Gender-based differences in the clustering of metabolic syndrome factors in children and adolescents.

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Background

There are key aspects of metabolic homeostasis that are regulated differently in males and females and it has been reported that the prevalence of different combinations of Metabolic syndrome (MS) factors are otherwise expressed by gender.
The major contributors of gender dimorphisms in glucose, lipid and energy homeostasis are "activation" effects of estrogens and androgens acting on their receptors after the onset of puberty. Gender-based differences in metabolic risk in children with obesity as well as interactions between gender and pubertal development on metabolic homeostasis and different MS combinations, are not fully detailed in pediatric age.
The aim of this cross sectional study was to describe the gender differences in MS clustering before and after puberty in children and adolescents, in order to identify early childhood prevention intervention and treatments for at high risk children.

Patients and methods

From October 2016 to October 2018, 1079 Caucasian children and adolescents (529 females and 550 males) aged 2-18 years, referred to our outpatients' clinic for auxological evaluation or obesity by their general practitioner or primary care pediatrician, were consecutively included in the study.
According to the Italian Society for Pediatric Endocrinology and Diabetology (ISPED) criteria, the subjects were classified as normal weight, body mass index (BMI)<75th percentile; overweight, BMI 75-95th percentile; with obesity, BMI>95th percentile
Physical examination of the participants included evaluation of height, weight, waist circumference, BMI (calculated as body weight in kilograms divided by height in meters squared), pubertal stage according to Marshall and Tanner (stage characteristics corresponding to Tanner stage 1), and blood pressure (BP) measurement. Waist to height ratio (WHtR) was also calculated to estimate adiposity distribution.
we diagnosed MS according to the modified criteria from the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATPIII), the World Health Organization and the International Diabetes Federation. Patients were classified as having MS if they met 3 of the following criteria for age and sex: BMI >95th percentile, TG level >95th percentile, HDL cholesterol level <5th percentile, SBP and/or DBP >95th percentile, FBG >100 mg/dl and/or HOMA-IR >97.5th percentile. For further details please refer to our previous studies

Results

Clinical and metabolic data
No statistical differences were found between males and females for age and pubertal stage.
Compared to females, males showed higher BMIs (p=0.01), WC (p=0.003), glucose levels, (<0.001), systolic blood pressure (p<0.01), tryg index (p=0.04) and WHtR (p=0.007).
All parameters included in the evaluation were significantly different in prebupertal *vs* pubertal stage (for all p<0.01), except HDL- and total-cholesterol and WHtR. The difference between gender is evident both before and post-puberty for BMI and WHtR (p=0.01 and p=0.02, respectively).

Clustering of dismetabolic factors
Based on the BMI percentiles threshold, 190 of the 1079 patients (17.6%) were normal weight, 271 (25.11%) overweight and 618 (57.27%) affected by obesity.
The percentage of patients with pathological auxological and metabolic parameters are reported in Figure 1.
The prevalence of dismetabolic factors was similar in males and females with no difference between genders (Figure 1), except for pathological BP that was higher in males than females (p=0.02).
Compared to pre-pubertal children, pubertal subjects showed a higher prevalence of pathological HOMA-IR (p=0.001), Tryg index (p=0.002) and WHtR (p=0.02), with no difference between gender.
MS was detected only in patients with obesity (14.27%). The prevalence of MS was higher in pubertal than pre-pubertal subjects (16.1 vs 10.3 p=0.01), without any significant difference between males and females (Figure 1).

Combination of metabolic syndrome components
As reported in Figure 2, dismetabolic factors presented alone or associated with 1 to 4 other parameters, with different combinations according to gender and puberty.
In pre-puberty, the most common combination was obesity (HBMI) +hypertension (HBP)+hyperglycemia/insulin resistance (HGLY/IR) followed by HBMI+low HDL-levels (LHDL) + HGLY/IR in females and HBMI+HBP+ HGLY/IR followed by HBMI+HBP+LHDL in males.
In pubertal period, the most prevalent combination remained similar to pre-puberty in females and males, additionally in both sexes the combination HBMI+HBP+ LHDL+ HGLY/IR was also detected.

Figure 1. Distribution of prevalence of metabolic syndrome and its components in pre-pubertal and pubertal females and males (BMI=body mass index; Glyc=glycemia; HOMA-IR=homeostasis model assessment for insulin resistance ; HDL-Chol=HDL-Cholesterol; BP=Blood Pressure)

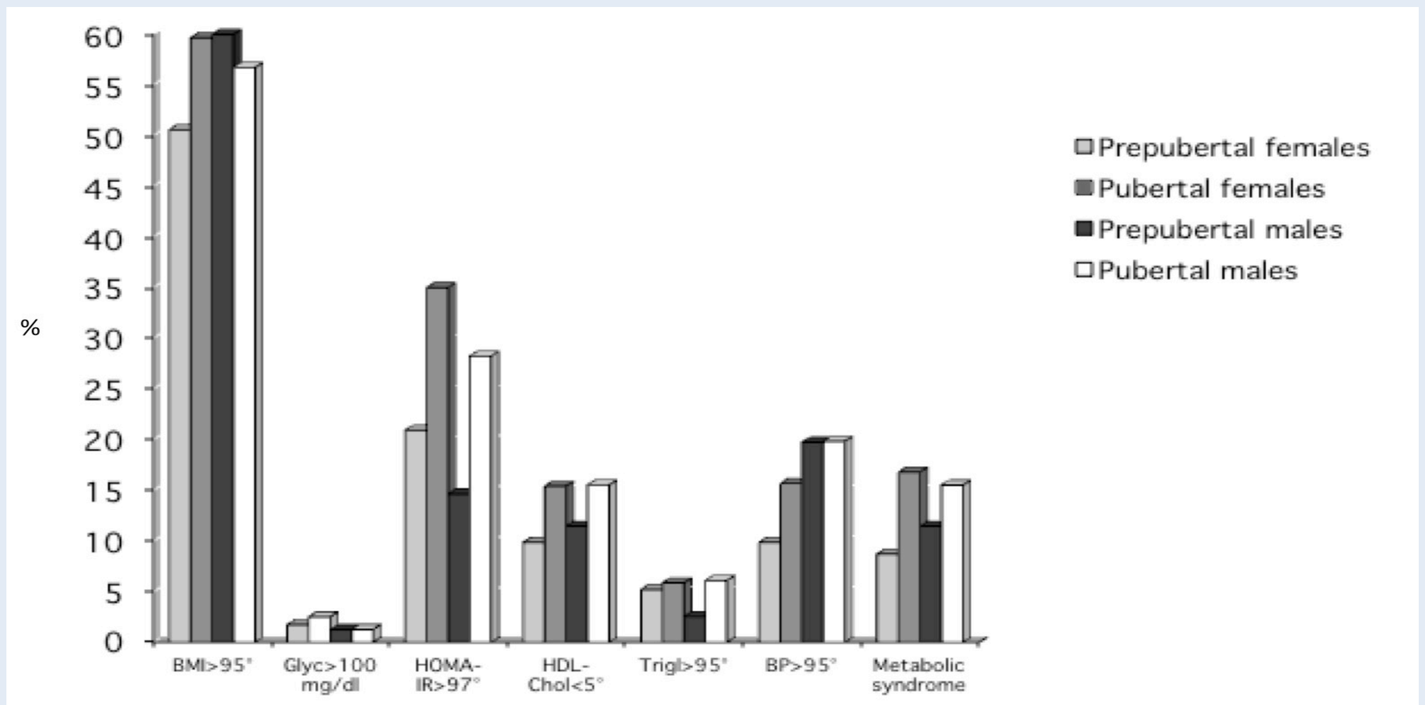
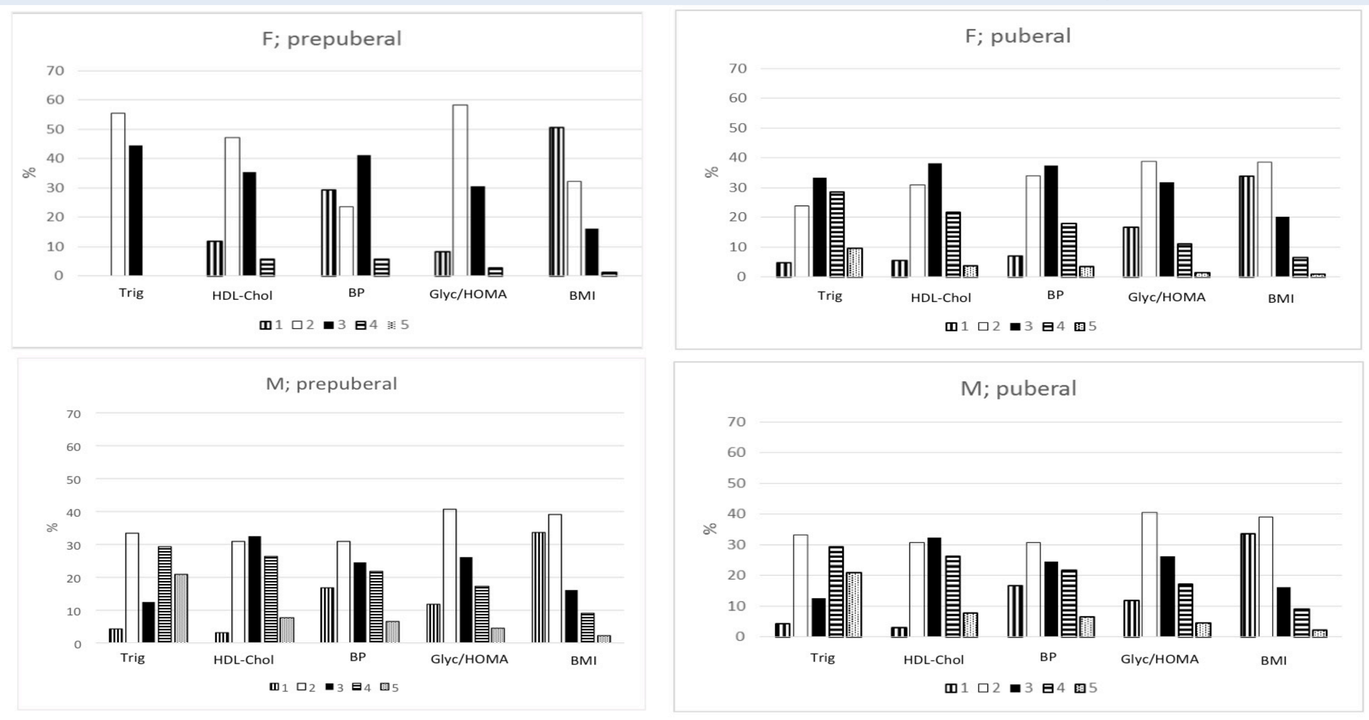


Figure 2. Distribution of **c**ombination of 1 to 5 pathological metabolic syndrome components according to pubertal stage and gender (BMI=body mass index; Glyc=glycemia; HOMA-IR=homeostasis model assessment for insulin resistance ; HDL-Chol=HDL-Cholesterol; BP=Blood Pressure)



Conclusions

In conclusion, our results indeed confirm that MS is an important consequence related to obesity, particularly in post-puberty period. No significant difference in prevalence of MS was noted between females and males, however some gender-based differences observed in our sample should be deeper investigated and considered in order to develop gender specific preventive strategies, particularly when puberty begins.