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ARÁN

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Trabajo Original

Obesidad y síndrome metabólico

Acantosis nigricans is associated with risk factors related to cardiovascular disease in Mexican children with obesity

La Acantosis nigricans *se asocia con factores de riesgo para enfermedades cardiovasculares en niños mexicanos con obesidad*

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Abstract

Introduction: The prevalence of obesity in Mexican children has increased during the last decade, as has the risk of early onset metabolic disorders and cardiovascular disease.

Objective: To determine the association of *Acantosis nigricans (AN)* with dyslipidemia, high blood pressure, body mass index (BMI), and risk factors related to eating behavior in overweight and obese children.

Patients and methods: This transverse analytical study, conducted in two Mexico City primary schools, included 300 boys and girls. Information was gathered on hereditary and perinatal background. A physical examination provided data on the presence/absence of *AN*, blood pressure, weight and height. The BMI and Z-score were calculated. The serum concentration of glucose, cholesterol and triglycerides was quantified and the lipoprotein profile determined.

Results: The prevalence of AN was 41.7%. An association was found between *AN* and risk factors for cardiovascular disease, including BMI (rS 0.432; $p < 0.0001$), systolic and diastolic blood pressure above the 90th percentile (rS 0.231, $p < 0.0001$; rS 0.128, $p = 0.026$; respectively), hypertriglyceridemia (rS 0.156; $p = 0.007$), and low levels of cHDL (rS -0.160; $p = 0.006$). *AN* was also associated with risk eating behavior, including dieting to lose weight ($p = 0.004$), losing control over eating ($p = 0.023$), and body fat percentage above the 90th percentile ($\chi^2 = 35.1$; $p = 0.0001$). No association was observed between *AN* and serum glucose concentration (rS -0.018; $p = 0.759$). Logistic regression analysis demonstrated an association of *AN* with a low concentration of cHDL (RM: 1.726; $p = 0.041$) and a high percentage of body fat (> 48%) (RM: 3.591; $p = 0.001$).

Conclusion: A high prevalence of *AN* was found in overweight and obese children. There was an association between *AN* and risk factors of cardiovascular disease, including Z-score, BMI, dyslipidemia, and high blood pressure.

Key words:

Acantosis nigricans. Dyslipidemia. Body mass index. Overweight. Obesity, Mexico.

Resumen

Introducción: la mayor prevalencia de obesidad en la población infantil mexicana durante la última década incrementa el riesgo de presentar trastornos metabólicos y enfermedades cardiovasculares a edades cada vez más tempranas.

Objetivo: determinar la asociación entre *Acantosis nigricans (AN)* con dislipidemia, hipertensión arterial, índice de masa corporal (IMC) y conductas alimentarias de riesgo en niños con sobrepeso y obesidad.

Pacientes y métodos: estudio transversal analítico realizado en dos escuelas públicas de la zona metropolitana de la ciudad de México donde participaron 300 niños, de ambos sexos, obteniéndose información de los antecedentes heredofamiliares y perinatales. Con la exploración física se valoró la presencia o ausencia de *AN* y presión sanguínea. Se pesó y midió a los escolares, se calculó el IMC y se estimó su puntaje Z. Se cuantificó la concentración sérica de glucosa, colesterol, triglicéridos y perfil de lipoproteínas.

Resultados: la prevalencia de *AN* fue 41,7%, al determinar la asociación entre la *AN* y los factores de riesgo cardiovascular, se identificó una asociación con el IMC (rS 0.432; $p < 0.0001$), entre las cifras de presión arterial sistólica y diastólica por encima del percentil 90 (rS 0.231; $p < 0.0001$) y (rS 0.128; $p = 0,026$) respectivamente, la hipertrigliceridemia (rS 0.156; $p = 0.007$), las bajas concentraciones de colesterol de lipoproteínas de alta densidad (cHDL) (rS -0,160; $p = 0,006$), así como la existencia de los trastornos de la conducta alimenticia; haber realizado dietas $p = 0.004$, ha perdido el control de lo que come $p = 0,023$ y cuando el porcentaje de grasa corporal fue superior al percentil 90, $\chi^2 = 35.1$; $p = 0.0001$, no se observó asociación con la concentración sérica de glucosa (rS -0.018; $p = 0,759$). En el análisis de regresión logística se observó que la presencia de AN mostró una asociación con las menores concentraciones de cHDL (RM: 1.726; $p = 0,041$) y con el porcentaje de grasa corporal (> 48%) (RM: 3.591; $p = 0,001$).

Conclusión: se observó una alta prevalencia de *AN* en niños con sobrepeso u obesidad y su asociación con factores de riesgo cardiovascular: puntaje Z del IMC, dislipidemia y las cifras tensionales elevadas.

Palabras clave:

Acantosis nigricans. Dislipidemia. Índice de masa corporal. Sobrepeso. Obesidad. México.

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INTRODUCTION

Overweight and obesity are defined as an abnormal or excessive accumulation of fat that implies a health risk. This phenomenon affects children as well as adults and is associated with the premature onset of chronic uninfectious diseases. In fact, some diseases before found only in adults, such as diabetes mellitus type 2 (DM-2) and high blood pressure, in some cases now appear very early in life (1,2).

Childhood obesity is one of the gravest public health problems of the 21st century, having become an emerging global epidemic that implies immediate and long-term effects. It is estimated that the percentage of obese children and adolescents has increased almost 50% in the last 20-30 years. In 2010 it was calculated that there were approximately 42 million overweight children in the world, of which about 35 million lived in developing countries. The Organization for Economic Cooperation and Development (OECD) classified Mexico as having the first place worldwide in overweight children (3).

This relatively recent, substantial increase in overweight and obese children does not bode well for the future, as these children have an eight-fold greater risk of remaining overweight or obese as adults. Indeed, 50% of children who are obese at 6 years of age and 80% of obese adolescents remain obese in adulthood (4,5). These children and adolescents also have a greater probability of early onset metabolic disorders (*e.g.,* dyslipidemia, insulin resistance, glucose intolerance and DM-2), some types of cancer, degenerative cardiovascular disease, dermatological/neurological/endocrine disorders, as well as alterations in the respiratory system, gastrointestinal tract and locomotor apparatus (6,7). All of these disorders involve, to a greater or lesser extent, a shorter life expectancy and a lower quality of life, and all are for the most part preventable (8). As can be seen, the importance of overweight and obesity go far beyond problems of self-image.

In Mexico the national prevalence of overweight and/or obese children in 2012 was estimated by the World Health Organization (WHO) to be 34.4% (19.8% for overweight and 11.8% for obesity), including 32% for Mexican girls (20.2% for overweight and 14.5% for obesity) and 36.9% for Mexican boys (19.5% for overweight and 17.4% for obesity) (9). This prevalence of obesity in Mexico is very similar to that of the United States and Chile. Furthermore, the rate of increase in childhood obesity in Mexico is greater than that seen in developed countries and other developing countries.

Generally, efforts to prevent and detect risk factors for chronic degenerative diseases, such as hypertension and DM-2, are aimed at adults. Therefore, risk factors tend to be identified once the damage is already done. However, the underlying problems exist in obese children and adolescents, giving rise to a deleterious, progressive and systemic effect that begins as subtle and undetectable changes in individuals with a normal and asymptomatic appearance (10). Hence, early detection of the presence and possibly the development of this series of disorders by non-invasive markers is of utmost importance to be able to intervene at an early stage in the population at risk and thus avoid greater complications later on (11).

In 2000, the American Diabetes Association established *Acantosis nigricans* (AN) as one criteria for identifying children at risk for DM-2. The increased incidence of AN runs parallel with that of obesity. Moreover, the diagnosis of AN is clinical, being formed by symmetrical, hyperpigmented, hypertrophic and varicose plaques that are in some cases papilloma. These skin areas appear velvety in texture and brownish-black in color, and are most commonly found on the underarm, back of the neck, flexing points of the upper and lower limbs, the naval, groin, breast folds, face, as well as peribuccal and perianal regions. The most common areas to find these skin blotches is on the back or side of the neck. *AN* is reportedly heavily influenced by genetic factors, being frequently found with Hispanic, Afro-American and Indian people, and infrequently encountered with Caucasians. This dermatological condition is associated with insulin resistance and metabolic disorders, and is known to be a good predictor of hyperinsulinemia, which can lead to DM-2 (12-14).

The prevalence of *AN* varies according to ethnic origin, with an incidence of 13% in blacks, 5% in Hispanics, and less than 1% in Caucasians. Gender and age are not risk factors. In adolescents with more than 200% of normal body weight, the prevalence of *AN* is 66% (15). This skin condition is now common in young people, especially in populations with a high prevalence of DM-2. Hence, this clinical condition may constitute a simple, economical and non-invasive technique for detecting hyperinsulinemia and the propensity for DM-2 and/or metabolic syndrome, especially in children. Its simplicity and low cost make it ideal for detection of these disorders in low income or marginalized communities, advantageous in relation to the traditional test for glucose tolerance or the determination of postprandial glucose or serum insulin (15,16).

Eating habits are formed for biological, psychological and cultural reasons, and when these habits alter normal metabolism they can represent a risk factor for obesity. It has been documented that poor eating habits that lead to overweight and obesity in adolescents are related to eating while doing other activities, such as watching TV, playing computer games, doing homework and working, as well as with prolonged fasts and an obsessive preoccupation with getting fat. Although poor eating habits probably begin in childhood, they are more evident in adolescence (19,20).

In spite of the aforementioned evidence, few studies have considered the role of body weight in the development of AN, or the latter as an independent marker of insulin resistance in school-age children (5-11 years old). The increased incidence of *AN* in the pediatric age parallels the rise in obesity, endocrine pathologies, genetic syndromes, DM-2, dyslipidemia, polycystic ovary syndrome, hypertension, and insulin resistance, the latter not necessarily associated with obesity (16). Consequently, the increase in prevalence of overweight and obesity in Mexican children during the last two decades could possibly be related to the risk of a higher rates of insulin resistance and metabolic syndrome at an ever younger age. On the other hand, it should be pointed out that overweight and obesity have social and emotional implications that are immediate, affecting the quality of life of the

child or adolescent in question, independently of the effects on physical health.

The aim of the present study was to determine whether, in a group of Mexican school children that reside in Mexico City, *AN* is associated with the Z-score of the body mass index (BMI), dyslipidemia, waist circumference, blood pressure and/or risk factors related to eating behavior.

MATERIAL AND METHODS

This is a transversal analytical study carried out from October of 2012 to June of 2013, with the participation of the Regional General Hospital (Hospital General Regional #196 of the Instituto Mexicano de Seguro Social), the National Institute of Perinatology (Instituto Nacional de Perinatología de la Secretaría de Salud) and the Superior School of Medicine (Escuela Superior de Medicina del Instituto Politécnico Nacional). After receiving permission from the school authorities, all students of the fourth, fifth and sixth grades on the morning shift of two primary schools were invited to participate in the study. Exclusion criteria included any chronic disease or any child under medication.

SUBJECTS

Based on a table of random numbers, statistical sampling was carried out in order to obtain a subset of the total population with characteristics similar to those found in each school grade. For this purpose, we used a list of students enrolled in the two schools involved in the present study, with a substitution technique in case a selected student did not want to participate. The sample had the following distribution: 79 (4^{th} grade), 110 (5^{th} grade) and 111 (6^{th} grade), with 133 boys and 167 girls from 9-11 years old. Informed consent was obtained from the parents or tutor, with the informed approval of the participating child. The protocol was approved by the Ethics in Research Committee of the Instituto Mexicano del Seguro Social. A clinical history was recorded for each child, with emphasis on hereditary family background as well as prenatal and pathological information.

Medical personnel carried out a physical examination. A family doctor and a pediatrician evaluated the presence/absence of *AN* in five distinct anatomical regions: on the back of the neck, underarms, the internal flexing areas of the elbows and knees, and the naval. The children were then divided into those with and without *AN* (*AN*+ and *AN*-).

ANTHROPOMETRIC MEASUREMENTS

Evaluation of body weight (kg) was done with a portable digital scale (SECA, model 803, with precision of 100 g). Height measurements (m) were made to 0.1 cm accuracy with a stadiometer (SECA, model 0123). Anthropometric measurements included the circumference of the waist and hip (cm), made with a medical tape measure (SECA, model 200), according to the criteria proposed by the WHO (17). The BMI was calculated with the Quetelet formula (weight in kilograms divided by the height in meters squared). The Z-score for age was also calculated according to the WHO standard, classifying the school children as normal (≤ 1) overweight (> 1 and ≤ 2) or obese (> 2). Z-scores were considered valid between -5.0 and +5.0.

Body fat was determined by measuring body perimeters by using a tape measure with 1 mm accuracy (Sanny medical). Measurement of fat folds was performed with a Vernier caliper (Harpenden). These non-invasive measurements were taken in the schools, averaging 4-5 minutes for each child. The protocols for these measurements were in accordance with the requirements of the International Society for the Advancement of Kinanthropometry.

CLINICAL EVALUATION

Blood pressure was determined after at least 10 minutes of rest, using a sphygmomanometer, a cuff adequate for the children and their complexion, and a stethoscope (Riester). The method utilized was auscultatory, since the records obtained were evaluated with the tables of the National High Blood Pressure Education Program. The pressure hoses used covered 2/3 of the arm, from the olecranon to the shoulder, and the inflatable cuff covered 80% of the circumference of the arm. Measurements were made in the morning, with the child seated, leaning on the backrest of the chair, feet on the floor and the right arm extended. The systolic and diastolic blood pressure (SBP and DBP) were recorded, utilizing the Korotkoff phases I and V as a reference, respectively. The measurement was taken three times because generally the readings tend to stabilize by adaptation of the child to the method and the corresponding diminishment of his/her anxiety. The latter two readings were averaged for the final value. In case the blood pressure reading was elevated, the parents were informed and it was recommended that they visit their pediatrician or family doctor.

The tables of blood pressure of the National High Blood Pressure Education Program were used as the criterion of classification, adjusting the percentile according to height and gender. Consequently, children with blood pressure below the 90^{th} percentile of the standard were considered to have normal blood pressure, while those from the 90^{th} to 94^{th} percentile were classified as pre-hypertensive and those from the 95^{th} percentile and above as hypertensive (18).

BIOCHEMICAL PROFILE

After a fast of 12 hours, with previous asepsis, blood samples were taken by venipuncture with the system of a Vacutainer vacuum. The tubes with blood were centrifuged for 10 min at 3,500 rpm to obtain serum, which was stored in different aliquots at -70 °C to await processing. In these serum samples, the concen-

tration of glucose (mg/dL), triglycerides (mg/dL) and cholesterol (mg/dL) was quantified with colorimetric enzymatic methods. cHDL (mg/dL) was evaluated by using a kit (HDL-Cholesterin/cholesterol, Roche Diagnostics).

EVALUATION OF RISK FACTORS RELATED TO EATING BEHAVIOR

Risk factors related to eating behavior were determined with the diagnostic criteria for eating disorders proposed by the *Diagnostic Manual and Statistics of Mental Disorders IV*. The resulting values were evaluated with the scale validated by Unikel et al. in a Mexican population. The results of using this scale have shown a reliability, according to Cronback's alpha, of 0.83 for women in Mexico City and 0.72 for women in the Mexico State (19).

This scale consists of 10 questions that evaluate the preoccupation with getting fat and other risk factors related to eating behavior in the three months prior to the survey. The answers were based on four Likert-type options (never or almost never = 0, sometimes = 1, frequently but less than two times per week = 2, very frequently or more than 2 times per week = 3 points). The degree of risk was scored as follows: less than 7 was considered to be without risk, 7-10 as moderate risk and > 10 high risk (19,20).

SOCIOECONOMIC LEVEL

This factor was determined by an interview with one of the parents or the tutor of each child, according to the standards of the Mexican Association of Market Research and Public Opinion (21). The interview consisted of 10 questions to establish scoring and overall classification in one of 6 levels of the standard of living: A/B = the highest, C+ = slightly above average, C = average, D+ = slightly below average, D = low or austere, and E = the lowest.

STATISTICAL ANALYSIS

A descriptive analysis was performed, utilizing absolute and relative (percentages) frequencies as well as the mean and standard deviation of quantitative variables to determine statistical difference and to test the hypothesis. The Shapiro Wild test was used to determine normal distribution of the sample. The Spearman's rank correlation for independent samples was employed to compare the groups. To evaluate the possible association between variables, the χ^2 non-parametric test of independence was applied. For non-parametric correlations, multiple logistical regression analysis was used. For analysis of multiple regression, all variables of confusion or modifiers of effect were included. Statistical significance was considered with $p < 0.05$. The information was recorded in the Microsoft EXCEL program and analysis was carried out in the SPSS version 15 for the Windows statistical program.

ETHICAL ASPECTS

Data gathering and analysis was confidential, taking into account ethical questions related to autonomy, information and security. The findings of the present study were included in a pamphlet given to all participants. The aim of this pamphlet was to provide guidelines for good eating habits in order to help the parents to establish good nutrition for their children. The present study was carried out following the guidelines established by the Official Mexican Norm (NOM-043-SSA2-2005) of the Secretary of Health in Mexico (22).

RESULTS

Of the 300 school children that participated in the study, 55.7% (167) were girls and 44.3% (133) were boys. Regarding socioeconomic level, 18 (6%) corresponded to a low or austere standard of living, 160 (53.3%) to an average level and 122 (40.7%) to a level slightly above average. Weight classification of the children was determined with the Z-score of the BMI according to age and gender, as proposed by the WHO, finding a 39.7% prevalence of obesity (119), 18.7% (56) overweight, 40.3% (121) normal and 1.3% (4) underweight. Overweight and obesity was more common among the girls (Table I).

The perinatal background of the children, according to information gathered from the mothers, indicated that at the time of birth the average number of weeks of gestation (WOG) was 38.4 ± 2.3%, with a weight of 3.183 ± 516 g, and a height of 49 ± 4.3 cm. Exclusive breastfeeding lasted an average of 8.5 ± 6.6 months, and for 20.7% (62) it lasted less than 3 months.

The average age of the mothers at the moment of the study was 35.7 ± 5.6 years, while that of the fathers was 35.7 ± 11.4 years, with 62.7% (188/300) of the mothers and 67.5% of the fathers having finished middle school. It was observed that 64.3% (193/300) of the mothers were overweight or obese and 71.2% (200/300) of the fathers, and that 36.7% (110/300) of both parents worked. Regarding the immediate family, there was a background for 53.3% (160/300) of the children of obesity, for 59.3% (178/300) of DM-2, and for 67.3% (202/300) of systemic high blood pressure.

Table I. Weight classification according to the Z-score of the BMI, considering age and gender

Weight classification	Boys n = 133 (%)	Girls n = 167 (%)	Total n = 300 (%)
Underweight	1 (25.0)	3 (75.0)	4 (1.3)
Normal	52 (43.0)	69 (57.0)	121 (40.3)
Overweight	21 (37.5)	35 (62.5)	56 (18.7)
Obese	59 (49.6)	60 (50.4)	119 (39.7)
Total	133 (44.3)	167 (55.7)	300 (100.0)

$\chi^2 = 3.08$; $p = 0.379$.

The average values of parameters for the children was the following: age, 10.1 ± 0.7 years; weight, 42.8 ± 10.9 kg; height, 143 ± 8 cm; BMI, 20.5 ± 3.8 kg/m^2; waist circumference, 68.8 ± 10.6 cm; hip circumference, 81.1 ± 8.9 cm; serum glucose, 98.5 ± 11.8 mg/dL; and serum cholesterol, 176.4 ± 48 mg/dL. There was glucose intolerance in 6 children and DM-2 in no children.

Regarding gender, there were no significant differences in any of the anthropometric, clinical or biochemical variables. Therefore, all of the children were included in the analysis of the association between variables, without carrying out stratification by gender.

AN was found in 41.7% (125) of the children, of which 37.6% (47/125) were overweight and 54.4% (68/125) obese. With a greater BMI there was a greater frequency of *AN*, while in the children with normal weight for their height, no *AN* was found. The children with *AN* not only had a tendency to higher weight but also lower height compared to the children without *AN* (see Table II).

Blood pressure was above the 90th percentile in 10.8% of the children. This high level of blood pressure was found in 6.5% of the children with normal BMI, 9% of those overweight, and 21% of those with obesity.

Serum cholesterol concentration was similar in the children with and without *AN*, while triglyceride concentration was much higher and cHDL concentration lower in the children with *AN* (Table II).

There was an association between *AN* and the following behavior: being preoccupied with getting fat ($\chi^2 = 4.09$; p = 0.043), dieting to lose weight ($\chi^2 = 8.2$; p = 0.004), losing control over eating ($\chi^2 = 5.13$; p=0.023), and a percentage of body fat above the 90th percentile ($\chi^2 = 35.1$; p = 0.0001) (Table III). No association was observed between *AN* and the length of breastfeeding, the weight of the parents, if both parents were working, if the parents did regular exercise, or a family background of DM-2, hypertension or obesity.

Table III. Association between the presence of *Acantosis nigricans* and risk factors in relation to eating behavior, n(%)

Risk factors	*Acantosis nigricans*		p
	Yes n = 125	No n = 175	
Preoccupation with getting fat	102 (34.0%)	125 (41.7%)	0.043
Dieting to lose weight	56 (18.7%)	50 (16.7%)	0.004
Losing control over eating	42 (14.0%)	38 (12.7%)	0.023

Table II. Anthropometric, clinical and biochemical characteristics of the school children under study, both with and without *Acantosis nigricans*

Variables	Total (mean ± SD)	With *AN* n = 125	Without *AN* n = 175	p
Age	10.1 ± 0.7	10.1 ± 0.7	10.06 ± 0.8	0.199
Anthropometric evaluation				
Weight (kg)	42.8 ± 10.9	48.1 ± 11.1	39.0 ± 9.2	< 0.0001
Height (m)	1.43 ± 0.08	1.45 ± 0.08	1.41 ± 0.08	< 0.0001
BMI (kg/m^2)	20.5 ± 3.8	22.5 ± 3.7	19.2 ± 3.3	< 0.0001
Waist circumference (cm)	69.0 ± 9.8	73.7 ± 9.9	65.7 ± 8.2	< 0.0001
Hip circumference (cm)	81.1 ± 8.9	85.2 ± 8.6	78.2 ± 7.8	< 0.0001
% of body fat	47.9 ± 10.0	52.3 ± 8.5	44.8 ± 9.9	< 0.0001
% of body fat in girls	48.9 ± 9.1	52.3 ± 7.9	46.6 ± 9.3	< 0.0001
% of body fat in boys	46.7 ± 10.9	52.3 ± 9.2	42.5 ± 10.3	< 0.0001
Blood pressure				
Blood pressure (mmHg)		81 ± 28	75 ± 12	0.013
Systolic (mmHg)	97.6 ± 14.7	101.1 ± 14	95.1 ± 14	< 0.0001
Diastolic (mmHg)	66.1 ± 12.3	67.8 ± 12	64.9 ± 12	0.044
Biochemical parameters				
Glucose (mg/dL)	98.5 ± 11.8	98.1 ± 11.4	98.8 ± 12.1	0.592
Cholesterol (mg/dL)	176.4 ± 48.0	173.3 ± 46.9	178 ± 50.4	0.342
Triglycerides (mg/dL)	118.3 ± 53.2	130.4 ± 57.8	110.2 ± 47.3	0.001
cHDL (mg/dL)	58.9 ± 12.6	46.2 ± 10.6	50.9 ± 13.6	0.001
cLDL (mg/dL)	103.8 ± 42.4	101.4 ± 40.9	105.7 ± 43.4	0.350

There was an association between *AN* and the BMI (rS 0.432; p < 0.0001), systolic blood pressure (rS 0.231; p < 0.0001), diastolic blood pressure (rS 0.128; p = 0.026), hypertriglyceridemia (rS 0.156; p = 0.007), and level of cHDL (rS -0.160; p = 0.006). No association was found between *AN* and the concentration of serum glucose (rS -0.018; p = 0.759) or low-density lipoprotein cholesterol (cLDL) (rS -0.042; p = 0.472) (Table IV).

The risk of having *AN* increased with a lower concentration of cHDL (RM: 1.726; p = 0.041) and a greater percentage of body fat (RM: 3.591; p = 0.001), according to calculations based on logistical regression (Table V).

DISCUSSION

Obesity is a public health problem that has currently become a worldwide epidemic. *AN* is now frequently found in children and adolescents, especially in populations with a high prevalence of obesity, insulin resistance and DM-2. Therefore, the present study explored the possible association of *AN* with the latter medical conditions, as well as the possibility of using *AN* as a marker so that family doctors and general practitioners can identify obesity in school children in a timely manner. This would allow for preventative measures to be implemented against the development of cardiovascular disease and DM-2 in overweight and obese children (23,24).

The incidence of *AN* in children has increased together with that of obesity and insulin resistance. For this reason, the American Diabetes Association has recommended the early detection of *AN* as a criterion for identifying children at risk for developing DM-2. The prevalence of *AN* in the present study was 41.7%, greater than that reported by Stoddart et al., who found 34.2% *AN* in a Cherokee Indian population (25). Meanwhile, Mukhtar et al. documented an 18.9% prevalence of *AN* in obese adolescents in New Mexico (26), Nguyen et al. reported 25% of *AN* in overweight Afro-American children (27), and Stuart et al. found 38% of *AN* in Native Americans (28). On the other hand, Thivel D and Maisonneuve B have reported the prevalence of *AN* to be as high as 68 and 69.9%, respectively, in obese children (29,30). These differences in prevalence of *AN* have been related to the proportion of overweight and obesity in the groups under study.

With the presence of *AN* associated with obesity, there are important alterations in the metabolism of lipids. A group of children with *AN* in a previous study showed signs of greater risk for the development of atherosclerosis and cardiovascular disease (31). When comparing the children with and without *AN* in the present study, there was a lower serum concentration of cHDL (c-HDL 46 ± 10 *vs.* 50 ± 13 p = 0.001) and a higher serum concentration of triglycerides (129 ± 58 *vs.* 110 ± 47 p = 0.002). Numerous studies have demonstrated the association between the risk of developing cardiovascular disease and low serum concentrations of cHDL (32) as well as hypertriglyceridemia. The latter condition gives rise to changes in the composition of cLDL, favoring the appearance of phenotype B that is characterized by the presence of small cLDL, which is more susceptible to oxidation and therefore can lead to atherosclerosis (33,34).

One of the most relevant findings of the present study is the early age (10.1 ± 0.7 years) at which a group of children with obesity and *AN* were found to have hypertriglyceridemia as well

Table IV. Bivariate association between *Acantosis nigricans* and distinct risk factors (Spearman's rank correlation)

Variable	Spearman's rank correlation r	p
Weight	0.418	< 0.0001
Height	0.218	< 0.0001
BMI	0.432	< 0.0001
Waist circunference	0.429	< 0.0001
Systolic blood pressure	0.231	< 0.0001
Diastolic blood pressure	0.128	0.026
Glucose	-0.018	0.759
Triglycerides	0.156	0.007
cHDL	-0.160	0.006
cLDL	-0.042	0.472

Table V. Variables associated with the presence of *Acantosis nigricans*

Variable	Beta	RM	IC 95%	p
Losing control over eating	0.362	1.436	0.815-2.529	0.210
Dieting to control weight	-0.282	0.754	0.442-1.288	0.310
Low concentration of cHDL	0.546	1.726	1.024-2.911	0.041
High level of body fat (> 48%)	1.279	3.591	2.011-6.414	0.001
High systolic blood pressure (> 100 mmHg)	0.442	1.558	0.899-2.691	0.114
High concentration of triglycerides (> 100 mg/dL)	-0.140	0.607	0.510-1.482	0.607
Constant	-1.403	0.246		0.001

The other variables were not significant in the model.

as a reduced concentration of serum cHDL and a high concentration of cLDL, which probably will favor the development of cardiovascular disease at a very early age. This observation is in agreement with Fishbein in the United States (35). Additionally, the alterations found in the profile of lipoproteins is also in accordance with Skhonthachit P et al. in Thai children (36) and with Boyd GS et al. (37), who both found a high prevalence of dyslipidemia in overweight and obese children and adolescents.

The existence of dyslipidemia is often reported in the many studies that have provided evidence of the association between obesity and the risk of cardiovascular disease. Within this context, the greatest prevalence found has been hypertriglyceridemia. Almost 1 of 2 children in the present study presented concentrations of triglycerides in the range considered as high risk, while 1 of 3 children showed hypercholesterolemia and 1 of 4 mixed dyslipidemia. This fact should be alarming to the authorities in the area of public health due to the combination of obesity and an alteration in the profile of lipids in a significant percentage of children, leading to a high risk of cardiovascular and metabolic diseases at an early age (38). For this reason, children with obesity should be a target group for the implementation of measures aimed at diminishing the aforementioned metabolic alterations. Such measures should include the modification of eating habits and lifestyle (including more exercise) in order to attain a loss of weight. Additionally, there should be constant monitoring of the lipid profile in obese children and adolescents, especially if they have *AN*, as recommended by the American Heart Association (39).

On the other hand, there is a widely recognized relation between systemic high blood pressure and obesity caused by poor diet and lack of exercise. A greater percentage of obesity has been found among a population of hypertensive children and adolescents in Cuba. Furthermore, with a reduction in weight, blood pressure was normalized in this population. Nevertheless, there are few studies that take into account the relation between the degree of obesity, time of evolution, the age of appearance, and the distribution of body fat in obese and hypertensive children and adolescents.

Different studies have shown the relation of obesity in children/adolescents with systemic high blood pressure, especially in those with a greater degree of obesity and lipid anomalies. The present study demonstrates higher blood pressure in children with obesity and *AN* than in children with normal weight. The greatest difference was found in systolic blood pressure, in accordance with the study by Dong B et al. on children and adolescents in China (40), by Chiolero A. on children of the Republic of Seychelles in Africa (41), by Moser on Brazilian children (42), and by Hoog who studied the association between blood pressure and BMI in children from different ethnic groups (43).

In the present study, 10.8% of the children had systolic or diastolic blood pressure above the 90th percentile, a figure slightly less than that reported by Bojórquez Díaz et al. (44), who detected high blood pressure in 12.7% of primary school children in the State of Sonora, Mexico. However, the figure from the present study is higher than the 7.6% reported by Salvadori et al. (45) in a study on rural children in Canada and the 4.2% of children from 5 to 12 years old and 6% of adolescents from 13 to 18 years old found by Díaz (46) in a study in Argentina. Additionally, in Cuba Suárez Cobas et al. (47) reported a group of adolescents with high blood pressure above the 90th percentile, made up of 7.6% boys and 2.4% girls from 15 to 17 years old, while in the city of Merida, Venezuela, there were 6.3% of adolescents from 15 to 17 years old (48) with this condition, and in Spain 1.7% of boys and the 3.05% of girls (49). Hence, the prevalence of obesity in the present study and a previous study in Mexico is higher than that found in children of Canada, Argentina, Venezuela and Spain. Due to the foreboding presence of high blood pressure at such an early age in Mexico, especially when found in overweight and obese children, an early detection of obesity and high blood pressure is of great importance since these conditions increase the risk of health problems in adolescence and early adulthood (50).

On the other hand, the present study confirmed the positive and significant association of *AN* with obesity (percent of body fat) and dyslipidemia (low cHDL), based on the statistical analysis with the Spearman's rank correlation and multiple logistical regression (RM: 3.591; $p = 0.001$, RM: 1.726; $p = 0.041$; respectively). This suggests that *AN* reflects the increase in obesity in Mexico, which is a risk factor for cardiovascular disease and is associated with dyslipidemia, high blood pressure and a greater risk of developing DM-2 (38,39).

Regarding risk factors in relation to eating behavior, the present study evidences the greater prevalence of *AN* among those that worry about getting fat, that had dieted to lose weight, and were not able to control what they eat, confirming a study on a group of adolescents (20). However, it should be stated that poor eating habits are often accompanied by an inadequate weight, including overweight and obesity, and that this is in turn associated with the alteration of hormones like insulin that are known to provoke the development of *AN* (11). The only variables associated with *AN* in the present study were low cHDL and a high percentage of body fat.

In summary, the results of the present study highlight the high prevalence of *AN* in overweight and obese children, and its association with two risk factors for cardiovascular disease, the distribution of body fat and dyslipidemia. This suggests that it is necessary to take early preventative measures, such as carrying out a follow-up in relation to the high risk that these children will later develop DM-2, other metabolic disorders, and/or cardiovascular disease. Such measures would represent an improvement in the medical attention and quality of life for Mexican children.

One of the limitations of the present study is that the data do not come from a representative sample of all children of primary schools of Mexico. Nonetheless, the sample is made up of a homogeneous population in a certain age group. Another limitation of this study was the fact that the serum concentration of insulin was not determined, and that information was not gathered in regard to the physical activity of the children.

These limitations could in part be overcome by carrying out a follow-up prospective cohort study of this population to see if they indeed develop DM-2, atherosclerosis, and/or polycystic ovary syndrome. In spite of the limitations of the present study, one of the main contributions is the association found of *AN* with obesity, certain risk

factors for cardiovascular disease, and metabolic disorders in children, who are one of the most vulnerable groups of the world population.

CONCLUSION

A*cantosis nigricans* is easy to evaluate in a clinical setting. The present study found a high prevalence (41.7%) of AN in overweight and obese children. Certain variables were associated with the presence of *AN*, including a low concentration of cHDL, a high percentage of body fat, and high blood pressure, but not eating behavior disorders.

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CONFLICT OF INTEREST

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