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Prevalence of metabolic syndrome among adolescents in a city in the Mediterranean area: comparison of two definitions

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Abstract

Background and objective: **there are few studies on the prevalence of metabolic syndrome (MetS) in European adolescent populations, and some have reported a higher prevalence in the Mediterranean basin area. Our objective was to examine the prevalence of MetS in adolescents in a Mediterranean city of Spain, comparing two different definitions of MetS and the associated risk factors.**

Methods and results: **a cross-sectional population-based study was conducted among 379 adolescents aged 12-16.9 years, selected using a random sampling method. Anthropometric measurements and fasting blood samples were obtained. The definitions of MetS used were that of the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATPIII) and that of the International Diabetes Federation (IDF). *Kappa* coefficient was used to measure the agreement between definitions and a multivariate logistic regression model to determine the associated risk factors.**

Results: **the prevalence of MetS was 5.7% (95%CI 3.33-8.07) according to the NCEP-ATPIII definition and 3.8% (95%CI 1.85-5.75) according to the IDF definition. No differences between the sexes or by age groups were found. The agreement between the two definitions was very good (*kappa* 0.815), especially in the obese subsample, but was lower in normal weight adolescents (*kappa* 0.497). Insulin resistance and obesity were associated with both definitions.**

Conclusions: **the prevalence of MetS in our adolescent population is higher than the European media. Although the overall agreement between both definitions was very good, the prevalence was higher using the NCEP-ATPIII criteria. Independently of the definition used, obesity and insulin resistance were risk factors for MetS.**

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Key words: *Metabolic syndrome*. *Prevalence*. *Adolescent*. *Metabolic syndrome definition*. *Insulin resistance*.

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PREVALENCIA DE SÍNDROME METABÓLICO EN LA POBLACIÓN GENERAL ADOLESCENTE DE UNA CIUDAD DEL ÁREA MEDITERRÁNEA: COMPARACIÓN DE DOS DEFINICIONES

Resumen

Introducción y objetivos: **existen escasos estudios acerca de la prevalencia de síndrome metabólico (MetS) en la población general adolescente en Europa. Algunos resultados muestran mayor prevalencia en adolescentes del área mediterránea. Nuestro objetivo fue estudiar la prevalencia de MetS en la población general adolescente de una ciudad del área mediterránea en España, comparando dos definiciones de MetS y los factores de riesgo asociados.**

Material y métodos: **estudio epidemiológico observacional sobre una muestra de base poblacional, elegida de forma aleatoria, representativa de los adolescentes de 12 a 16,9 años escolarizados en la ciudad de Almería. Se recogieron variables antropométricas y analíticas. Se compararon dos definiciones de SM para población adolescente: *National Cholesterol Education Program* (NECP-ATPIII) e *International Diabetes Federation* (IDF). *Estadística:* coeficiente *kappa* para analizar la concordancia entre definiciones y regresión logística múltiple para el estudio de factores de riesgo asociados.**

Resultados: **la prevalencia de MetS fue 5,7% (95%IC 3,33-8,07) con la definición NECP-ATPIII y 3,8% (95%IC 1,85-5,75) con los criterios IDF. No se encontraron diferencias entre sexos ni entre grupos de edad. La concordancia entre ambas definiciones fue muy buena a nivel global (*kappa* 0,815) y especialmente en el grupo de obesos, pero empeoró entre adolescentes con normopeso (*kappa* 0,497). Los factores asociados a ambas definiciones fueron obesidad y resistencia insulínica.**

Conclusiones: **nuestros resultados muestran una prevalencia de MetS en adolescentes mayor a la media europea. Aunque la concordancia entre definiciones fue muy buena a nivel global, la prevalencia fue mayor con la definición NECP-ATPIII. Obesidad y resistencia insulínica fueron los factores de riesgo asociados.**

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Palabras clave: *Síndrome metabólico*. *Prevalencia*. *Adolescente*. *Definición de síndrome metabólico*. *Insulinorresistencia*.

Abbreviations

BMI: body mass index
ESeC: The European Socioeconomic Classification
HDL: high-density lipoproteins
HOMA-IR: Homeostasis Model Assessment of Insulin Resitance
IDF: International Diabetes Federation
IOTF: International Obesity Task Force
IR: insulin resistance
LDL: low-density lipoproteins
MetS: metabolic syndrome
NCEP-ATPIII: National Cholesterol Education Program's Adult Treatment Panel III
TG: triglycerides
95%CI: Confidence Interval at 95%

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Introduction

Metabolic syndrome (MetS) is a cluster of cardiovascular risk factors secondary to an inflammatory and insulin resistance state that increases the risk of cardiovascular disease and type 2 diabetes mellitus in adulthood[1-3]. In Europe, few population-based studies have been performed on the prevalence of MetS among adolescents[4-6], but in recent years some studies have reported a higher prevalence of MetS in the Mediterranean basin, in comparison with published average levels for Europe. This prevalence reaches levels between 5.8% and 8% depending on the definition used[7,8].

MetS is strongly related to obesity, and its prevalence in SE Spain and Mediterranean area is higher than in Spain as a whole and than the European average[9,10]. In this area, the prevalence of Mets in the adulthood is higher than the Spanish figures[11] and, in addition, levels of glucose and triglycerides are higher among schoolchildren, in comparison with other Spanish provinces[12].

The purpose of this study is to examine the prevalence of obesity and MetS among adolescents in Almería, a Mediterranean city for which there are no previous data in this respect, applying and comparing the two most frequently definitions of MetS used for adolescents and considering the risk factors associated with each definition.

Material and methods

This observational epidemiological study was conducted on a population-based representative sample of adolescents aged 12-16.9 years in the city of Almería (SE Spain), selected by multistage probabilistic sampling. In the first stage of the study, six schools were selected, using a table of random numbers. In the second stage, three different classes from each of the grades were randomly selected. Criteria for inclusion were: resident in Almería city, aged 12-16.9 years, with informed consent from parents or legal guardians as well as from the participants themselves. Any subject with a chronic endocrine or systemic disease that, due to the disorder itself or to its treatment, might affect the test results was excluded. The participation rate was 81.6%.

The field research was implemented between January and June 2008, and all actions complied with the stipulations of the 1975 Helsinki Declaration, were approved by the Research and Ethics Committee of Torrecárdenas Hospital (Almería).

A complete physical examination was conducted, anthropometric measurements were obtained (weight, height and waist circumference) and blood pressure measurements were obtained using calibrated equipment and following standard methods. Tables by Moreno *et al.*[13,14] were used to compare the waist circumference with the reference population and to carry out the standard score (z-score) calculation. The body mass index (BMI) was calculated by dividing weight by height squared (kg/cm^2). Overweight and obesity were determined based on the internationally accepted thresholds of BMI for sex and age as published by the International Obesity Task Force[15]. Systolic or diastolic prehypertension and hypertension was defined above the 90^{th} age-, sex- and height-specific percentiles based on the 2004 Task Force Report templates[16]. The interviewers and researchers were physicians who had previously completed a training and standardisation programme. Concordance among researchers was assessed, and a concordance correlation coefficient of between 0.83 and 0.90 was obtained.

The subjects' parents were asked about the family background, including parent obesity and type 2 diabetes prevalence, and socioeconomic level. The European Socioeconomic Classification (ESeC) (17) was used to classify the socioeconomic level.

The analytical determinations were performed after night fasting. Plasmatic glucose, high-density lipoproteins (HDL cholesterol), low-density lipoproteins (LDL cholesterol) and triglycerides (TG) were measured using a Cobas® c-501 analyser (Roche Diagnostics, Basel, Switzerland). Insulin was determined by an in vitro immunological test (Sandwich ELISA) using a Cobas® c-601 analyser (Roche Diagnostics, Basel, Switzerland). The insulin resistance index (HOMA-IR) was calculated as the product of fasting insulinaemia (uU/ml) and fasting glucose (mg/dl) divided by 405.

In the absence of a universally accepted criteria for adolescents, two different definitions of MetS were used and subsequently compared. The election of these two definitions was based on its widely used in previously published studies in adolescents[5,6,7,18]:

The definition by the National Cholesterol Education Program Program's Adult Treatment Panel III (NCEP-ATPIII) revised by Cook /Ford[19,20]. According to this definition, a diagnosis of MetS is made when three of the following five risk factors are present: waist circumference ≥ p90 according to age and sex, fasting glucose ≥ 100 mg/dl, TG ≥ 110 mg/dl, HDL-COL < 40 mg/dl, systolic or diastolic blood pressure ≥ p90 according to age, sex and height.

According to the definition offered by the International Diabetes Federation (IDF)[21] for children and adolescents, MetS can be diagnosed when the individual presents abdominal obesity defined as waist circumference ≥ p90, plus two of the following criteria: fasting plasma glucose ≥ 100 mg/dl or previous diagnosis of diabetes mellitus type 2, TG ≥ 150 mg/dl, HDL-COL < 40 mg/dl, systolic blood pressure ≥ 130 mmHg, or diastolic blood pressure ≥ 85 mmHg.

Statistical Methods

Sample size calculation: a total of 9823 adolescents aged 12-16.9 years attending one of the 38 secondary schools in Almería were eligible to participate. The sample size was calculated with an assumed MetS prevalence rate of 10%[19], a 95% confidence interval and 4% precision, applying a design effect of 1.5. A 15% extra was considered in order to offset possible losses. Finally, a total of 366 subjects were required.

The qualitative variables were expressed as percentages with confidence intervals (95%CI), and group differences were evaluated by the *Chi-square* test. The quantitative data were described by the mean and the standard deviation. The *Kolmogorov-Smirnov* test was used to examine whether the analytical variables were normally distributed. *Student's t-test* was applied to compare means. The degree of concordance between the definitions of MetS was assessed by the *Kappa* (κ) coefficient. Multiple and binary logistic regression analysis was used to study the association of dependent variables (MetS definitions by NCEP-ATPIII and IDF) and independent variables. The multiple logistic regression models showed there was no collinearity between the independent variables, using the variable inflation factor and studying goodness of fit by the *Hosmer-Lemeshow* test. In all cases, a *p*-value of less than 0.05 ($p<0.05$) was considered to be significant. Epidat 3.0 software was used for the sample calculation and SPSS 15.0 program for the statistical analysis.

Results

379 adolescents were included, 58.05% were males. Medium age was 14.08 (95%CI 13.95-14.21) years. Clinical and analytical characteristics of the sample population are described in table I. There were no significant differences in the prevalence of overweight and obesity between sexes. Females presented higher z-scores of waist circumference but there were no significant differences in the prevalence of abdominal obesity (p 0.08). Males presented higher levels of systolic blood pressure and fasting glucose than females

Table I
Clinical and analytical characteristics of the sample population by sex

Variable	*Total (95% CI)*	*Females (95% CI)*	*Males (95% CI)*	*p-value*
Age (years)	14.08 (13.95 – 14.21)	14.13 (13.93 – 14.33)	14.04 (13.87 – 14.21)	0.495
Waist circumference (Z-score)	1.03 (0.86 – 1.19)	1.36 (1.09 – 1.62)	0.79 (0.57 – 1.01)	0.001
Systolic blood pressure (mmHg)	118.15 (117.05 – 119.25)	114.58 (112.57 – 116.59)	120.89 (119.13 – 122.65)	<0.001
Diastolic blood pressure (mmHg)	62.87 (62.03 – 63.71)	63.48 (62.22 – 64.74)	62.40 (61.28 – 63.52)	0.214
Blood glucose level (mg/dl)	83.59 (82.68 – 84.50)	81.77 (80.48 – 83.06)	84.92 (83.68 – 86.16)	<0.001
HDL-Cholesterol (mg/dl)	54.86 (53.60 – 56.12)	57.11 (55.29 – 58.93)	53.21 (51.52 – 54.90)	0.003
LDL-Cholesterol (mg/dl)	81.01 (78.95 – 83.07)	80.09 (76.76 – 83.42)	81.68 (79.07 – 84.29)	0.454
Triglycerides (mg/dl)	72.32 (69.05 – 75.59)	71.29 (66.91 – 75.67)	73.08 (69.12 – 78.48)	0.596
HOMA-IR	2.06 (1.90 – 2.22)	2.19 (1.97 – 2.41)	1.97 (1.75 – 2.19)	0.164
Prevalence of abdominal obesity	19.5% (17.53 – 21.47)	24.1% (19,76 – 28,44)	16.7% (12.91 – 20.49)	0.080
Prevalence of overweight	21.3% (17.16 – 25.44)	18.3% (14.41 – 22.19)	23.6% (19.32 – 27.88)	0.209
Prevalence of obesity	8% (5.25 – 10.75)	5.7% (3.37 – 8.03)	9.7% (6.72 – 12.68)	0.152

BMI: Body Mass Index; Z-score: standard score; HDL: high-density lipoproteins; LDL: low-density lipoproteins; HOMA-IR: Homeostasis Model Assessment of Insulin Resitance; 95%CI: Confidence Interval at 95%; p-value: significance level.

(p<0.001). In contrast, HDL-Cholesterol levels were higher in females (p 0.003).

The global prevalence of MetS was 5.7% (95%CI 3.33-8.07) according to the modified NCEP-ATPIII definition, and 3.8% (95%CI 1.85-5.75) according to the IDF definition for adolescents. 45.5% of the adolescents presented at least one criteria of the NCEP-II-IIII definition, and 40.2% presented at least one criteria of the IDF definition. Abdominal obesity was the most frequent component in both definitions (19.5%).

There was no significant difference in the prevalence of MetS by sex or age groups. MetS was more prevalent among obese and overweight adolescents regardless of the definition applied. There was a very good overall concordance between the two definitions (κ=0.815). These agreement remains good in the analysis by sex, age, and in obese and overweight individuals, although the concordance fell to moderate (κ=0.497) with respect to normal-weight patients (Table II).

In the binary logistic regression analysis, both definitions were associated with obesity and higher values of HOMA-IR. These associations persisted in the multiple logistic regression analysis. Sex, age, socioeconomic level of the parents and family records of obesity and diabetes mellitus were not associated with neither of the two definitions (Tables III and IV).

Discussion

The prevalence of MetS in adolescents in our study was 5.7% according to the modified NCEP-ATPIII definition, and 3.8% according to the IDF definition. This prevalence is higher than has been observed in studies carried out in Central and Northern Europe. Thus, in Finnish adolescents the MetS prevalence was 2.1% with the NECP-ATP III definition and 2.4% with the IDF criteria[5]. In a multicentre study among adolescents aged 15 years from Denmark, Estonia and Portugal[6], the global prevalence, according to the IDF definition, was 1.4%. Nevertheless, our results are in agreement with studies in the Mediterranean basin, that reveal a higher prevalence in the latter area than the European average[7,8,22]. The prevalence of MetS observed in our study is similar to the 5.8% recorded for adolescents in the Balearic Islands (Spain), using NCEP-ATPIII definition[7], although it is still lower than the 8% observed in Greek adolescents using the IDF definition[8]. Theses geographic differences can be explained, partly, by the differences in the obesity prevalence. Thus, the North-South gradient in the obesity prevalence described in Europe[9,10,23,24] could explain the differences with Central and Northern Europe studies. Our results confirm the higher prevalence of obesity and overweight among adolescents. Obesity is known to be a risk factor for MetS both in adolescence and adulthood[4,5,7,19,25-27] and this is also confirmed by the results reported here. Other factors, like differences in dietary patterns or physical activity between countries has been described as possible explanations[28,29].

Regarding the differences between both definitions, IDF definition showed a lower prevalence of MetS than the NCEP-ATPIII criteria. These results are consistent with previous data[22,30]. Thus, Noto *et al.* obtained a MetS prevalence of 5.2% with the NCEP-ATPIII

Table II
Prevalence of metabolic syndrome and concordance between the two definitions

	NCEP-ATPIII (95% CI)	*IDF (95% CI)*	*Kappa*
TOTAL	5.7% (3.33-8.07)	3.8% (1.85-5.75)	0.815
SEX			
Females	3.2% (1.4-5.0)	1.9% (0.51-3.29)	0.774
Males	7.6% (4.89-10.31)	5.2% (2.93-7.47)	0.836
p-value	0.072	0.105	
AGE			
12-14.9 years old	5% (2.77-7.23)	3.6% (1.7-5.5)	0.835
15-16.9 years old	6.7% (4.15-9.25)	4% (2.0-6.0)	0.790
p-value	0.51	0.857	
BMI			
Normal weight	1.5% (0.26-2.74)	0.4% (0.24-1.04)	0.497
Overweight	12.0% (8.68-15.32)	7.8% (5.06-10.54)	0.688
Obesity	28.6% (23.98-33.22)	28.6% (23.98-33.22)	1
p-value	<0.001	<0.001	

BMI: Body Mass Index; 95%CI: Confidence Interval at 95%; *Kappa*: *kappa* coefficient; p-value: significance level.

Table III
Adjusted and unadjusted odds ratio of the different risk factors by the NCEP/ATPIII definition

	UNADJUSTED OR (95% CI)	*p-value*	*ADJUSTED OR (95% CI)*	*p-value*
Male	2.33 (0.83 – 6.54)	0.081	3.31 (0.38 – 28.91)	0.278
Age	1.08 (0.77 – 1.53)	0.644	1.06 (0.55 – 2.06)	0.864
Obesity (IOTF)	10.83 (3.98 – 29.51)	<0.001	6.27 (0.51 – 76.76)	0.015
HOMA-IR	2.42 (1.73 – 3.39)	<0.001	2.58 (1.46 – 4.57)	0.001
Father low socioeconomic level (Class 3)	1.10 (0.38 – 3.17)	0.860	1.45 (0.16 – 13.10)	0.741
Mother low socioeconomic level (Class 3)	1.12 (0.25 – 4.92)	0.881	2.59 (0.28 – 23.72)	0.399
Family history of obesity	0.49 (0.06 – 3.98)	0.510	0.08 (0.01 – 19.34)	0.368
Family history of type 2 diabetes	1.76 (0.21 – 14.91)	0.603	5.97 (0.03 – 10.41)	0.5

Hosmer-Lemeshow test: Chi2=7.403, p=0.494.
BMI: Body Mass Index; IOTF: International Obesity Task Force; HOMA-IR: Homeostasis Model Assessment of Insulin Resitance; 95%CI: Confidence Interval at 95%; p-value: significance level.

Table IV
Adjusted and unadjusted odds ratio of the different risk factors by the IDF definition

	UNADJUSTED OR (95% CI)	*p-value*	*ADJUSTED OR (95% CI)*	*p-value*
Male	2.79 (0.77 – 10.19)	0.119	2.85 (0.06 – 14.27)	0.6
Age	1.02 (0.68 – 1.54)	0.907	1.51 (0.56 – 4.02)	0.418
Obesity (IOTF)	22.27 (7.05 – 70.37)	<0,001	75.97 (2.41 – 239.92)	0.014
HOMA-IR	2.67 (1.75 – 4.06)	<0,001	2.16 (1.17 – 3.97)	0.013
Father low socioeconomic level (Class 3)	0.99 (0.27 – 3.66)	0.994	1.07 (0.03 – 40.01)	0.97
Mother low socioeconomic level (Class 3)	0.43 (0.07 – 2.67)	0.364	0.37 (0.05 – 26.58)	0.652
Family history of obesity	0.74 (0.13 – 4.22)	0.735	0.18 (0.02 – 21.43)	0.484
Family history of type 2 diabetes	3.18 (0.36 – 28.2)	0.299	7.63 (0.15 – 39.03)	0.215

Hosmer-Lemeshow test: Chi2=13.18, p=0.106.
BMI: Body Mass Index; IOTF: International Obesity Task Force; HOMA-IR: Homeostasis Model Assessment of Insulin Resitance; 95%CI: Confidence Interval at 95%; p-value: significance level.

definition but only 0.9% with the IDF one in males aged 13-14 years living in the Mediterranean area[22]. This disparity may be explained by two main factors. First, IDF paediatric definition maintains the elevated triglyceride and high blood pressure thresholds used in the IDF adult definition. Therefore, this approach has been questioned[31]. Second, the IDF paediatric definition requires the presence of abdominal obesity as an essential criterion for diagnosis. For this reason, a lower prevalence was observed among normal-weight adolescents, resulting in a lower concordance in this subgroup than that for overweight and obese individuals. This observation coincides with the conclusions of other studies in which no differences were found between the two definitions with respect to MetS among obese adolescents[32,33].

Although these differences in the prevalence figures, both definitions showed a very good overall agreement and they were independently associated with the increased estimates of the HOMA index. High values of the latter index has shown an evident association with MetS both among the general population and among obese adolescents[26,34]. These results reflect the key role that insulin resistance plays in the development of the anomalies associated with MetS.

There was no difference by sex, although males showed a higher trend to present MetS. In general terms, studies conducted on adolescent populations have confirmed this trend[18,20], and in some cases the differences were statistically significant[7]. In spite of the absence of differences in the prevalence of MetS by sex, males in our study presented higher values of systolic blood pressure and fasting plasma glucose. Several previous studies conducted on adolescents have also observed this feature among males[4,7,12]. Moreover, females presented higher waist circumference z-scores, which has been previously described in adolescents[4,7], although there was no difference in the prevalence of abdominal obesity by sex, with a high prevalence among both sexes. This may reflect the trend to central fat accumulation, which has been observed previously in studies of Spanish children[35]. Abdominal obesity was the most prevalent component for both definitions of MetS, as it has been shown in other European studies[6]. It has also shown to be a marker of obesity and MetS later in life[36].

We observed no differences by age in our study. Nevertheless, it has been described an increase in the prevalence of MetS with age when school children are compared with adolescents or children with adults[6,25]. However, the studies examining age groups similar to that of the present analysis have reported no differences in the prevalence of MetS; indeed, it has been observed that while the highest prevalence in males occurs from the age of 14 years, in females it occurs between the ages of 10 and 13 years, and subsequently falls[37]. Regarding the educational and sociocultural level of the parents, it has been reported that a low socioeconomic level is related to a higher prevalence of MetS in adult population in the Mediterranean area[38], but this relationship has not been observed for Mediterranean basin adolescents[7] as has been shown in our study.

Finally, our data coincides with those reported previously, in that the parents' obesity and diabetes are not associated with a higher prevalence of MetS[37,39]. Even so, opinions differ in this respect[6,40] and it is undeniable the importance of genetic factors[41]. These disparities among studies might be due, in part, to the different methods used to obtain data for the parents' weight, i.e., surveys, anthropometry measurements or medical records. For example, in our country half of patients affected by DM type 2 ignore they have this condition[42]. In the present case, weight and size data, and diabetes records were collected by means of a survey, and so the prevalence of parental obesity and of a pathological background may have been underestimated.

Another limitation of the present study is that, due to its cross-sectional design, causal relationships could not be established. Nevertheless, the sample technique used was appropriate and the sample size measurement was addressed seeking to maximise representativeness. The non-response rate was lower than 20%, although there could be a bias if the non-responders were healthy. As in any other study on the prevalence of MetS, the definition applied does influence the results. In order to minimise this problem, two definitions were used, and so the results obtained could be compared with those from most previously published studies, since the NCEP-ATPIII and IDF definitions are by far the most commonly used in population studies.

In conclusion, the present study confirms the higher prevalence of MetS among adolescents in the Mediterranean region than in Central and Northern Europe. The NCEP-ATPIII definition produces a higher prevalence of MetS than when the IDF criteria are used, although there is a very good overall concordance between them. The main difference was the detection of MetS among patients with normal weight, which was higher with the NCEP-ATPIII definition. Obesity was the main risk factor for MetS, regardless of the definition applied and there was a positive correlation between the HOMA index and the higher prevalence of MetS. These data suggest there is a need to reinforce strategies to combat obesity and its morbility in the countries of the Mediterranean basin.

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