

Body mass index associated with hyperglycemia and alterations of components of metabolic syndrome in Mexican adolescents

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Abstract

Objective. This research aims to describe the epidemiology of obesity and its association with alterations in some components of metabolic syndrome, such as serum concentrations of glucose, insulin, and some lipids in a sub-sample of the Mexican Health Survey (MHS) of youth ages 10 to 19 years. **Material and Methods.** This analysis is based on a randomly selected sub-sample of the MHS of 20% of the youth ages 10 to 19 years (n=1977), carried-out in Mexico in the year 2000 and distinguishes differences between national, rural and urban areas as well as four geographical country regions. Serum concentrations of glucose, insulin, triglycerides (TG), total cholesterol (TC) and HDL-cholesterol (HDLc) were measured. The protocol was approved by the Ethics Committee of the Mexican National Institute of Public Health. **Results.** Overall, 14.8% of the individuals were overweight, 6.7% were obese and 37.5% had a family history of type 2 diabetes mellitus (DM2). The overall mean concentrations of glucose, insulin, total cholesterol, and triglycerides were significantly higher and those of HDLc were significantly lower in obese subjects than in individuals with normal Body Mass Index (BMI) ($p < 0.05-0.001$). The probability ratio (PR) of being in quintile 5 for glucose distribution was significantly higher for obese males and females (RP=2.1, $p < 0.001$) than for their non-obese counterparts. It was also higher for females with a history of DM2 (RP=1.12, $p < 0.02$), but not for males. The PR of being in quintile 5 for insulin distribution was significantly higher for obese males (RP=3.51, $p < 0.001$) and females (RP=3.3, $p < 0.001$) than for non-obese counterparts. It was

Resumen

Objetivo. Esta investigación tiene como objetivo describir la epidemiología de la obesidad y de su asociación con alteraciones de algunos componentes del síndrome metabólico, tales como las concentraciones séricas de glucosa, insulina y algunos lípidos en una muestra de jóvenes con edades entre 10-19 años estudiados en la Encuesta Nacional de Salud (ENSA). **Material y métodos.** El presente análisis está basado en una submuestra de 20% de los sujetos de la ENSA, realizada en México en el año 2000, con edades entre 10-19 años (n=1977) seleccionada aleatoriamente, con poder para distinguir diferencias a nivel nacional, urbano rural y por cuatro regiones geográficas del país. Se midieron en el suero las concentraciones de glucosa, insulina, colesterol total (CT), triglicéridos (TG) y colesterol-HDL (cHDL). El protocolo fue aprobado por el Comité de Ética del Instituto Nacional de Salud Pública. **Resultados.** El 14.8% de la muestra tuvieron sobrepeso, 6.7% obesidad y 37.5% tenían una historia familiar de diabetes mellitus tipo2 (DM2). La media de las concentraciones de glucosa, insulina, CT y TG fueron significativamente mayores y los de cHDL significativamente menores en los sujetos obesos que en los que tenían índice de Masa Corporal (IMC) normal ($p < 0.05-0.001$). La razón de probabilidades (RP) de estar en el quintil 5 de la distribución de glucosa fue significativamente mayor para los hombres y mujeres con obesidad (RP=2.1, $p < 0.001$) que para sus contrapartes no obesos, para la mujeres con historia familiar de DM2 (1.12, $p < 0.02$), pero no para los hombres. La RP de estar en el quintil 5 de la distribución de insulina fue mayor para los hombres

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also higher for male (RP=1.28, $p<0.02$) and female (RP=1.27, $p<0.02$) subjects with a history of DM2. Finally, the PR for being in quintile 5 for TG distribution was significantly higher for obese males (RP=4.71, $p<0.001$) and females (RP=1.75, $p<0.001$) than for their non-obese counterparts. **Discussion.** A strong association between obesity and the risk of higher concentrations of glucose, insulin, TG, and TC and a lower concentration of HDLc in youth has been demonstrated. These findings stress the risk of obesity at these early ages, with alterations in some of the components of metabolic syndrome.

Key words: obesity; adolescents; hyperglycemia; insulin; cholesterol; HDL-cholesterol

(RP=3.51, $p<0.001$) y para las mujeres (RP=3.3, $p<0.001$) con obesidad que para aquellos con IMC normal, así como para los hombres (RP=1.28, $p<0.02$) y las mujeres (RP=1.27, $p<0.02$) con historia familiar de DM2. La RP de estar en el quintil 5 de la distribución de triglicéridos fue mayor en los hombres (RP=4.71, $p<0.001$) y las mujeres (RP=1.75, $p<0.001$) obesos que en los no obesos. **Conclusiones.** Se observó una fuerte asociación entre la obesidad y el riesgo de tener altas concentraciones de glucosa, insulina, TG y CT y bajas de cHDL en jóvenes. Tales hallazgos confirman el riesgo que tiene la obesidad de asociarse con anomalías de algunos componentes del síndrome metabólico en jóvenes.

Palabras clave: obesidad; adolescentes; hiperglicemia; insulina; colesterol; HDL-colesterol

In Mexico, the prevalence of obesity and type 2 diabetes mellitus (DM2) have steadily grown over the last 10 years,¹⁻³ closely following global tendencies. The prevalence of obesity among women 12 to 48 years of age doubled in 11 years, according to the 1988 and 1999 Mexican National Nutrition Surveys (NNSs).^{2,4} Most probably, the prevalence of obesity in males in the same age group has followed a similar pattern, although no data trends are available. Data from the 2000 Mexican Health Survey (MHS) reported a similar prevalence of overweight and obesity among males and females.⁵ In 1999, the combined prevalence of overweight and obesity in children and adolescents was already high, varying from 5 to 25%, with a positive association with age.⁶ The prevalence of both overweight and obesity increased five percentage points between 1988 and 1999.^{6,7} In other countries, the prevalence of overweight and obesity in children and adolescents increased three-fold in the last decade.⁸ The increasing prevalence of obesity at early ages is an alarming public health problem because 25% of obese six year-olds and 75% of 12 year-olds will remain obese in adulthood.⁹

In addition, obesity is etiologically associated with other components of metabolic syndrome (such as hypertension, high glucose concentrations, triglycerides, total cholesterol, low concentrations of HDL-cholesterol, insulin resistance and truncal obesity). All of these alterations have been identified as risk factors for atherosclerosis, cardiovascular diseases and DM2.¹⁰ Although DM2 is more frequent in adults, its prevalence in children, and especially in adolescents,¹¹ has increased ten-fold in the last two decades.¹² Those figures may be underestimated because DM2 is often misclassified, not diagnosed or not frequently reported.^{13,14} Thus, it is accepted that obesity in childhood is a risk factor for

metabolic syndrome, DM2 and cardiovascular diseases in adult life.

The National Cholesterol Education Program of the United States has targeted obesity as one of the main objectives in the primary prevention of cardiovascular diseases.^{15,16}

In Mexico, the information available on the magnitude and distribution of the components of metabolic syndrome and its association with obesity in children comes from non-probabilistic studies,¹⁷ some of which are from the Mexican-American population.¹⁸⁻²⁰

This research was designed to describe the epidemiology of obesity and its association with several components of metabolic syndrome, such as serum concentrations of glucose, insulin and some lipids in a sample of youths ages 10 to 19 years selected from the MHS (2000).

This information can be useful for the design of interventions and as evidence of the effect of this public health epidemic on Mexican youth.

Material and Methods

Data for this analysis was obtained from the Mexican Health Survey (MHS) (2000). The methodology has been published in detail elsewhere.²¹ Briefly, the sample was selected based on the geographical characteristics of the localities and the states, which were obtained from available georeferential databases administered by the National Institute of Statistics, Geography and Informatics. This probabilistic survey has the statistical basis for being representative at the national and regional levels. The survey was carried out from November 1999 to June 2000 in 47 000 households. The sampling was multistage and multistratified. Sampling units were

households included one adult older than 20 years of age, one youth between 10 to 19 years old and one child younger than 10 years were surveyed. The male:female ratio was 49.3:50.7%.

For the purpose of this study, a sub-sample of 1 997 subjects was randomly selected, representing 10% of the total sample of 19 735 youth 10 to 19 years of age. The sub-sample was representative of national rural and urban areas and four regional populations. The sub-sample was balanced according to gender, age, urban and rural areas, and geographic location. Rural households were defined as those located in communities of less than 2 500 inhabitants. Four geographic regions were selected to represent the degree of general economic development based on the classification previously used for the National Nutrition Survey (1999), in which the northern region was the most developed and the southern region the least developed. Central and Mexico City regions are considered intermediate. The regions were composed of the following states: 1) northern: Baja California, Baja California Sur, Coahuila, Chihuahua, Durango, Nuevo Leon and Sonora, 2) central: Aguascalientes, Colima, Guanajuato, Jalisco Mexico, Michoacan, Morelos, Nayarit, Queretaro, San Luis Potosi, Sinaloa and Zacatecas, 3) Mexico City, a region by itself, and 4) southern: Campeche, Chiapas, Guerrero, Hidalgo, Oaxaca, Puebla, Quintana Roo, Tabasco, Tlaxcala, Veracruz and Yucatan.

Variables for each subject selected were extracted from the general database and are described below. Serum samples were identified and extracted from a serum bank where the samples were stored at -70°C. Original blood samples were obtained during the survey house visit, occurring between 8:00 am and 6:00 pm, thus, an undetermined proportion of blood samples with less than two hours of fasting were obtained.

Variables

Selected variables included: age, gender, housing, family history of DM2 and hypertension, height and body weight measurements and other socioeconomic variables. Serum samples frozen at -150°C were used to determine the concentrations of glucose, total cholesterol (TC), triglycerides (TG) and HDL-cholesterol (HDLc) in a Prestige semiautomatic analyzer, model 24i (Tokyo Boeki Medical System LTD, Tokyo, Japan). Insulin concentrations were measured by immunoassay in an automatic analyzer (TOSOH, model AIA 600, Tosoh, Inc, Tokyo, Japan).

Overweight and obesity were classified based on reference data for BMI (kg/m^2) from Cole et al, specific for age and gender with the following cut-off values:

1) normal <85th percentile, 2) overweight 85th-95th percentile and 3) obesity >95th percentile.²²

Statistical analysis

Due to the characteristics of the survey design, in the present study the estimates were calculated using the complex survey STATA 8.2 "SVY" module (College Station, TX). This program makes adjustments based on the sample design and allows for the results to be generalized to those individuals in the population.* First, a descriptive analysis of the population characteristics was conducted. Gender-specific means and 95% confidence intervals (95%CI) were calculated for age, glucose, insulin, total cholesterol, HDL-cholesterol and triglycerides. Age-adjusted, gender-specific means were then estimated and stratified by BMI or by quintiles. Next, non-conditional multivariate logistic regression models, in order, were estimated for the purpose of analyzing the association between the main independent variables –BMI (normal, overweight and obese) and previous family history of diabetes– and gender, the prevalence of subjects in quintile 5 for distributions of glucose, insulin, total cholesterol, triglycerides or quintile 1 for HDL-Cholesterol. The model's adjustment was carried out using maximum likelihood estimates and a *p*-value cutoff point of >0.05, which indicated an appropriate adjustment. Probability ratios (PR) were estimated from odds ratios using the method proposed by Zhang.^{23,24}

Ethical considerations

Consent for participation was obtained from a parent (usually the mother) or caregiver of all participants. The project was approved by the scientific and ethics committees of the Mexican National Institute of Public Health. In addition, data collection respected the confidentiality and reserve rights stipulated by the Mexican Statistical and Geographic information law.²⁵

Results

The analysis included 1 997 youths ages 10 to 19 years, with a balanced distribution by gender (females= 50.5%) and urban and rural areas (urban= 44.5%). Overall, 14.8% of the youths were overweight and 6.7% were obese. A total of 37.5% had a family history of DM2. Mean serum concentrations of glucose, insulin, TG,

* Stata Corp. Stata reference manual. Release 8.2. College Station, TX: Stata Press, 2001.

TC, and HDLc were within the normal limits proposed by the Atherosclerosis, Hypertension, and Obesity in Youths Committee.¹⁵ There were no significant gender differences between these variables (Table I).

The variations across quintiles 1 through 5 in mean concentrations of glucose (53.4-107 mg/dl), TG (69.2-277 mg/dl), TC (124.7-207.5 mg/dl) tended to be lower and those of insulin (5.2-67.4 uU/ml) tended to be higher for females compared to males. No statistical differences were found. Mean HDLc concentrations (females: 28.4-50.4 mg/dl) were comparable between genders (Table II). The overall mean concentrations of glucose, insulin, TC, and TG were significantly higher and those of HDLc were significantly lower in obese subjects compared to those with normal BMI ($p < 0.05-0.001$), (figure 1).

The PRs for being in quintile 5 for glucose distribution were significantly higher for obese males and females (PR= 2.1, $p < 0.001$) than for their non-obese counterparts, and for female subjects with a history of DM2 (PR= 1.12, $p < 0.02$), but not for males. The PRs for being in quintile 5 for insulin distribution were significantly higher for obese males (PR= 3.51, $p < 0.001$) and females (PR= 3.3, $p < 0.001$) than for their non-obese counterparts, and for male (PR= 1.28, $p < 0.02$) and female (PR= 1.27, $p < 0.02$) subjects with a history of DM2. The PRs for being in quintile 5 for TG distribution were significantly higher for obese males (4.71, $p < 0.001$) and females (1.75, $p < 0.001$) than for their non-obese counterparts. Family history of DM did not increase the PRs. The PRs of being in quintile 5 for TC distribution were significantly higher for obese males (2.43, $p < 0.001$) and females

Table I
DISTRIBUTION BY GENDER OF SOME CHARACTERISTICS OF THE SAMPLE.
DATA FROM THE MEXICAN NATIONAL HEALTH SURVEY, 2000

	Total sample 1997	Female 1053 (50.5)	Male* 944 (49.5)
Means (95 % CI)			
Age (years)	12.6 (12.5, 12.7)	12.5 (12.3, 12.6)	12.7 (12.5, 12.9)
Glucose (mg/dl)	78.5 (76.3, 80.6)	76.4 (74.2, 78.6)	80.6 (77.1, 82.4)
Insulin (mcg/dl)	23.0 (21.2, 24.9)	25.9 (23.1, 28.8)	20.1 (17.7, 22.4)
Triglycerides (mg/dl)	137.6 (132.9, 142.2)	140.1 (133.8, 146.1)	134.9 (128.8, 141.1)
Total Cholesterol (mg/dl)	161.4 (159.2, 163.6)	163.5 (160.6, 166.3)	159.3 (156.3, 162.3)
HDL-Cholesterol- (mg/dl)	38.3 (37.7, 38.9)	38.4 (37.6, 39.2)	38.2 (37.2, 39.1)
N (%)			
Body Mass Index			
Normal	1 441 (76.9)	756 (75.4)	685 (78.5)
Overweight	376 (16.4)	213 (17.9)	163 (14.8)
Obesity	147 (6.7)	67 (6.7)	80 (6.7)
Family history of DM2			
No	1 245 (62.8)	656 (63.1)	589 (62.5)
Yes	712 (37.2)	378 (36.9)	334 (37.5)
Region			
Northern	442 (17.1)	222 (15.7)	220 (18.5)
Central	794 (41.9)	410 (40.9)	384 (42.8)
Mexico City	42 (7.0)	24 (8.3)	18 (5.8)
Southern	719 (34.0)	397 (35.1)	322 (32.9)
Housing			
Urban	909 (43.3)	472 (42.2)	437 (44.4)
Rural	1 085 (56.7)	578 (57.8)	50 (55.6)

Percentage and CI 95% are expanded values. Expanded cases= 1 982 463

* None of the differences were significant by t test, the Fisher's exact test or χ^2 at $p < 0.05$

Table II
MEAN CONCENTRATIONS AND 95% CONFIDENCE INTERVALS FOR SOME COMPONENTS OF METABOLIC SYNDROME
BY QUINTILES. DATA FROM THE MEXICAN NATIONAL HEALTH SURVEY, 2000

	I Mean (CI 95%)	II Mean (CI 95%)	III Mean (CI 95%)	IV Mean (CI 95%)	V Mean (CI 95%)
Females					
Glucose	53.4 (51.6, 55.1)	69.1 (68.6, 69.6)	77.8 (77.2, 78.4)	87.5 (86.8, 88.2)	107.0 (104.1, 109.8)
Insulin	5.2 (4.8, 5.5)	10.4 (10.2, 10.7)	17.4 (17.0, 17.8)	29.6 (28.6, 30.6)	67.4 (59.3, 75.5)
Triglycerides	69.2 (66.4, 72.1)	97.1 (98.8, 98.5)	123.4 (121.3, 125.4)	159.8 (156.7, 162.9)	277.0 (260.6, 293.3)
Total Cholesterol	124.7 (122.2, 133.3)	147.6 (146.7, 148.5)	162.1 (161.5, 162.8)	177.1 (176.1, 178.1)	207.5 (203.4, 211.5)
HDL-Cholesterol	28.4 (28.0, 28.8)	33.5 (33.3, 33.8)	37.2 (36.9, 37.5)	41.2 (40.9, 41.5)	50.4 (48.9, 51.9)
Males					
Glucose	54.0 (51.6, 56.3)	72.4 (71.8, 72.9)	81.7 (81.3, 82.1)	92.7 (91.9, 93.5)	124.8 (113.1, 136.5)
Insulin	3.7 (3.5, 3.9)	7.4 (7.2, 7.6)	12.3 (11.9, 12.6)	20.5 (19.8, 21.1)	56.9 (48.6, 65.1)
Triglycerides	66.7 (64.3, 69.2)	95.0 (93.6, 96.4)	122.8 (120.9, 124.7)	161.0 (158.9, 163.1)	285.7 (265.6, 305.8)
Total Cholesterol	122.3 (120.3, 124.4)	142.4 (141.2, 143.6)	159.4 (158.2, 160.5)	176.7 (175.3, 178.1)	210.8 (205.6, 216.0)
HDL-Cholesterol	27.6 (27.1, 28.1)	32.9 (32.7, 33.2)	36.7 (36.5, 37.0)	41.3 (41.0, 41.7)	50.9 (49.7, 52.2)

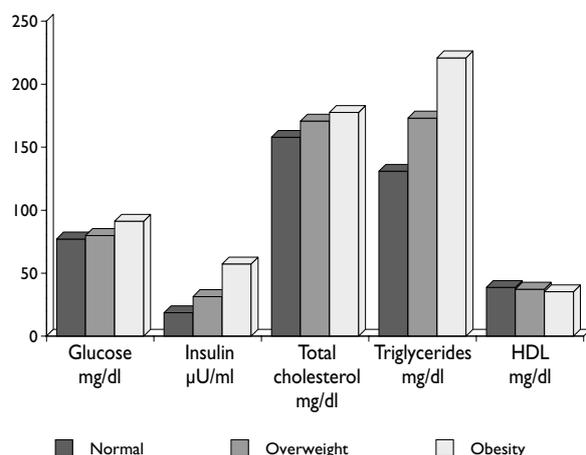


FIGURE 1. ADJUSTED MEANS FOR SOME COMPONENTS OF THE METABOLIC SYNDROME BY BMI CATEGORY, CONCENTRATIONS OF GLUCOSE, INSULIN, TRIGLYCERIDES, AND TOTAL CHOLESTEROL WERE SIGNIFICANTLY GREATER AND THOSE OF HDL-CHOLESTEROL WERE SIGNIFICANTLY LOWER IN OBESE SUBJECTS THAN IN NORMAL BMI SUBJECTS. $P < 0.001$ FOR ALL THE VALUES FOR TEST FOR TENDENCIES

(1.53, $p < 0.001$) than for their non-obese counterparts. Family history of DM did not increase the PRs for being in quintile 5 for total cholesterol. Neither obesity nor having a family history of DM2 increased the PRs for being in quintile 5 for HDLc distribution (Table III).

Discussion

A strong association between obesity and the risk of higher serum concentrations of glucose, insulin, TG, TC and HDLc in youths was observed in this national survey. Several studies have shown that overweight and obesity in early years are risk factors for coronary disease and metabolic syndrome in adult life.^{26,27} Also, hyperinsulinemia and insulin resistance play a role in the pathogenesis of hypertension.²⁸ Hyperinsulinemia and hypertension are known risk factors for coronary heart disease.²⁹ In addition, obesity and hyperinsulinemia are considered risks for type 2 diabetes mellitus, for which the prevalence is increasing at an alarming rate, especially in adolescents.^{29,30} Our data show that these risks are already present in a significant number of Mexican youth, especially in those that are obese. Identification of alterations in the components of metabolic syndrome has clinical and epidemiological relevance because these DM2 and cardiovascular disease risk factors can be reduced by individual and public health interventions.³¹⁻³³ Even small reductions in body weight are able to correct abnormalities in the components of metabolic syndrome, such as hyperglycemia, hyperinsulinemia, and dislipidemias.^{32,33} Interventions aimed at increasing physical activity and improving the diet are cost effective for reducing the risk of chronic diseases associated with obesity.^{31,34}

The authors recognize that a limitation of this study is the inability to determine whether the cases were or were not in fasting condition. Thus, we were unable to

Table III
PREVALENCE RATIOS (PR) AND 95% CONFIDENCE INTERVALS (95% CI) FOR CASES IN QUINTILE 5
FOR SOME COMPONENTS OF METABOLIC SYNDROME. DATA FROM THE MEXICAN NATIONAL HEALTH SURVEY, 2000

	Glucose Quintile V PR (95%CI)	Insulin Quintile V PR (95%CI)-	Triglycerides Quintile V PR (95%CI)	Total cholesterol Quintile V PR (95%CI)	HDL-Cholesterol Quintile I PR (95%CI)
Females					
Body mass index					
Normal*	1.00	1.00	1.00	1.00	1.00
Overweight	1.51 (1.09,2.09)	1.94 (1.38,2.72)	1.79 (1.28,2.50)	1.42 (1.03,1.95)	1.30 (0.91,1.88)
Obesity	2.16 (1.30,3.63)	3.29 (1.94,5.60)	1.75 (1.08,2.83)	1.53 (0.96,2.44)	1.31 (0.79,2.15)
p [‡]	< 0.001	< 0.001	< 0.001	< 0.001	0.18
Family history of DM2					
No*	1.00	1.00	1.00	1.00	1.00
Yes	1.12 (0.84,1.51)	1.27 (0.98,1.64)	1.03 (0.80,1.32)	1.00 (0.74,1.36)	0.88 (0.68,1.15)
p [‡]	0.02	0.02	0.95	0.09	0.21
Males					
Body mass index					
Normal*	1.00	1.00	1.00	1.00	1.00
Overweight	1.01 (0.74,1.39)	1.88 (1.35,2.62)	1.84 (1.28,2.60)	1.38 (0.99,1.93)	0.85 (0.60,1.20)
Obesity	2.10 (1.39,3.18)	3.51 (2.37,5.20)	4.71 (3.13,7.09)	2.43 (1.62,3.64)	1.67 (1.09,2.56)
p [‡]	< 0.001	< 0.001	< 0.001	< 0.001	0.35
Family history of DM2					
No*	1.00	1.00	1.00	1.00	1.00
Yes	1.16 (0.90,1.48)	1.28 (0.97,1.70)	0.89 (0.69,1.17)	0.99 (0.74,1.27)	0.73 (0.54,1.00)
p [‡]	0.39	0.02	0.43	0.27	< 0.001

The regression models were adjusted by age and housing

* Reference category

‡ p values for test for tendencies

estimate the prevalence of abnormal concentrations of glucose, insulin and lipids. However, total cholesterol concentrations from this study are remarkably similar to those found for Mexican-Americans participating in NHANES.³⁵ The companion paper, reporting the distribution of dyslipidemias in adults (see Barquera et al), found a prevalence of >60% for males and females with HDL-cholesterol values <40 mg/dL, and >70% for individuals between 20 and 29 years of age. The prevalence of this abnormality was not significantly associated with obesity. However, in our sample, the mean concentrations of HDLc were significantly lower in non-obese subjects than in those who were overweight and obese. In addition, there was no reason to assume that the distribution of fasting/non fasting cases varies across BMI groups; thus, it is believed that the observed associations are not biased.

The interpretation of TG data in our study must be carefully considered since TG serum concentration increases in the absorptive state. On the other hand, serum HDLc concentrations show negligible changes in the absorptive state.^{36,37}

In summary, our findings support the notion of a relevant association between obesity at these early ages and the development of alterations in the components of metabolic syndrome. These findings must be included in the development of informed interventions through primary prevention aimed at the prevention and reduction of cardiovascular risk factors.

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