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Study of the Prevalence of Metabolic Syndrome in Pediatric Obesity Patients

Treball Final de grau

Marina Relancio Ardanuy

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Facultat de Farmàcia i Ciències de l'Alimentació
Departament de Bioquímica i Fisiologia

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Marina Relancio Ardanuy[1]

[1]Departament of Biochemistry and Physiology, Faculty of Pharmacy and Food Science, Campus of Torribera, University of Barcelona, Barcelona, Spain

ABSTRACT

Objective: The aim of this study was to evaluate the prevalence of Metabolic Syndrome (MetS) in Spanish children from three different cohorts, according to the definition by Ahrens et al. (2014) (IDEFICS study, action level). Additionally, it analyzed the components of MetS in each cohort to evaluate their impact on MetS prevalence across pediatric populations.

Study design: The study comprised 2,411 participants aged between 3 and 18 years from three Spanish cities: Santiago de Compostela (N = 1,497), Zaragoza (N = 396), and Córdoba (N = 518). In all cohorts, recruited from hospital settings, anthropometric and biochemical data were collected and analyzed to determine the prevalence of MetS and to compare among cohorts.

Results: MetS prevalence was notably high in children with obesity across all cohorts (Córdoba: 91.3%; Santiago de Compostela: 92.7%; Zaragoza: 86.8%). Additionally, MetS prevalence increased with pubertal development, rising from 11.3% in prepubertal children to 37.5% in pubertal children in the Córdoba cohort. The same trend was observed in the Santiago and Zaragoza cohorts. Regarding socioeconomic status, Córdoba had the highest proportion of families with low parental education (45.0%) compared to Santiago (11.6%) and Zaragoza (5.8%).

Conclusion: In conclusion, significant regional, pubertal, and socioeconomic differences highlight the influence of biological and contextual factors on metabolic risk, emphasizing the urgent need to develop unified consensus guidelines for pediatric MetS.

Keywords: Metabolic Syndrome; Pediatric obesity; Spanish children; Prevalence; Risk factors; ObMetrics

RESUM

Objectiu: L'objectiu d'aquest estudi va ser avaluar la prevalença de Síndrome Metabòlica (MetS) en nens espanyols de tres cohorts diferents, d'acord amb la definició d'Ahrens et al. (2014) (IDEFICS study, action level). A més, es van analitzar els components de la MetS de cada cohort per avaluar el seu impacte en la prevalença de la MetS en poblacions pediàtriques.

Disseny de l'estudi: L'estudi va incloure 2.411 participants d'entre 3 i 18 anys, de tres ciutats espanyoles: Santiago de Compostel·la (N = 1.497), Saragossa (N = 396), i Còrdova (N = 518). A totes les cohorts, reclutades a entorns hospitalaris, es van recollir i analitzar dades antropomètriques i bioquímiques per a determinar la prevalença de MetS i comparar entre les cohorts.

Resultats: La prevalença de MetS va ser notablement alta en nens amb obesitat a totes les cohorts (Còrdova 91,3%; Santiago: 92,7%; Saragossa: 86,8%). Tanmateix, la prevalença de MetS va augmentar amb el desenvolupament puberal, passant de l'11,3% en nens prepuberals al 37,5% en nens puberals a la cohort de Còrdova. Es va observar la mateixa tendència en les cohorts de Santiago i Saragossa. Pel que fa al nivell socioeconòmic, Còrdova va presentar la proporció més alta de famílies amb un nivell educatiu parental baix (45,0%) en comparació amb Santiago (11,6%) i Saragossa (5,8%).

Conclusió: En conclusió, les diferències regionals, puberals i socioeconòmiques posen de manifest la influència de factors biològics i de l'entorn en el risc metabòlic, destacant la urgent necessitat de desenvolupar guies consensuades i unificades per a la MetS pediàtrica.

Paraules clau: Síndrome Metabòlica; Obesitat pediàtrica; Nens espanyols; Prevalença; Factors de risc; ObMetrics

Sustainable Development Goals (SDGs): This final project is focused on studying the prevalence of Metabolic Syndrome in the pediatric population with obesity. Consequently, it aligns with some of the goals proposed by the United Nations, mainly SDG2 (Zero Hunger) and SDG3 (Good Health and Well-being). Regarding SDG3, the findings of this study contribute specifically to achieving targets 3.4 (which aims to reduce mortality from non-communicable diseases through prevention and treatment) and 3.8 (which seeks to achieve universal health coverage, including access to essential and affordable health.
services). This is supported by the identification of which factors contribute to increasing metabolic risk, including among them, environmental factors. In relation to SDG2, that project addresses target 2.2 (which focuses on ending all forms of malnutrition). Childhood obesity, recognized as an increasingly prevalent form of malnutrition in many populations, is a key aspect of this work.

Introduction

Metabolic syndrome (MetS) is characterized by a combination of metabolic abnormalities commonly found in patients with obesity that significantly increases the risk of developing cardiovascular disease (CVD)[1] and type II diabetes (T2DM)[2]. The main components that define MetS include increased abdominal adiposity, elevated blood pressure (BP), hyperglycemia and dyslipidemia. To classify an individual as having MetS, disorders at least three of these components must be present[3,4]. Recent studies reveal the global impact of obesity, exposing an alarming prevalence of this condition within pediatric and adult populations. The high prevalence of pediatric obesity affects 107.7 million children[5,6]. In Spain, a prevalence of MetS of 18% (using the criteria of Cook et al.[7]) and of IR of 35% has been found in children with moderate obesity aged between 4 and 18 years[8].

Currently, clinical obesity is defined as a systemic disorder characterized by dysfunction at the organ and tissue levels, primarily driven by excess adiposity. This shift emphasizes the importance of incorporating metabolic health indicators into clinical evaluations and therapeutic strategies[9,10]. Thus, implementing early strategies to prevent MetS is crucial to mitigate the development of serious health problems in the future in pediatric patients with pre-clinical and clinical obesity[11,12].

However, despite this need, the absence of an international agreement on the most appropriate definitions of MetS in children and adolescents is still a limitation, especially given that the definitions applied to adults cannot be directly used to the pediatric population[13]. In contrast to the assessment of MetS in adults, pediatricians must utilize cutoff points adjusted by age, sex, height, and ethnicity[14,15].

Today, there is still no consensus on which components should be included and how important each one is for the definition of MetS in children and adolescents[16,17]. Some definitions do not consider the evaluation of insulin resistance (IR), which plays a pivotal role in the pathophysiology of the MetS[18]. Additionally, most of the reference populations used to define pediatric MetS are biased because the great majority are based on the North American Caucasian population, with limited representation of other ethnicities, particularly those from low- and middle-income countries. This lack of diversity in reference standards complicates the application of these definitions globally and highlights the need for representative datasets including varied ethnic and geographic backgrounds.

In this context, several authors have evaluated the prevalence of MetS in study populations of children and adolescents using different classification definitions of MetS, and clarifying which cutoff points and reference tables should be followed. Nowadays, the most widely accepted and utilized definition of MetS is the Zimmet et al. (2007) definition (IDF)[19,20], which stipulates that diagnosis is only possible after the age of 10 years. In addition to MetS classification definitions, there are also definitions, such as those proposed by Ahrens et al. (2014) (IDEFICS) and Stravnsbo et al. (2018), that allow the calculation of both global MetS z-scores and z-scores for individual MetS components[21,22], providing robust and comprehensive tools for pediatric research. More detailed information in **Table 1**.

In this study, we used ObMetrics (https://obmetrics.es/), an application developed by a research group of the University of Granada. This app simplifies the calculation, data analysis, and interpretation of Metabolic Syndrome outcomes according to multiple definitions in epidemiological studies of pediatric populations (3-18 years).

Using ObMetrics the prevalence of MetS was estimated in Spanish children of three different cohorts using the definition proposed by Ahrens et al. (2014). Additionally, the individual components of MetS within each cohort have been analysed to evaluate their impact on the overall prevalence of MetS across pediatric populations.

Methods

Study populations

Data from three pediatric Spanish cohorts with different geographical backgrounds were collected. It is important to note that the whole population is a clinical cohort derived from a hospital setting where the prevalence of overweight and obesity is higher than that reported in the general population. Detailed methodologies for sample collection, as well as anthropometric and biochemical measurements, are described in previous publications[23-30]. The anthropometric and metabolic characteristics of all the subjects studied are detailed in **Table 2**.

Definition of Metabolic Syndrome

In this study, the Action Level definition proposed by Ahrens et al. (2014) within the framework of the IDEFICS study was chosen to classify metabolic risk[21]. This decision was based on several relevant criteria related to the population characteristics of the present study.

Firstly, this definition was specifically developed for the European paediatric population. All children included in our cohorts are Caucasian, which aligns with the population characteristics used in the original IDEFICS study, thus supporting the external validity of the results. Secondly, it targets children aged 2 to 10.9 years, a range that closely corresponds to our sample. Additionally, the fact that the population was recruited in a hospital setting justifies the use of the Action Level cut-offs, which are more stringent than population-based monitoring cut-offs and therefore more appropriate for a hospital-based cohort.

Therefore, it has been considered that this definition allows for a standardised and comparable assessment of metabolic risk in Spanish children.

Furthermore, z-score for each component of MetS was calculated based on the reference population from the IDEFICS study. Knowing that a z-score is a statistical measurement that indicates how many standard deviations a value is from the mean of a reference population, it helps to determine whether a value is typical or atypical compared to that reference population.

Use of ObMetrics tool

The ObMetrics web-based application (https://obmetrics.es/) was used to process the anthropometric and biochemical data. This tool automatically classified each participant as having or not having Metabolic Syndrome, according to the selected definition, by applying the appropriate age- and sex-specific thresholds. It was also used to calculate z-scores, allowing for a standardized assessment and comparison of metabolic variables across the pediatric population.

Statistical analysis

All statistical analyses were performed using R Commander version 4.4.0. Categorical variables are presented as both total numbers and percentages, whereas continuous variables are reported as medians with 25th to 75th percentile interquartile ranges. To compare categorical variables, Pearson’s Chi-square or Fisher’s exact tests were used, and the Kruskal-Wallis test was used for numerical variables due to the non-normal distribution of the data. A p-value less than 0.05 was considered statistically significant.

Results

General description of study population

This study included 2,411 participants, of whom 2,373 were selected for inclusion in the data analysis. The remaining 38 were excluded for not meeting the selection criteria **(Table 2)**. In the overall study population, more than 50% of participants were female, accounting for 52.01%. The median (interquartile range) age was 10.55 (8.80, 12.50) years. The median (interquartile range) BMI z-score was 2.14 (0.96, 3.19).

Regarding obesity status according to Cole's criteria, 19.86% of participants had normal weight, 24.73% were classified as overweight, and 55.41% were categorized as having obesity. Based on the Tanner index, 59.22% of the participants were in the prepubertal stage, while 40.78% were in the pubertal stage. When assessing abdominal adiposity using waist circumference, 75.40% of participants showed altered values indicating excess adiposity, whereas 24.60% were within normal ranges.

The median (interquartile range) values for the z-scores of individual metabolic components were as follows: blood pressure, 0.06 (−0.93, 0.56); triglycerides (TAG), 0.63 (0.07, 1.13); HDL-cholesterol (HDL-C), −0.13 (−0.93, 0.56); glucose, −0.34 (−0.96, 0.25); and insulin resistance, 0.74 (−0.20, 1.66). Additionally, the median height z-score was 0.55 (−0.16, 1.26).

Lastly, when analyzing parental educational level, it was observed that 10.89% of the children had parents with a low level of education, including individuals with no formal education, illiteracy, or only primary schooling **(Appendix 1)**. A total of 78.46% had parents with a medium educational level, corresponding to those with secondary education. Finally, 10.65% were classified as having a high educational level, referring to individuals with tertiary education.

General description of the three study cohorts

This study included 2,373 participants across the three cohorts **(Table 3)**. In all three populations, nearly 50% of the children were female, with 49.40% in Córdoba, 52.80% in Santiago de Compostela, and 52.30% in Zaragoza.

The median (interquartile ranges) age was 9.44 (8.10, 10.80) years in the population of Córdoba, 10.87 (8.85, 13.00) in the population of Santiago de Compostela and 10.79 (9.00, 12.80) years in the population of Zaragoza.

The median (interquartile range) BMI z-score was 1.68 (0.01, 3.13) in the population of Córdoba, 2.42 (1.49, 3.27) in the population of Santiago de Compostela, and 1.69 (-0.04, 2.81) in the population of Zaragoza.

In terms of obesity status based on Cole's criteria, the proportion of normal-weight participants was 37.00% in Córdoba, 10.00% in Santiago de Compostela, and 33.30% in Zaragoza. Overweight prevalence was 18.70%, 27.80%, and 21.20%, while obesity prevalence was 43.80%, 62.20%, and 45.50% in each cohort, respectively.

With respect to pubertal development, 90.90% of participants in Córdoba were in the prepubertal stage, compared to 53.00% in Santiago de Compostela and 41.00% in Zaragoza. The pubertal stage was reached by 9.10%, 47.00%, and 59.00% of participants in each cohort, respectively.

For abdominal adiposity (based on waist circumference), 42.00% of the Córdoba participants had normal values, compared to 10.60% in Santiago de Compostela and 38.30% in Zaragoza. The proportion with altered (excess) adiposity was 57.40%, 89.40%, and 61.70%, respectively.

Given the higher prevalence of obesity in the cohort of Santiago compared to the populations of Córdoba and Zaragoza, higher values were observed for all cardiometabolic complications, except for plasma triacylglycerols (TAG), glucose, and insulin resistance, which were higher in the children of Zaragoza.

The median height z-score was 0.42 (−0.37, 1.12) in the population of Córdoba, 0.60 (−0.12, 1.28) in the population of Santiago de Compostela, and 0.56 (−0.13, 1.26) in the population of Zaragoza.

Regarding parental educational level, in the Córdoba population, 45.00% were classified as having a low educational level. A total of 52.50% were classified as having a medium educational level, and 2.50% as having a high educational level. In the Santiago population, 11.60% were classified as having a low educational level, 77.70% as medium, and 10.70% as high. Finally, in the Zaragoza population, 5.80% were classified as having a low educational level, 82.90% as medium, and 11.30% as high.

Differences in MetS prevalence between cohorts

The MetS prevalence was estimated according to the selected definition, with obesity status determined by BMI according to Cole's criteria published by the International Obesity Task Force (IOTF)[31]. **Table 4** presents the MetS prevalence in the three studied populations.

For the population of Córdoba, the prevalence of MetS in children with overweight was 8.70%. On the other hand, the prevalence of MetS in children with obesity was 91.30% . For the population of Santiago de Compostela, the prevalence of MetS in children with overweight was 7.30%. In contrast, the prevalence of MetS in children with obesity was 92.70%. For the population of Zaragoza, the prevalence of MetS in children with overweight was 13.2%. Whereas the prevalence of MetS in children with obesity was 86.80%.

For the population of Córdoba, the prevalence of MetS in female participants was 13.60%. On the other hand, the prevalence of MetS in male participants was 9.80%. For the population of Santiago de Compostela, the prevalence of MetS in female participants was 21.10%. In contrast, the prevalence of MetS in male participants was 17.40%. For the population of Zaragoza the prevalence of MetS in female participants was 17.40%, and the prevalence of MetS in male participants was 20.50%.

For the population of Córdoba, the prevalence of MetS in prepubertal stage children was 11.30%. Whereas the prevalence of MetS in pubertal stage children was 37.50%. For the population of Santiago de Compostela, the prevalence of MetS in prepubertal stage children was 18.30%. In contrast, the prevalence of MetS in pubertal stage children was 27.60%. Finally, for the population of Zaragoza, the prevalence of MetS in prepubertal stage children was 14.10%. On the other hand, the prevalence of MetS in pubertal stage children was 30.00%.

When BMI z-score was analysed across the three cohorts, stratified by obesity status (**Table 5**), significant differences were observed. Among children with normal weight, the median BMI z-score was -0.28 (-0.67, 0.13) in Córdoba, -0.16 (-0.59, 0.27) in Santiago, and -0.42 (-0.78, -0.05) in Zaragoza. Among children classified as overweight, the median BMI z-score was 1.11 (0.80, 1.37) in Córdoba, 1.44 (1.13, 1.75) in Santiago, and 1.34 (1.10, 1.68) in Zaragoza. And among children with obesity, the median BMI z-score was 3.59 (2.54, 4.31) in Córdoba, 3.28 (2.48, 3.73) in Santiago, and 3.40 (2.46, 3.86) in Zaragoza.

Overall, the prevalence of MetS was predominantly higher in children with obesity than in children with overweight, when the same MetS definition was used. Additionally, the prevalence of MetS increased as Tanner index increased in all three cohorts.

Discussion

The results of this study show a high prevalence of MetS among patients with obesity across the three Spanish cohorts. Using the Action Level definition by Ahrens et al. from the IDEFICS study, more than 85% of children with obesity were classified as having MetS in all populations, highlighting the serious impact that childhood obesity has on metabolic health.

In relation to the differences in the prevalence of MetS by sex, no significant differences were found between the cohorts. In Córdoba and Santiago, prevalence was higher in females, while in Zaragoza, MetS prevalence was higher in males. Although some previous literature has suggested a greater cardiometabolic risk in males, particularly during adolescence, the current data do not provide sufficient evidence to draw firm conclusions[32].

A clear increase in the prevalence of Metabolic Syndrome (MetS) during puberty has been observed. For example, in Córdoba, the prevalence increased significantly from 11.3% in prepubertal children to 37.5% in pubertal children. This trend is similar in Santiago de Compostela and Zaragoza. This increase may be attributed to physiological changes that take place during puberty, such as body fat redistribution and hormonal fluctuations. This, also could be related to the fact that childhood obesity is a factor that causes earlier puberty, as explained in previous studies[33]. Therefore, these findings show that puberty is an important stage when metabolic problems can start to appear in children. Geographical variability was also evident. Santiago de Compostela presented the highest proportion of children with obesity (62.2%) and one of the highest MetS prevalence rates (92.7%) among children with obesity. Although the Córdoba cohort included a younger, predominantly prepubertal population, the prevalence of MetS in children with obesity was high (91.3%).

Also, it should be noted that none of the children with a normal weight were diagnosed with Metabolic Syndrome. Another interesting result is that overweight children in Zaragoza have a higher prevalence of MetS compared to overweight children in the other regions. However, when we look at the average BMI z-scores in overweight children, the values are higher in Santiago than in Zaragoza. This is a relevant observation because it shows that weight

and metabolic health are not always directly connected. A higher BMI does not necessarily correlate with a worse metabolic profile, suggesting that BMI alone may not be a sufficient indicator of a child's health, especially because it does not consider body composition differences. Moreover, a possible reason for the higher prevalence of metabolic disorders among overweight children in Córdoba, even though having a lower average BMI, could be their lower socioeconomic status.

Parental education level appeared to be a potential socioeconomic indicator linked to MetS risk. In Córdoba, where 45% of parents had a low educational level (the highest prevalence among the three cohorts), the prevalence of obesity and MetS was notably high. This observation supports existing evidence between lower parental education and socioeconomic status with higher risk of childhood obesity and metabolic issues[34].

These regional differences may reflect differences in dietary habits, levels of physical activity, or access to healthcare services, suggesting that local environmental and socioeconomic factors could affect children’s metabolic health.

Conclusion

In conclusion, this study confirms that Metabolic Syndrome is very common among children with obesity in a hospital population in Spain. Notable differences were found by region, pubertal status, and socioeconomic background, suggesting that biological and contextual factors contribute to metabolic risk. These findings underscore the need to implement screening and intervention programs, to prevent the impact of metabolic disease in adult life.

Table 1. Definitions proposed for the metabolic syndrome classification and z-scores in children and adolescents

Metabolic syndrome classification								
			Components of metabolic syndrome					
Definitions	**Study population**	**Age range**	**Excess adiposity**	**Blood pressure**	**Triacylglycerols**	**HDL-C**	**Glucose**	**Insulin resistance**
Cook *et al.* (2003) (NCEP ATP III)	White, Black, and Mexican American 12-19 years old (N = 2420, NHANES III, 1988-1994)	2-18 years old	WC ≥ 90th percentile (age, sex and ethnic-specific, NHANES III)	SBP or DBP ≥ 90th percentile (age, sex and height percentile specific, NHBPEP)	TAG ≥ 110 mg/dL (NCEP)	HDL-C ≤ 40 mg/dL (NCEP)	Glucose ≥ 110 mg/dL (ADA)	Insulin resistance is not considered
de Ferranti *et al.* (2004)	White, Black, and Mexican American 12-19 years old (N = 1960, NHANES III, 1988-1994)	2-18 years old	WC ≥ 75th percentile (age, sex and ethnic-specific, NHANES III)	SBP ≥ 90th percentile (age, sex and height percentile specific NHBPEP)	TAG ≥ 100 mg/dL (NCEP)	HDL-C ≤ 50 and ≤ 45 mg/dL for age <15 and ≥ 15 respectively	Glucose ≥ 110 mg/dL	Insulin resistance is not considered
Ford *et al.* (2005)	White, Black, and Mexican American 12-17 years old (N = 1370, NHANES, 1999-2000)	2-18 years old	WC ≥ 90th percentile (age, sex and ethnic specific, NHANES III)	SBP or DBP ≥ 90th percentile (age, sex and height percentile specific, NHBPEP)	TAG ≥ 110 mg/dL (NCEP)	HDL-C ≤ 40 mg/dL (NCEP)	Glucose ≥ 100 mg/dL	Insulin resistance is not considered
Viner *et al.* (2005)	White, Black, South Asian, and other or mixed ethnicity 2-18 years old (N = 103, everyone with obesity)	2-18 years old	BMI ≥ 95th percentile (Cole *et al.* 2000)	SBP ≥ 95th percentile (age, sex and height percentile specific, NHBPEP)	TAG ≥ 150 mg/dL	HDL-C ≤ 35 mg/dL	Glucose ≥ 110 mg/dL or Insulin ≥ 15 µUI/ml ≥ 30 µUI/ml and ≥ 20 µUI/ml for pre-, mid- and postpubertal children, respectively.	
Zimmet *et al.* (2007) (IDF)	It was a report.	10-18 years old	WC ≥ 90th percentile or adult cutoff-points if lower (age ≤ 16, sex and ethnic-specific, NHANES III) and adult cutoff-points (age > 16, sex and ethnic-specific)	SBP or DBP ≥ 130 or 85 mmHg	TAG ≥ 150 mg/dL (NCEP)	HDL-C ≤ 40 mg/dL (age ≥ 16, NCEP) and HDL-C ≤ 40 mg/dL in males and 50 mg/dL in females (age ≥ 17, NCEP)	Glucose ≥ 100 mg/dL (ADA)	Insulin resistance is not considered
Olza *et al.* (2011)	White European (Spanish) 5-10.9 years old N=930	4-18 years old	BMI ≥ 95th percentile (Cole *et al.* 2000) (2-18 years old)	SBP or DBP ≥ 90th percentile (age, sex and height percentile specific, NHBPEP) (2-18 years old)	TAG ≥ 90th percentile (age and sex specific, NCEP) (0-19 years old)	HDL-C ≤ 10th percentile (age and sex specific) (4-19 years old)	Glucose ≥ 100 mg/dL	HOMA-IR ≥ 2.5 and ≥ 5.38 for prepubertal (Tanner I) and pubertal children (Tanner II-IV)
Ahrens *et al.* (2014) (IDEFICS study, monitoring/action level)	European 2-10.9 years old (N=18745, IDEFICS)	3-10 years old	WC ≥ 90th/95th percentile (age and sex specific, IDEFICS)[23]	SBP or DBP ≥ 90th/95th percentile (age, height and sex specific, IDEFICS)[23]	TAG ≥ 90th/95th percentile / HDL-C ≤ 10th/05th percentile (age and sex specific, IDEFICS)[23]		Glucose/HOMA-IR ≥ 90th percentile or (age and sex specific, IDEFICS)[23]	
Metabolic syndrome z-scores								
Ahrens *et al.* (2014) (IDEFICS study)	European 2-10.9 years old (N=18745, IDEFICS)	3-10 years old	WC z-score	BP z-score	Lipid z-score		HOMA-IR z-score	
Stravnsbo *et al.* (2018)	European (Denmark, Estonia, Portugal, Switzerland) and United States 6-18 years old (N = 22479, EYHS, CoSCIS, PANCS, KISS and NHANES studies)	6-18 years old	WC z-score	BP z-score	Lipid z-score		HOMA-IR z-score	

Table 2. Anthropometric and metabolic characteristics of the study population

Whole population (ages 3-18)	
Variable	**(N = 2,373) a**
Sex	
Female	1234 (52.01%)
Male	1139 (47.99%)
Age (years)	10.55 (8.80, 12.50)
Obesity Status (Cole)	
Normal weight	470 (19.86%)
Overweight	585 (24.73%)
Obesity	1311 (55.41%)
Tanner Index	
Prepubertal	1403 (59.22)
Pubertal	966 (40.78)
Excess adiposity (WC)	
Normal	325 (24.60)
Altered	996 (75.40)
Z-scores components	
Blood pressure	0.06 (-0.93, 0.56)
TAG	0.63 (0.07, 1.13)
HDL-C	-0.13 (-0.93, 0.56)
Glucose	-0.34 (-0.96, 0.25)
Insulin resistance	0.74 (-0.20, 1.66)
BMI z-score	2.14 (0.96, 3.19)
Height z-score	0.55 (-0.16, 1.26)
Parental Education Level	
Low	134 (10.89%)
Medium	965 (78.46%)
High	131 (10.65%)

a n (%); Median (IQR). Abbreviations: TAG, Triacylglycerols; HDL-C, High-Density Lipoprotein-Cholesterol; BMI, Body Mass Index.

Table 3. Anthropometric and metabolic characteristics of the three study cohorts

	Whole population (N = 2,373)			
Variable	**Córdoba (N = 514) a**	**Santiago de Compostela (N = 1,463) a**	**Zaragoza (N = 396) a**	**p-value b**
Sex				0.4072
Female	254 (49.40%)	773 (52.80%)	207 (52.30%)	
Male	260 (50.60%)	690 (47.20%)	189 (47.70%)	
Age (years)	9.44 (8.10, 10.80)	10.87 (8.85, 13.00)	10.79 (9.00, 12.80)	<2.2e-16
Obesity Status (Cole)				<2.2e-16
Normal weight	193 (37.00)	145 (10.00%)	132 (33.30%)	
Overweight	96 (18.70%)	405 (27.80%)	84 (21.20%)	
Obesity	225 (43.80%)	906 (62.20%)	180 (45.50%)	
Tanner Index				<2.2e-16
Prepubertal	467 (90.90%)	774 (53.00%)	162 (41.00%)	
Pubertal	47 (9.10%)	686 (47.00%)	233 (59.00%)	
Excess adiposity (WC)				<2.2e-16
Normal	170 (42.00%)	76 (10.60%)	79 (38.3%)	
Altered	229 (57.40%)	640 (89.40%)	127 (61.70%)	
Components z-scores				
Blood pressure	-0.09 (-0.93, 0.75)	0.16 (-0.44, 0.75)	0.01 (-0.65, 0.69)	0.0001074
TAG	0.59 (0.09, 1.03)	0.62 (0.04, 1.18)	0.71 (0.13, 1.20)	0.4883
HDL-C	0.22 (-0.49, 0.86)	-0.41 (-1.12, 0.21)	0.17 (-0.63, 0.93)	<2.2e-16
Glucose	-0.47 (-1.00, 0.01)	-0.40 (-1.04, 0.23)	0.11 (-0.47, 0.56)	2.121e-15
Insulin resistance	0.40 (-0.40-1.15)	0.86 (0.04, 1.76)	0.98 (-0.02, 1.95)	1.743e-14
BMI z-score	1.68 (0.01, 3.13)	2.42 (1.49, 3.27)	1.69 (-0.04, 2.81)	<2.2e-16
Height z-score	0.42 (-0.37, 1.12)	0.60 (-0.12, 1.28)	0,.56 (-0,13, 1.26)	0.007607
Parental Education Level				4.093e-12
Low	18 (45.00%)	94 (11.60%)	22 (5.80%)	
Medium	21 (52.50%)	629 (77.70%)	315 (82.90%)	
High	1 (2.50%)	87 (10.70%)	43 (11.30%)	

a n (%); Median (IQR). b Pearson's Chi-squared test; Kruskal-Wallis chi-squared. Abbreviations: TAG, Triacylglycerols; HDL-C, High-Density Lipoprotein-Cholesterol; BMI, Body Mass Index.

Table 4. Prevalence of metabolic syndrome in study populations

Whole population (ages 3-18) Ahrens *et al.* (IDEFICS study, action level)									
Variable	**Córdoba (N = 514)**			**Santiago de Compostela (N = 1,463)**			**Zaragoza (N = 396)**		
	No MetS a (N = 344)	**Yes MetS a (N = 46)**	**p-value b**	**No MetS a (N = 566)**	**Yes MetS a (N = 137)**	**p-value b**	**No MetS a (N = 165)**	**Yes MetS a (N = 38)**	**p-value b**
Sex			0.2443			0.1807			0.3387
Female	178 (86.40%)	28 (13.60%)		310 (78.90%)	83 (21.10%)		95 (82.60%)	20 (17.40%)	
Male	166 (90.20%)	18 (9.80%)		256 (82.60%)	54 (17.40%)		70 (79.50%)	18 (20.50%)	
Obesity Status (Cole)			3.571e-12			4.536e-12			0.002053
Normal weight	152 (44.20%)	0 (0.00%)		70 (12.40%)	0 (0.00%)		72 (43.60%)	0 (0.00%)	
Overweight	69 (20.10%)	4 (8.70%)		152 (26.90%)	10 (7.30%)		34 (20.60%)	5 (13.2%)	
Obesity	123 (35.80%)	42 (91.30%)		344 (60.80%)	127 (92.70%)		59 (35.80%)	33 (86.80%)	
Tanner Index			0.02275			0.1452			0.3084
Prepubertal	339 (88.70%)	43 (11.3%)		503 (81.70%)	113 (18.30%)		122 (85.90%)	20 (14.10%)	
Pubertal	5 (62.50%)	3 (37.5%)		63 (72.40%)	24 (27.60%)		42 (70.00%)	18 (30.00%)	

a n (%); Median (IQR). b Pearson's Chi-squared test; Kruskal-Wallis chi-squared.

Table 5. BMI z-score distribution by obesity status in the three study cohorts

Whole population (N = 2,373)				
	BMI z-score			
	Córdoba (N = 514) a	**Santiago de Compostela (N = 1,463) a**	**Zaragoza (N = 396) a**	**p-value b**
Obesity Status (Cole)				0.00001135
Normal weight	-0.28 (0.67,013)	-0.16 (-0.59, 0.27)	-0.42 (-0.78, -0.05)	
Overweight	1.11 (0.80, 1.37)	1.44 (1.13, 1.75)	1.34 (0.10, 1.68)	
Obesity	3.59 (2.54, 4.31)	3.28 (2.48, 3.73)	3.40 (2.46, 3.86)	

a Median (IQR). b ANOVA.

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Appendix 1: Classification of Parental Educational Levels

¿Qué estudios ha realizado el **padre** del niño/a?	¿Qué estudios ha realizado la **madre** del niño/a?
☐1 Sin estudios	☐1 Sin estudios
☐2 No sabe leer o escribir	☐2 No sabe leer o escribir
☐3 Estudios de 1º Grado (Estudios primarios, EGB hasta 5º)	☐3 Estudios de 1º Grado (Estudios primarios, EGB hasta 5º)
☐4 Estudios de 2º Grado, primer ciclo (Graduado escolar, EGB hasta 8º, Bachiller elemental)	☐4 Estudios de 2º Grado, primer ciclo (Graduado escolar, EGB hasta 8º, Bachiller elemental)
☐5 Estudios de 2º grado, segundo ciclo (Bachiller Superior, FP, BUP, Aprendizaje y Maestría industrial, COU)	☐5 Estudios de 2º grado, segundo ciclo (Bachiller Superior, FP, BUP, Aprendizaje y Maestría industrial, COU)
☐6 Estudios de 3º grado, primer ciclo (Perito, Ingeniero técnico, Escuelas Universitarias, Magisterio)	☐6 Estudios de 3º grado, primer ciclo (Perito, Ingeniero técnico, Escuelas Universitarias, Magisterio)
☐7 Estudios de 3º grado, segundo y tercer ciclo (Ingeniero superior, Licenciado, Doctorado, Master)	☐7 Estudios de 3º grado, segundo y tercer ciclo (Ingeniero superior, Licenciado, Doctorado, Master)
☐98 NS/NC	☐98 NS/NC