International Journal of Contemporary Pediatrics
*Caballero-Noguez B et al. Int J Contemp Pediatr. 2020 Dec;7(12):2255-2259*
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20204941

**Original Research Article**

# Blood glucose levels in children with acanthosis nigricans associated with obesity

**Bonifacio Caballero-Noguez[1]*, Marco A. Cardoso-Gomez[2], Maria L. Ponce-Lopez[2], Antonio Mendez-Duran[3], Ulises Reyes-Gomez[4]**

[1]Obstetric and Perinatal Care Division, [3]Medical Care Unit, Mexican Social Security Institute, Mexico City, Mexico
[2]Faculty of Higher Studies (FES) Zaragoza, National Autonomous University of Mexico, Mexico City, Mexico
[4]Mexican Academy of Pediatrics, Mexico City, Mexico

**Received:** 15 October 2020
**Revised:** 26 October 2020
**Accepted:** 27 October 2020

***Correspondence:**
Dr. Bonifacio Caballero-Noguéz,
E-mail: bonicaballero1@gmail.com



## ABSTRACT

**Background:** A body mass index ≥95 percentile increases 40 times the risk of diabetes. The hyperinsulinemia secondary to the resistance of insulin and obesity is associated to the development of acanthosis nigricans. The objective of current study was to associate acanthosis nigricans with childhood obesity with alterations in the curve of glucose tolerance.
**Methods**: In current study 90 children were evaluated with obesity and acanthosis nigricans of which only 34 concluded the study. Glucose, cholesterol and triglycerides levels were determined while in fasting state, and glucose tolerance curve was conducted. The statistical analysis was done by determining $X^2$, Fisher´s test and U, Mann Whitney test.
**Results**: Statistically significant difference was found between glucose levels at 2 hours and the presence of obesity and acanthosis nigricans ($p<0.01$).
**Conclusions**: It is important that all the children with obesity and Acanthosis nigricans apply for a curve of glucose tolerance.

**Keywords:** Childhood obesity, Overweight, Acanthosis nigricans, Type 2 diabetes mellitus, Body mass index

## INTRODUCTION

Recent studies show that the incidence and prevalence of obesity has alarmingly increased in the past 60 years and has since become an epidemic in the last 20 years, ranging from 10 to 20% in childhood and 30 to 40% in adolescents. In Mexico, the National health and nutrition survey (ENSANUT) conducted in 2018 found that the prevalence of overweight in children between 5 and 11 years of age was 18.1% and 17.5% for obesity, with a combined prevalence of 35.6% and, according to the type of locality, a combined prevalence of 37.9% for the urban region and 29.7% for the rural region.[1]

In reference to ENSANUT 2018, the combined prevalence of overweight and obesity in girls was 32.8% and 33.7% in boys, while the obesity figures are currently increasing significantly in this age group.[2]

Childhood obesity is a function of genetic predisposition, habits and customs of the family organization and of the city or place where one lives, the availability, costs and ease of acquiring food, public health policies and the possibility of exercising in open spaces, since all of these predisposes children to develop unhealthy behaviors and to live in obesogenic environments.[3,4]

The implications of obesity in school-age girls and boys are increased blood pressure, increased blood lipids, altered metabolism, high blood glucose, low self-esteem and distorted body image.[5,6]

Therefore, obese children are at higher risk for developing type 2 diabetes mellitus (T2DM), insulin resistance, respiratory diseases, psychological problems, some malignancies, orthopedic problems and cardiovascular disease. Currently, T2DM is increasing dramatically in children in parallel with pediatric obesity.[7] Obesity has been associated with insulin resistance and hyperinsulinemia in multiple studies.[8] It is estimated that 90% of T2DM cases are attributable to obesity.[9]

The risk of developing T2DM progressively increases as the body mass index (BMI) increases. Thus, the risk of developing T2DM is 40 times higher for people with a BMI ≥95 percentile than for those with a BMI <95 percentile, so childhood obesity is a risk factor for the early development of T2DM.[10,11]

Acanthosis nigricans (AN) is classically characterized by the presence of velvety hyperpigmented plaques on the axillary skin and on the neck. Other areas may also be affected. This disorder is caused by hyperinsulinemia secondary to insulin resistance associated with obesity, which is why an increase in the prevalence of AN is expected to parallel the increase in obesity. Insulin resistance is a key fact in T2DM.[12]

Based on the foregoing and with the purpose of contributing to a broader understanding of childhood obesity, the objective of this study was to associate AN and obesity with alterations in the glucose tolerance curve.

## METHODS

The objective of the research was to associate the presence of AN with childhood obesity and with alterations in the glucose tolerance curve. As part of a research line of the project "Diabetes, a Multidisciplinary Care Program (DUPAM)".

Current study is a prospective, cross-sectional, comparative, observational study, carried out through simple random sampling, which included 805 children, aged between 8 and 12 years, who were in fourth, fifth and sixth grade of primary school, of the morning shift in four public schools. Primary schools located in the municipality of Nezahualcóyotl City, a marginal urban community, in the state of Mexico, in the central area of the country, from May 1 to July 15 2019.

Weight, height, waist and hip circumference, body mass index determination, in addition to the search for AN skin lesions associated with obesity were recorded in all children.

In first stage, the prevalence of overweight and obesity in this population was established. In the second stage, AN skin lesions associated with obesity were searched to determine variations in blood glucose levels on an oral glucose tolerance test (OGTT).

The processing of blood samples was carried out at the University Clinic for Health Care "Tamaulipas" (CUAS Tamaulipas), Faculty of Higher Studies (FES) Zaragoza, National Autonomous University of Mexico (UNAM) and the Regional General Hospital No. 25 of the Mexican Social Security Institute (IMSS).

Children who, despite being obese, did not present AN type lesions were excluded. Those boys and girls whose parents did not agree to participate in the study or who dropped out were also excluded.

Consent was obtained under written information, from one or both of the parents before the children were admitted to the study and the protocol was approved by both the ethics and research committees of both institutions. Out of the selected girls and boys, 90 met the inclusion criteria and were admitted to the study. They were followed up at the CUAS Tamaulipas for medical consultation and baseline blood glucose, cholesterol and triglycerides were quantified in the fasting state, as well as a blood glucose determination 2 hours after the ingestion of 75 g of glucose dissolved in 1 liter of drinking water. The samples were processed by the same laboratory technician and with the same procedure, the foreseeable error was previously determined.

For weight measurement, an EF221BW Camry para scale was used and a MSEC208 Seca stadiometer was used to measure height. A measuring tape was used to determine the waist and hip circumference. To determine the degree of obesity, the centers for disease control and prevention (CDC) tables were used. Triglyceride, cholesterol and blood glucose samples were processed by automated method (ADVIA 1200 chemistry system).

For the analysis of the results, a group was formed with a sample size similar to the group of children who concluded the study (N=34), matched by age, gender, BMI and degree of obesity without AN lesions, which was considered as a control group.

For statistical analysis, the $X^2$ nonparametric association tests and Fisher's exact test were used, and Mann Whitney U test was applied using the statistical program SPSS version 25 as a comparison test of means with a level of statistical significance of $p<0.05$.

## RESULTS

Somatometry, BMI and waist-hip measurements were taken from children from the four schools, who were in the fourth, fifth and sixth grade of primary school; 400 women (49.68%) and 405 men (50.31%).

Out of these, 5.3% presented malnutrition, 63.4% normal weight, 16.8% overweight and 14.2% obesity. The highest number of obese and overweight children was found in the in children who were in the fifth grade.

Out of the 805 children, 90 were selected for presenting obesity and AN, of which only 34 completed the study; of those 18 were men (52.94%) and 16 women (47.05%). Of the 34 children in the group, 14.7% (n=5) women and 14.7% (N=5) men had a weight greater than 60 kg, 2.9% (n=1) of women and 8.8% (n=3) of men weighed from 55 to 60 kg, 5.8% (n=2) of women and 11.7% (n=4) of men had weights of 50-55 kg, in the same way 5.8% (n=2) of women and 11.7% (n=4) in men had a weight of 45-50 kg, 8.8% (n=3) women and 2.9% (n=1) men had weighed from 40 to 55 kg and 8.8 % (n=3) of women and 2.9% (n=1) of men had a weight of 35-40 kg. There was a greater weight in men in relation to women (Figure 1).

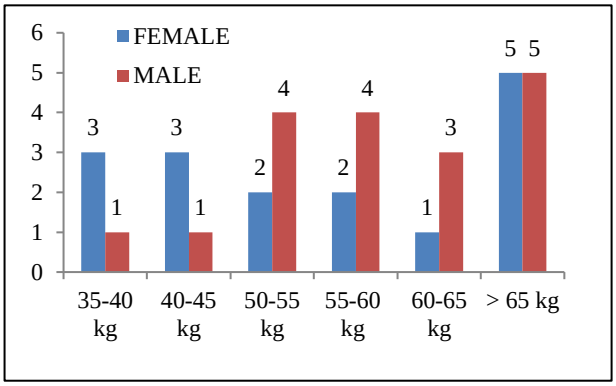


**Figure 1: General distribution of weight in the study group (n=34).**

Regarding age, the children were between 8 and 12 years old. The distribution by sex and age was: women; 2 with 8 years, 5 with 9 years, 4 with 10 years, 3 with 11 years and 2 with 12 years. Men; 2 with 8 years, 8 with 9 years, 5 with 10 years, 2 with 11 years and 1 with 12 years. The average weight of the total of the 34 children in the study was 54.33±11.06 kg. The range for weight was 44 to 81 kg. The average height was 144.9±9.08 cm. Values ranged from 133 to 164 cm. The average BMI was 26.35±3.9 kg/m$^2$.

In 2.73% of the cases (n=22), the BMI was found above the 95th percentile. The average waist and hip circumference were 88.05±9.75 cm and 89.94±9.2 cm respectively. The average value of the waist-hip index was 0.97±0.06. The number of cases by gender according to the degree of AN is shown in Figure 2.

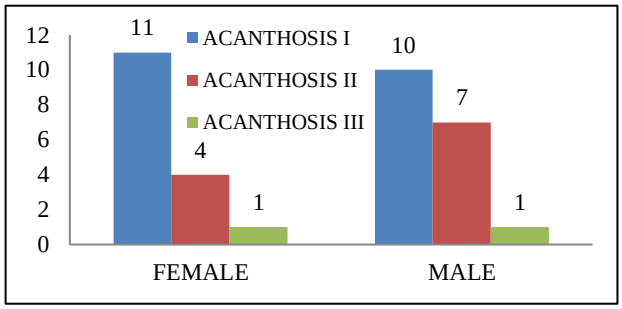


**Figure 2: Degree of acantosis by gender (n=34).**

The blood glucose value prior to ingesting the glucose water solution in the group of obese children with AN were 90.67±6.79 mg/dl (p<0.04) and 97.17±15.37 mg/dl for the samples 2 hours after ingestion, the difference between both groups was significant (p<0.01).

In a girl and a boy in the group with AN, there was an alteration in blood glucose value (>140 mg/dl) in the blood sample 2 hours after ingesting the glucose water solution.

Statistically significant difference was observed between blood glucose levels at 2 hours and the presence of obesity associated with AN grade II and III (n=13), with respect to children who presented AN grade I (n=21) regardless of the gender (p<0.049).

Regarding the serum cholesterol figures, this was 162.41±40.58 mg/dl. There was a statistically significant difference between blood cholesterol levels in obese children with AN lesions (p<0.03).

The mean value of triglycerides was 170.82±61.29 mg/dl. Triglyceride blood values in obese children with AN did not show a statistically significant difference compared to the control group (p=28.96).

Age, BMI, as well as the result of the fasting blood glucose level, blood glucose level 120 minutes later, and cholesterol and blood triglycerides levels are shown in (Table 1).

**Table 1: General characteristics of the groups.**

| Indicator | Control group (n=34) | Study group (n=34) | P value |
|---|---|---|---|
| **Average age (years)** | 9.7±1.19 | 9.7±1.23 | Not significant |
| **IMC (kg/m$^2$)** | 26.11±3.7 | 26.35±3.9 | Not significant |
| **Basal glucose (mg/dl)** | 83.95±4.67 | 90.67±6.79 | P<0.04 |
| **Glucose 120 minutes (mg/dl)** | 90.12±4.33 | 97.17±15.37 | P<0.01 |
| **Total cholesterol (mg/dl)** | 133.58±26.61 | 162.41±40.58 | P<0.03 |
| **Triglycerides (mg/dl)** | 169.93±62.19 | 170.82±61.29 | Not significant |

## DISCUSSION

In the present study it was found that the group of children with obesity had a statistical significance in the serum glucose levels, in the OGTT and when there were skin lesions of AN, the latter was considered as an indicator related to resistance to the insulin.

In current study, differences were found between blood glucose values before and after the glucose tolerance test, which was carried out in children with obesity without reaching values of glucose intolerance, since the most important and frequent metabolic complication is resistance to the peripheral action of insulin. For the quantification of insulin resistance (IR), there are several indices, such as performing the OGTT at different times for its calculation. It has recently been found that the transition from normal glucose tolerance to glucose intolerance and from glucose intolerance to T2DM in obese adolescents is closely related to the significant increase in body weight over time, as reported in some studies.[13]

Likewise, two cases of children with AN and glucose intolerance (<140 mg/dl) were reported, this raises the suspicion that the progression towards glucose intolerance states in obese children and adolescents is due to a lower sensitivity to glucose and an impaired peripheral action of insulin which, in turn, triggers a compensatory hyperinsulinic state sufficient to maintain the euglycemic state for some time. Once this secretory capacity of the pancreatic beta cells is exceeded, T2DM manifests itself clinically, and this may be one of the factors or mechanisms involved in the genesis of glucose intolerance in obese children and adolescents.[14]

In children with obesity, alterations in glucose levels and the degree of AN I showed a difference between these groups compared to children with degrees of AN II and III, this skin alteration has been associated with rare genetic defects in the action of the insulin, that is, insulin resistance and impaired carbohydrate metabolism such as glucose intolerance. Therefore, AN may be a clinical marker for hyperinsulinemia and/or other endocrinopathies.[15]

In the group of obese children, serum cholesterol levels were not reported above the recommended parameters, however, there were differences between those who did not present AN and those who did. Triglycerides levels reached an average value of 170 mg/dl and although there were no significant differences between children with AN and obesity and the comparison group, the reported values were above the allowed limits, so it can be assumed that the presence of AN associated with obesity produces significant alterations in lipid metabolism and presents risk factors related to an increased risk of developing atherosclerosis and cardiovascular disease.[16]

## CONCLUSION

There is a significant relationship between the existence of AN and endocrinopathies, such as insulin resistance. This reaffirms the importance of a comprehensive and holistic evaluation of children with skin alterations, as these are invaluable signs that can guide clinical suspicion in everyday medical practice. The presence of in obese children defines a group of children with metabolic alterations associated with an increased risk of developing cardiovascular diseases and T2DM. In our experience, we were able to verify that there is no obesity prevention culture, since 56 of the children selected for the study were eliminated due to the little or no interest of parents in knowing the health status of their children.

## ACKNOWLEDGEMENTS

We acknowledge and thank all the health personnel who have worked for several decades at the Regional General Hospital No. 25 of the Mexican Social Securiy Institute (IMSS), Mexico City, Mexico, always committed to providing care to the population of the state of Mexico and Mexico City. The authors thank Francisca Nayely Caballero-Noguéz and José Daniel Caballero-Flores for the review and editorial support for the manuscript.The participation of the Doctors Alicia González-Carmona, Christian Fabiola Yazmín Martínez-Jiménez and Diana Zamudio-Sánchez for the collection of information is appreciated.

*Funding: National Autonomous University of Mexico (DGAPA-PAPIIT: IN405319)*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Encuesta Nacional de Salud y Nutrición 2018. Available at: https://ensanut.insp.mx/encuestas/ensanut2018/doctos/informes/ensanut_2018_presentacion_resultados.pdf. Accessed on 24 September 2020.
2. Instituto Nacional de Salud Pública-Secretaría de Salud. Encuesta Nacional de Salud y Nutrición de Medio Camino 2016 (ENSANUT 2016), informe final de resultados. Available at: https://www.insp.mx/images/stories/2017/Avisos/docs/180315_encuesta_nacional_de_salud_y_nutricion_de_medio_Capdf. Accessed on 24 September 2020.
3. Kaufer-Horwits M, Perez-Lizaur AB, Arroyo P. Nutriología médica. 4th ed. México: DF Editorial Médica Panamericana SA; 2015.
4. Vega-Rodríguez P, Álvarez-Aguirre A, Bañuelos-Barrera Y, Reyes-Rocha B, Hernández Castañón MA. Lifestyle and nutritional status among school children. Enferm univ.2015;12(4):197-203.
5. Elizondo ML, Serrano MG, Ugalde CP, Cuello GC, Borbolla EJR. Metabolic syndrome risk factors

among a sample of overweight and obese Mexican children. J Clin ypertense. 2010;12(5):380-7.
6. Ávila-Curiel A, Galindo-Gómez C, Juárez-Martínez L, Osorio-Victoria ML. Síndrome metabólico en niños de 6 a 12 años con obesidad, en escuelas públicas de siete municipios del Estado de México. Salud Publica Mex. 2018;60:395-403.
7. American Diabetes Association. 12. Children and adolescents: standards of medical care in diabetes-2018. Diabetes Care. 2018;41(Suppl 1):S126-36.
8. Genoni G, Menengon V, Secco G, Sonzini M, Martelli M, Castagno M, et.al. Insulin resistance, serum uric acid and metabolic syndrome are linked to cardiovascular dysfunction in pediatric obesity. Int J Cardiol. 2017;249:366-71.
9. Barrera-Cruz A, Rodríguez-González A, Molina-Ayala MA. Escenario actual de la obesidad en México. Rev Med Inst Mex Seguro Soc. 2013;51(3): 292-9.
10. Murillo Valles M, Bel Comós M. Obesidad y síndrome metabólico. Protoc diagn ter pediatr. 2019;1:285-94.
11. Zhu H, Zhang X, Li M, Xie J, Yang X. Prevalence of type 2 of diabetes and pre-diabetes among overweight or obese children in Tianjin, China. Diabetic Med. 2013;30(12):1457-65.
12. Slyper AH, Kashmer L, Huang W-M, Re'em Y. Acanthosis nigricans, vitamin D, and insulin resistance in obese children and adolescents. J Pediatr Endocrinol Metab. 2014;27(11-12):1107-11.
13. Yeste D, Carrascosa A. Obesity-related metabolic disorders in childhood and adolescence. Ann Pediatr. 2011;75(2):135.e1-9.
14. Weiss R, Caprio S. The metabolic consequences of childhood obesity. Best Pract Res Clin Endocrinol Metab. 2005;(19):405-19.
15. Rafalson L, Pham TH, Willi SM, Marcus M, Jessup A, Baranowski T. The association between acanthosis nigricans and dysglycemia in an ethnically diverse group of eighth grade students. Obesity (Silver Spring). 2013;21(3):E328-33.
16. Ordoñez M, Luzuriaga A, Flores M, Suquilanda D. Acanthosis nigricans as a practical diagnosis of endocrine diseases in pediatrics. Dermatol Rev Mex. 2019;63(1):3-7.

**Cite this article as:** Caballero-Noguez B, Cardoso-Gomez MA, Ponce-Lopez ML, Mendez-Duran A, Reyes-Gomez U. Blood glucose levels in children with acanthosis nigricans associated with obesity. Int J Contemp Pediatr 2020;7:2255-9.