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Article *in* Metabolic syndrome and related disorders · February 2014

DOI: 10.1089/met.2013.0127 · Source: PubMed

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METABOLIC SYNDROME AND RELATED DISORDERS
Volume 12, Number 4, 2014

Pp. 202–209
DOI: 10.1089/met.2013.0127

Variations in the Prevalence of Metabolic Syndrome in Adolescents According to Different Criteria Used for Diagnosis: Which Definition Should Be Chosen for This Age Group?

Gloria M. Agudelo, MSc,[1] Gabriel Bedoya, MSc,[2] Alejandro Estrada, MSc,[3] Fredy A. Patiño, MSc,[4] Angelica M. Muñoz, ND,[5] and Claudia M. Velásquez, MSc[6]

Abstract

Background: Despite the increasing prevalence of metabolic syndrome in adolescents, there is no consensus for its diagnosis.
Methods: A cross-sectional study was conducted to compare the prevalence of metabolic syndrome in adolescents by different definitions, evaluate their concordance, and suggest which definition to apply in this population. A total of 851 adolescents between 10 and 18 years of age were evaluated. Anthropometric (weight, height, waist circumference), biochemical (glucose, lipid profile), and blood pressure data were taken. The prevalence of metabolic syndrome was determined by the definitions of the International Diabetes Federation (IDF) and four published studies by Cook et al., de Ferranti et al., Agudelo et al., and Ford et al. Concordance was determined according to the kappa index.
Results: The prevalence of metabolic syndrome was 0.9%, 3.8%, 4.1%, 10.5%, and 11.4%, according to the IDF, Cook et al., Ford et al., Agudelo et al., and de Ferranti et al. definitions, respectively. The most prevalent components were hypertriglyceridemia and low high-density lipoprotein cholesterol, whereas the least prevalent components were abdominal obesity and hyperglycemia. The highest concordance was found between the definitions by Cook et al. and Ford et al. (kappa = 0.92), whereas the greatest discordance was between the de Ferranti et al. and IDF definitions (kappa = 0.14).
Conclusions: Metabolic syndrome and its components were conditions present in the adolescents of this study. In this population, with a high prevalence of dyslipidemia and a lower prevalence of abdominal obesity and hyperglycemia, the recommendation to diagnose metabolic syndrome would be that used by Ford et al.

Introduction

The increase in the prevalence of overweight in adolescents favors the presence of metabolic syndrome, a condition that groups different metabolic disorders and that increases the risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) in adulthood.[1] Therefore, early identification of risk factors and preventive treatment are desirable strategies to deal with the epidemic of noncommunicable chronic diseases, today considered public health problems.[2]

Metabolic syndrome has been defined as the simultaneous presence of lipid and nonlipid risk factors of a metabolic origin, characterized by abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, and insulin resistance.[3,4] The presence or absence of metabolic syndrome in

[1]Clinical Nutrition, Vidarium Research Group, Nutrition, Health and Wellness Research Center, Nutresa Business Group (Grupo Empresarial Nutresa), Medellín, Colombia.
[2]Biology, Molecular Genetics Group, Universidad de Antioquia (UdeA), Medellín, Colombia.
[3]Epidemiology, School of Nutrition and Dietetics, Universidad de Antioquia (UdeA), Medellín, Colombia.
[4]Public Health, Research Group of Sciences Applied to Physical Activity and Sports, Universidad de Antioquia (UdeA), Medellín, Colombia.
[5]Research Group in Food and Human Nutrition, Universidad de Antioquia (UdeA), Medellín, Colombia.
[6]Basic Biomedical Sciences, Research Group in Food and Human Nutrition, Universidad de Antioquia (UdeA), Medellín, Colombia.

an individual is determined by genetic components that predispose the subject to the disorder,[5] as well as environmental factors, such as physical inactivity and inadequate eating habits, which enhance its development.[6]

The concept of metabolic syndrome in adolescents is recent,[7] still controversial, and more common than reported. Metabolic syndrome develops progressively with age according to changes in puberty,[8] and its prevalence increases with obesity.[1,6,9] For young people, at least 40 definitions of metabolic syndrome have been proposed, and all of them include elements used in defining metabolic syndrome in adults with modifications in the cutoff values.[10] Among other factors, the same cutoff for all ages, the moderate alteration observed in the metabolic indicators in adolescence, the physiological insulin resistance proper to puberty, and the differences in the lipid concentrations among ethnic groups, make consensus difficult in defining metabolic syndrome in this age group.[2,11–13] Many definitions have been used with criteria and cutoff points that respond to different interests. For example, the International Diabetes Federation (IDF) seeks to identify adolescents at risk for diabetes,[14] Cook et al.[7] and Ford et al.[15] favor cardiovascular risk, and Ford et al.'s definition is more sensitive to capturing adolescents with hyperglycemia. Other definitions include more liberal cutoff points, such as de Ferranti et al.[16] and other different components to evaluate, for example, obesity, as in Agudelo et al.[17]

Some authors consider that the model to diagnose metabolic syndrome in adolescents is not fulfilling the purpose of early identification of CVD and T2DM and propose focusing actions on established risk factors more than on its diagnosis.[8] Others argue that regardless of the criteria for its diagnosis, this condition is a reality in youth and only its early detection and prevention will decrease its presence and consequences.[18]

This study aimed to compare the prevalence of metabolic syndrome in a group of adolescents according to different definitions and assess their concordance to recommend which definition to use in this population group.

Methods

Cross-sectional descriptive study

The adolescents were recruited from the study population ''Metabolic Syndrome in overweight youth: Identification of risk factors and evaluation of an intervention.'' The sample consisted of 851 adolescents, beneficiaries of a health-promotion company in the city of Medellín, Colombia. We included adolescents of both sexes, between 10 and 18 years of age, whose parents or guardians voluntarily agreed to participate in the study and signed the written informed consent. Adolescents with physical disabilities that would limit the collection of anthropometric data and those who were pregnant or breastfeeding were excluded.

Socioeconomic stratum

This was determined according to Colombia's National Administrative Department of Statistics (DANE), which is reported in the public utility bill. It was classified as low (strata 1 and 2), medium (3 and 4), and high (5 and 6).

Anthropometric assessment

Weight, height, and waist circumference (WC) were measured according to international standards.[19,20] The body mass index (BMI) was calculated (kg/m^2), and obesity was determined according to the cutoff used by each author group in their definition.

Pubertal maturation

This was conducted by following the methodology defined by Tanner according to the development of secondary sexual traits.[21,22] Each adolescent evaluated his or her state of sexual maturity in a self-report that identified the visual image closest to his or her development in the graphic material designed for this purpose.

Blood pressure

This measure was taken with a mercury sphygmomanometer (Riester®, Germany) with adolescent-appropriate cuffs, following the methodology described in the Fourth Task Force.[23] The cutoff suggested by the authors in the definition of metabolic syndrome was applied for the classification.

Biochemical tests

The blood samples were taken from fasting subjects by puncturing the antecubital vein; serum was obtained after centrifugation at 2500 rpm for 10 min and was used to determine glucose concentration by standard enzymatic colorimetric methods. High-density lipoprotein cholesterol (HDL-C) and triglycerides (TGs) were determined using a spectrophotometry RA50 (Bayer, Series 71663) photocolorimeter, using specific enzymatic colorimetric kits (BioSystems). The results obtained were classified according to the cutoff established by the authors' definitions of metabolic syndrome.

Diagnosis of metabolic syndrome

The prevalence of metabolic syndrome and its components were evaluated according to five definitions: Cook et al. 2003,[7] de Ferranti et al. 2004,[16] Ford et al. 2007,[15] IDF 2007,[14] and Agudelo et al. 2008.[17] The IDF defines metabolic syndrome as the presence of abdominal obesity plus two other components, whereas the other four groups of authors define it as the presence of three or more components out of five possible, which combine criteria and cutoff points of the World Health Organization (WHO) and the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) (Table 1).

This project was approved by the Bioethics Committee of the University of Antioquia University Research Center (Sede de Investigación Universitaria, SIU), certificate number 10-11-328.

Statistical analysis

The prevalence of metabolic syndrome was calculated for each definition in the total sample by sex, age, pubertal maturation, and socioeconomic classification; the association among these factors was conducted by the chi-squared test of independence. The change in prevalence among each

TABLE 1. CRITERIA AND CUTOFF POINTS FOR THE DIAGNOSIS OF METABOLIC SYNDROME IN ADOLESCENTS

Criterion	*Cook et al. 2003*	*de Ferranti et al. 2004*	*Ford et al. 2007*	*Agudelo et al. 2008*	*IDF consensus definition 2007*
Triglycerides	≥ 110 mg/dL	≥ 100 mg/dL	≥ 110 mg/dL	≥ 110 mg/dL	≥ 150 mg/dL
HDL-C	≤ 40 mg/dL	< 50 mg/dL < 45 in men. 15–19 years old	≤ 40 mg/dL	≤ 40 mg/dL	< 40 mg/dL
Fasting glucose	≥ 110 mg/dL	≥ 110 mg/dL	≥ 100 mg/dL	≥ 100 mg/dL	≥ 100 mg/dL
Blood pressure (mmHg)	≥ 90th percentile By age, gender and height	≥ 90th percentile By age, gender and height	≥ 90th percentile By age, gender and height	≥ 90th percentile By age, gender and height	SBP ≥ 130 mmHg DBP ≥ 85 mmHg
Waist circumference	≥ 90th percentile By age and gender	> 75th percentile By age and gender	≥ 90th percentile By age and gender	None	≥ 90th percentile By age and gender
BMI	None	None	None	≥ 95th percentile	None
Metabolic syndrome diagnosis	Presence of three or more criteria	Presence of three or more criteria	Presence of three or more criteria	Presence of three or more criteria	High waist circumference + two other criteria[a]

[a]Adolescents > 16 years; waist circumference in men > 102 cm and in women > 88 cm; triglycerides > 150 mg/dL; HDL-C in men < 40 mg/dL and in women < 50 mg/dL; blood pressure ≥ 130/85 mmHg or treatment for previously diagnosed hypertension; glucose ≥ 100 mg/dL or diagnosed for type 2 diabetes mellitus (T2DM).

IDF, International Diabetes Federation; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index.

definition was carried out by the McNemar test for change control, and the concordance among them by the kappa index. In all cases, a $P < 0.05$ was considered significant. The statistical analysis was performed using the Statistical Package for the Social Sciences, SPSS® v. 20.0 program.

Results

The final sample consisted of 851 adolescents between 10 and 18 years old; 55.5% were between 10 and 13 years of age, 52.1% were women, and 80.0% belonged to the medium and low socioeconomic classifications.

Figure 1 shows the prevalence of the metabolic syndrome components according to the cutoffs used in the five definitions analyzed here. De Ferrati et al. 2004 showed the highest prevalence of hypertriglyceridemia (45.3%) and low HDL-C (43.8%). Hyperglycemia had the highest prevalence according to Ford et al. 2007, Agudelo et al. 2008, and the IDF (2.8%). The prevalence of high blood pressure was 10.3% for the cutoff defined by Cook et al. 2003, Ford et al. 2007, and Agudelo et al. 2008; high WC, according to de Ferranti et al. 2004, was present in 18.9% versus 3.4% with the other definitions. Finally, the BMI ≥ 95th percentile criterion, used to define obesity in adolescents by Agudelo et al. 2008, had a prevalence of 29.1%.

The prevalence of metabolic syndrome according to the five definitions discussed above and to sociodemographic variables is shown in Table 2. The highest prevalence of metabolic syndrome was found when the definitions by the Ferranti et al. 2004 and Agudelo et al. 2008 were applied (11.4% and 10.5%, respectively), whereas the lowest prevalence was found by the IDF (0.9%). Using the definition of metabolic syndrome proposed by Agudelo et al. 2008, prevalence was significantly greater in men than women ($P = 0.01$) and lower in men with high socioeconomic strata ($P = 0.041$). With the definition of de Ferranti et al. 2004, prevalence was significantly greater in prepubertal than pubertal and postpubertal adolescents ($P = 0.01$).

The change in prevalence among the different definitions and the concordance among them is shown in Table 3. No differences were found in the metabolic syndrome classification when comparing the definitions of Cook et al. 2003 and Ford et al. 2007, nor between de Ferranti et al. 2004 and Agudelo et al. 2008. The greatest concordance was between Cook et al. 2003 and Ford et al. 2007, whereas the greatest discordance was between de Ferranti et al. 2004 and the IDF. The other definitions showed significant changes and lower concordances in the classifications of metabolic syndrome.

Discussion

The prevalence of metabolic syndrome in adolescents, depending on the criteria used for its diagnosis, has been reported between 0% and 19.2%, with the average being 3.3%.[2] In this study, it was found to be between 0.9% and 11.4%, depending on the definition employed. The main differences among the definitions were: The IDF uses a strict cutoff for hyperglycemia, it is less rigorous for TGs and blood pressure, but it has the condition of a high WC to diagnose metabolic syndrome. The definition of de Ferranti et al. 2004 is the strictest in the classification of TGs, HDL-C, and WC, whereas that of Agudelo et al. 2008 includes the BMI and not the WC as a diagnostic criterion.

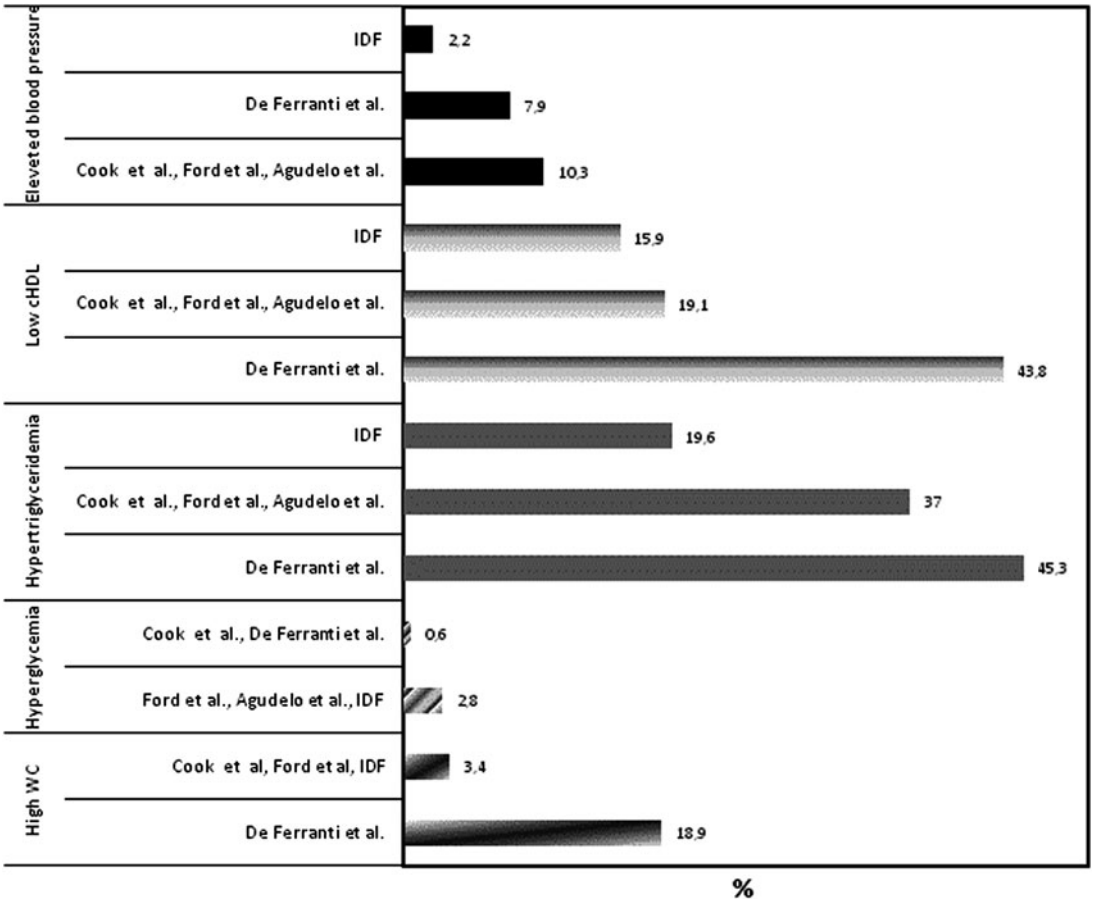

FIG. 1. Prevalence of the metabolic syndrome components in the study population according to the cutoff points of the five definitions.

A recent systematic review reported a greater prevalence of metabolic syndrome in young men than young women and in men of old age.[2] In the sample of adolescents from Medellín analyzed here, a difference by gender, but not by age, was found in Agudelo et al. 2008. This study found a lower prevalence of metabolic syndrome, according to the definition by de Ferranti et al. 2004, in the high socioeconomic category; however, results of other studies are conflicting and there is insufficient evidence for this association. The significantly greater prevalence of metabolic syndrome,

Table 2. Prevalence of Metabolic Syndrome in the Study Group According to Different Definitions

			Prevalence of adolescents with metabolic syndrome									
			Cook et al.		*Ford et al.*		*de Ferranti et al.*		*Agudelo et al.*		*IDF*	
Variable	n	%	n	%	n	%	n	%	n	%	n	%
Total	851	100	32	3.8	35	4.1	97	11.4	89	10.5	8	0.9
Gender												
Men	408	47.9	17	4.2	19	4.7	49	12.0	54	13.2 [a]	6	1.5
Women	443	52.1	15	3.4	16	3.6	48	10.8	35	7.9	2	0.5
Age (years)												
10–13	472	55.5	16	3.4	17	3.6	61	12.9	46	9.7	5	1.1
14–18	379	44.5	16	4.2	18	4.7	36	9.5	43	11.3	3	0.8
Socioeconomic classification												
Low	340	40.0	16	4.7	18	5.3	41	12.1	36	10.6	3	0.9
Medium	354	41.6	12	3.4	12	3.4	47	13.3	41	11.6	4	1.1
High	157	18.4	4	2.5	5	3.2	9	5.7	12	7.6 [a]	1	0.6
Pubertal maturation												
Prepubertal	147	17.3	5	3.4	4	2.7	30	20.4[a]	18	12.2	2	1.4
Pubertal	243	28.6	7	2.9	8	3.3	23	9.5	20	8.2	1	0.4
Postpubertal	459	54.1	20	4.4	23	5.0	43	9.4	51	11.1	5	1.1

[a]Chi-squared test $p < 0.05$ by classification of metabolic syndrome for each of the variables.
IDF, International Diabetes Federation.

Table 3. Change in the Prevalence According to the Definition of Metabolic Syndrome

Definition of metabolic syndrome	*Ford et al.*		*de Ferranti et al.*		*Agudelo et al.*		*IDF*	
	Have	*Not have*	*Have*	*Not have*	*Have*	*Not have*	*Have*	*Not have*
Cook et al.								
Have	31	1	31	1	32	0	8	24
Not have	4	815	66	753	57	762	0	819
McNemar*	0.375		0.000		0.000		0.000	
Kappa**	(0.92; 0.000)		(0.45; 0.000)		(0.50; 0.000)		(0.39; 0.000)	
Ford et al.								
Have			31	4	34	1	8	27
Not have			66	750	55	761	0	816
McNemar*			0.000		0.000		0.000	
Kappa**			(0.44; 0.000)		(0.52; 0.000)		(0.36; 0.000)	
de Ferranti et al.								
Have					63	34	8	89
Not have					26	728	0	754
McNemar*					0.366		0.000	
Kappa**					(0.64; 0.000)		(0.14; 0.000)	
Agudelo et al.								
Have							8	81
Not have							0	762
McNemar*							0.000	
Kappa**							(0.15; 0.000)	

*P from the McNemar test for change control.
**Kappa concordance index (indice; valor P).
IDF, International Diabetes Federation.

according to the definition of de Ferranti et al. 2004, in prepubertal compared to pubertal and postpubertal adolescents could be explained by the stricter cutoff that these authors used to classify high WC (>75th percentile). This strict cutoff can result in claiming abdominal obesity in prepubertal children when they could actually be under the effect of a fat wave prior to the normal growth spurt that occurs at this age. For this reason, the definition of de Ferranti et al. 2004 may overestimate the proportion of adolescents with metabolic syndrome.

In this study, regardless of the definition used, the most prevalent components of metabolic syndrome were hypertriglyceridemia, low HDL-C, and high blood pressure; the least frequent were hyperglycemia and high WC. These findings are similar to those reported by other studies in Colombian,[24,25] Mexican,[26,27] Turkish,[28] Iranian,[29] and Vietnamese[30] populations, but different from those found for Spanish,[31,32] American,[33] and Kuwaiti[34] adolescents, in whom abdominal obesity and high blood pressure were the most prevalent components. In Latino adolescents residing in the United States, a greater prevalence of abdominal obesity and low HDL-C was reported.[35] These results suggest that the particular genetic and environmental characteristics of each population may account for the differences. It is argued that one of the greatest difficulties in unifying the definition of metabolic syndrome in adolescents lies in generalizing criteria for populations with different ethnic backgrounds, because this may have an effect on the lipid patterns, body composition, and insulin resistance.[36]

Depending on the criteria used, the results of this study show significant variations, both in the presence of the components as well as in the diagnosis of metabolic syndrome in adolescents. The lower prevalence of metabolic syndrome was found with the IDF definition (0.9%), whereas the greatest prevalence was found with the definitions of de Ferranti et al. 2004 and Agudelo et al. 2008 (11.4% and 10.5%, respectively). When comparing these prevalences with others reported in Colombian adolescents living in urban areas, we found similar values in the prevalence of metabolic syndrome, the lowest using the IDF definition, followed by that of Cook et al.; the highest prevalence was that of de Ferranti et al.[24,37]

Unlike other authors, the definition by Agudelo et al. 2008 uses the BMI and not the WC to evaluate obesity. BMI has been identified as a risk factor predictor of CVD in children and adolescents.[6,36] However, BMI does not discriminate the distribution of body fat, an aspect that plays a decisive role in sensitivity to insulin; a high concordance has been found between visceral obesity, metabolic syndrome in adolescence and CVD in adulthood.[12] Other studies in Colombian adolescents[24,38] have not found abdominal obesity as one of the most frequent criteria for metabolic syndrome. This raises several considerations: (1) Although less specific, BMI would allow diagnosing more adolescents with metabolic syndrome; (2) in this age group, and for prevention purposes, it would be more appropriate to use a more stringent cutoff to diagnose abdominal obesity, such as that used by de Ferranti et al. 2004; (3) it is necessary to establish a WC cutoff for Colombian adolescents, as has been done in Canada, Italy, the United States, and the United Kingdom;[36] and (4) exploring other indicators of abdominal obesity, such as the waist-to-height ratio.[39]

In the study population of adolescents of Medellín, a significant prevalence of alterations in the lipid profile has been reported.[25,38,40] This could be explained not only by the obesogenic environmental factors specific to these adolescents, but also by their ancestral genetic composition, which consists, on average, of 78% European, 16%

Amerindian, and 6% African.[41] A strong European genetic composition is related to the high prevalence of lipid disorders; in contrast, the lower prevalence of insulin resistance is more associated with Amerindian ancestry.

Abdominal obesity and hyperglycemia were the least prevalent components of metabolic syndrome in the sample of adolescents from Medellín. In this regard, one of the differences in the definitions of this criterion is in the manner in which hyperglycemia is diagnosed.[10] It has been proposed that the natural history of metabolic syndrome first passes through abdominal obesity, then by a state of insulin resistance compensated to achieve normoglycemia, and finally reaches the β-cell failure with decreased insulin production and hyperglycemia. In this study, no adolescent showed abdominal obesity as one of the most prevalent components, and in those who presented it (3.4%), the existence of insulin resistance with normoglycemia was evident (unpublished data). This suggests that pancreatic β-cells compensate insulin resistance, which could explain the low prevalence of hyperglycemia in our sample. These results suggest that using the IDF cutoff to diagnose hyperglycemia excluded a number of adolescents with alterations in their lipid profiles and limits the early detection of a CVD risk factor in this population. Regarding blood pressure, the lowest prevalence in our sample was achieved with the IDF definition, which uses a cutoff normally used in adults, different from the rest of the definitions, which use cutoff points according to age, sex, and height.

The above results indicate that although the IDF definition could identify more adolescents at T2DM risk, it may underestimate the CVD risk at an early age; CVD represents the leading cause of death in Colombia.[42] Instead, the definition by de Ferranti et al. 2004, which proposes a more stringent cutoff for HDL-C and TGs, could overestimate the metabolic syndrome prevalence.

By applying the five definitions discussed here, the differences in the prevalence of metabolic syndrome are consistent with those published in other reports.[2,43] The results showed a high concordance between Cook et al. 2003 and Ford et al. 2007 and discordance between de Ferranti et al. 2004 and the IDF. Particularly striking is the prevalence of its individual components, which maybe of more concern than metabolic syndrome itself. It is important to remember that until they were included in this study these adolescents were ''apparently'' healthy, and many of them, although they might not have had metabolic syndrome, did present metabolic alterations that warrant timely intervention.

In the current context of noncommunicable chronic disease epidemiology and the conditions of the Colombian population, the recommendation to diagnose metabolic syndrome would be that used by Ford et al. 2007; however, similar studies with more subjects are needed to validate this criteria. This definition uses metabolic syndrome components recognized by the majority of the definitions, cutoff points supported by international agencies (National Cholesterol Education Program and International Diabetes Federation), and, among those applied, it seems that they neither overestimate nor underestimate conditions. Even though the definitions by Ford et al. and Cook et al. were the most consistent, the difference in the cutoff point for hyperglycemia permitted diagnosing four more adolescents with metabolic syndrome; although this difference is small, it is clinically important to begin early secondary prevention.

Therefore, the definition of Ford et al. 2007 would permit capturing both adolescents at risk for T2DM and CVD, as well as adolescents without metabolic syndrome but with lipid alterations or hyperglycemia that should be treated promptly with interventions that have demonstrated impact.[44] The early diagnosis and timely treatment of metabolic syndrome are relevant because longitudinal studies have shown that the risk of atherosclerosis increases exponentially with the presence of cardiovascular risk factors[45] and increases between 9 and 11 times the probability of suffering CVD and T2DM in adulthood, respectively.[46] Another study found that 25 years later, 19.4% of those who had been overweight or had had metabolic syndrome in their adolescence had experienced a significant cardiovascular event.[47]

Although neither this study nor the sample from which this work was derived was designed for a study of concordance, the findings described here illustrate the differences in the prevalence according to the definitions used in a population. This confirms the complexity of diagnosing metabolic syndrome in adolescents while offering guidelines on which definitions apply and how to interpret the results.

In conclusion, in this study with a high prevalence of dyslipidemia and a lower prevalence of abdominal obesity and hyperglycemia, the recommendation to diagnose metabolic syndrome would be that used by Ford et al. 2007. Due to the complexity of its definition, the utility of metabolic syndrome continues to be discussed; efforts are required by the medical and research communities to reach a consensus on its application. Studying the effect of genetic components and the utility of new biomarkers will contribute to understanding metabolic syndrome as a multifactorial condition. Finally, despite the diversity in its definition and the difficulties of its application, metabolic syndrome is present in adolescents and makes them a priority group in which to initiate early detection and timely treatment

Acknowledgments

This study was funded by resources from Colciencias contract 203 of 2010, Vidarium, and the University of Antioquia 2011–2012 and 2013–2014 Sustainability Strategy.

Author Disclosure Statement

No competing financial interests exist

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Address correspondence to:
Gloria M. Agudelo
Vidarium, Nutrition, Health and Wellness Research Center
Nutresa Business Group
(Grupo Empresarial Nutresa)
Calle 8 Sur 50–67
Medellín 050023
Colombia

E-mail: gmagudelo@serviciosnutresa.com