesterol <5th percentile, systolic and/or diastolic blood pressure >95th percentile and impaired glucose tolerance. In all patients calprotectin serum levels were also detected.

Results

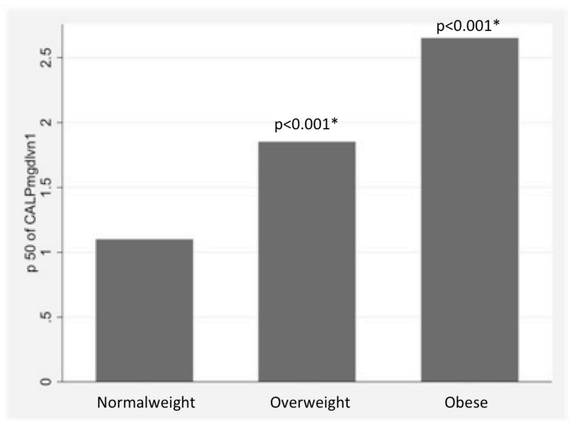
Based on the BMI percentiles threshold, 39 of the 131 (29.7%) enrolled patients were normal weight, 36 (27.4%) overweight and 56 (42.7%) obese. The clinical characteristics and metabolism-related laboratory data of the normal-weight and obese subjects are reported in table 1.
In both obese and overweight children, serum calprotectin level was higher compared to normal weight subjects (median 2.65 µg/mL and 1.85 µg/mL respectively *vs* 1.1 µg/mL; p<0.001). No significant difference between patients with obesity and overweight (p=0.07) was observed in calprotectin values.
Distribution of calprotectin levels into the three groups, according to body weight classification and sex, is reported in Figure 1. Calprotectin was higher in female than males (p=0.004). No significant difference in other metabolic parameters were noted between male and females, except for a higher pathological waist circumference in females (p=0.02).
Pathological calprotectin concentration (>1.6 µg/mL) was found in 42/56 children with obesity (75%), in 21/36 overweight children (58.3%) and in 15/39 normal weight ones (38.4%).
Overall prevalence of MetS was detected in 13 (10%) children either overweight or with obesity; 10 of these patients, exhibited elevated calprotectin. No normal weight subjects met the criteria for MetS.
Increased calprotectin was related to pathological fasting blood glucose (p<0.001) and insulin resistance (p=0.03). No significant correlation with other pathological clinical or biochemical parameters was reported.
Multiple regression analysis identified BMI (beta 1.28 C I95% 0.36-2.29 for overweight; beta 1.35 CI 95% 0.53-2.17, p=0.001 for obese) and diastolic pressure (beta 0.07 for 1-mmHg increase, CI 95% 0.02-0.11, p=0.001) as independent factors for increased serum calprotectin. Gender and age were not statistically significant.

Table 1. Clinical and metabolic parameters according to body weight classification.

Parameters	Normal weight (n=39)	Overweight (n=36)	Obesity (n=56)	p
Age (years)	12.3±5.1	11.4±4.0	11.4±3.0	0.52
Gender (M/F)	24/15	11/25	29/27	0.03
Pubertal stages				0.07
Tanner I	8	6	21	
Tanner II-III	18	23	23	
Tanner IV-V	13	7	12	
WC (cm)	63.7±6.5	78.9±10.4	84.5±9.2	0.03a
W/HtR	0.40±0.04	0.54±0.05	0.6±0.05	0.27
Fasting glucose (mg/dl)	70.7±7.3	71.9±8.4	72.0±15.2	0.41
Insulin (mU/L)	6.4±7.3	11.4±7.7	12.3±8.9	0.11
HOMA-IR	1.2±0.8	2.0±1.3	2.2±1.8	0.36
Triglycerides (mg/dl)	50.3±16.3	65.7±31.8	86.1±46.3	0.04
HDL-cholesterol (mg/dl)	54.1±11.0	50.7±12.8	47.6±10.2	<0.01b
Total cholesterol (mg/dl)	143.6±18.6	155.2±26.1	161.1±30.2	0.10
Systolic pressure (mmHg)	107.1±10.4	108.4±10.0	113.6±10.0	0.01c
Diastolic pressure (mmHg)	62.6±9.0	69.0±8.2	71.0±8.2	0.52
Calprotectin (µg/mL)*	1.1 (0.9-2.1)	1.85 (1.1-4.7)	2.65 (1.6-4.2)	<0.001d

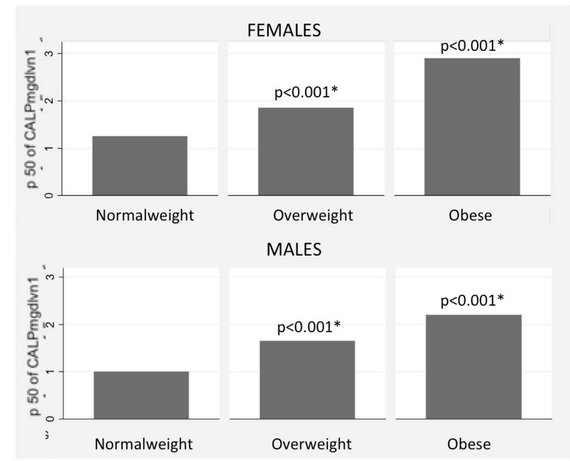
Figure 1. Distribution of calprotectin levels in normal-weight, overweight and obese children (Panel A) and according to sex (Panel B). Data are expressed as median values.

A



*p vs normalweight

B



*p vs normalweight

Conclusions

This study work supports a role of calprotectin as a marker of obesity-associated chronic low-grade inflammation in children and suggesting the potential utility of this biomarker in the monitoring of its metabolic complications.
Further research with larger sample, in multiple critical care units and even outside of clinical setting, would be valuable in order to confirm these results in pediatric age and apply these findings in clinical practice to identify young patients with no alarm symptoms present who require further invasive investigation to exclude metabolic and cardiovascular complications and designed personalized intervention.

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