



## LETTERS TO THE EDITOR

**Comment about the article:  
 ‘‘Association of metabolic  
 syndrome with low birth  
 weight, intake of high-calorie  
 diets and acanthosis nigricans  
 in children and adolescents  
 with overweight and obesity’’<sup>☆</sup>**



**Comentario sobre el artículo: «Asociación  
 del síndrome metabólico con bajo peso al  
 nacimiento, consumo de dietas hipercalóricas  
 y acantosis nigricans en escolares y  
 adolescentes con sobrepeso y obesidad»**

Dear Sir,

We have read with great interest the article entitled ‘‘Association of metabolic syndrome with low birth weight, intake of high-calorie diets and acanthosis nigricans in children and adolescents with overweight and obesity’’.<sup>1</sup> This study addresses a significant public health problem that is increasingly prevalent in Mexico.<sup>2</sup> We would like to discuss here some methodological aspects that may be beneficial for future studies.

First of all, overweight and obesity are highly prevalent conditions among Mexican schoolchildren.<sup>1</sup> To investigate them, the authors actually used a cross-sectional study, but they have wrongly reported it as a case–control study.<sup>3</sup> In cross-sectional studies, the proportion of subjects in a sample with a given condition is determined, while in a case–control study, the subject’s status (case or control) is already known, and separate sampling strategies are used for cases and controls.<sup>4</sup> In addition, studies conducted at hospitals and on subjects having several conditions and factors are susceptible to Berkson’s bias.<sup>5</sup> It is therefore quite possible that, in this study, the ‘‘exposure’’ variables studied (low birth weight, intake of high-calorie diets, and acanthosis nigricans, particularly the last two) were systematically greater in these cases only by hospital

sampling, which should have been mentioned as a limitation.

In addition, the variable acanthosis nigricans is a manifestation of insulin resistance, and cannot therefore be considered as an exposure variable for metabolic syndrome, but rather as a response variable to the former, based on the basic principle of the temporal relationship between variables.<sup>6</sup> Thus, both variables are already conceptually related, and OR calculation, although mathematically correct, is therefore not appropriate. Finally, measurement of the diet and weight variables may be biased. The 24-h recall is a tool that allows for the characterization of the current or recent intake patterns of a person, but it does not measure the intake of a high-calorie diet over long cumulative time periods nor does it necessarily result in metabolic syndrome.<sup>7</sup> As regards the evaluation of birth weight, this may be affected by the recall bias of the mother, because of the time elapsed.

Overall, we think that the study helps us to better understand the problem of overweight and obesity in Mexican children and adolescents. We also hope that the above comments may be taken into account in future studies aimed at better characterizing and understanding these public health problems that affect the pediatric population.

## References

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## Reply to the comment to our article titled: "Association of metabolic syndrome with low birth weight of birth, intake hypercaloric diets and acanthosis nigricans in childhood and teens with overweight and obesity"<sup>☆</sup>



### Respuesta al comentario a nuestro artículo titulado: «Asociación del síndrome metabólico con bajo peso al nacimiento, consumo de dietas hipercalóricas y acantosis nigricans en escolares y adolescentes con sobrepeso y obesidad»

Dear Editor,

With regard to the comments on our article entitled: "Association of metabolic syndrome with low birth weight, intake of high-calorie diets and acanthosis nigricans in children and adolescents with overweight and obesity",<sup>1</sup> we should like to make the following points:

Observational studies should be assessed using the guidelines of the *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) statement,<sup>2-5</sup> as recommended by the Cochrane Center,<sup>5</sup> which states that in case-control designs, "the eligibility criteria and the sources and methods to determine the cases and select the controls" should be provided, but does not mention as a prerequisite "an a priori selection", which would be methodologically better, but is not indispensable for this design. However, the eligibility criteria are discussed below.

According to Argimon Pallas and Jiménez Villa,<sup>6</sup> in case-control studies, cases are taken from a series of patients in whom the disease has already been diagnosed and who are available for the study. The study was conducted in ambulatory obese children who attended a hospital. Children with metabolic syndrome were the cases,

while those without the syndrome were used as controls. Potential exposure factors, including low birth weight, a history of intake of high-calorie diets and acanthosis nigricans, were identified and considered retrospective factors. Even if this is not considered to be a case-control study, it is an analytical cross-sectional study, and odds ratio calculation is also applicable. In our opinion, however, the study has the basic structure of a case-control design because it is retrospective and longitudinal, and because there is a time period between the consequence (metabolic syndrome) and exposure factors, which are retrospective (e.g. low birth weight).

As regards exposure criteria, they were defined in the article as follows: low birth weight according to the World Health Organization criteria,<sup>7</sup> high-calorie diets using the criteria of the American Academy of Pediatric Nutrition,<sup>8</sup> and acanthosis nigricans according to the Simone et al. criteria.<sup>9</sup> The commentators disagree with our criteria, but give no particulars.

In the study discussion, we state in the first paragraph that the study population came from a third level hospital, and that this was why there was a high rate of metabolic syndrome. However, "selection or Berkson's bias occurs when the combination of exposure and the disease under study increases the chance of hospital admission".<sup>2</sup> In our case, the frequency of exposure would be higher in these cases than in hospital controls. Thus, at least as regards "low birth weight", we think that it does not increase their chance of hospital admission at 10 and 15 years of age. Moreover, obese children and adolescents were not admitted to hospital, but were ambulatory and attended an overweight and obesity program.

As regards acanthosis nigricans, we recognize its scientific (both clinical and biochemical) relationship to insulin resistance, mentioned in the text, but acanthosis nigricans has not been shown to be a definite marker of insulin resistance, as explained by Zhu et al.,<sup>10</sup> and is therefore not considered a confounding variable. The authors cite Chiarpenello et al., who reported that 60% of the population had high insulin levels with a gradual increase in the prevalence of acanthosis nigricans, but this is not a sufficient pathological or epidemiological explanation for regarding acanthosis nigricans as a marker of insulin resistance. Consistent evidence is lacking.

The most important concept in this study is the association of fetal programming and the development of metabolic changes, which other authors have considered (Barker's theory). In particular, birth weight has a special relevance for Mexican women, but it should be admitted that retrospective studies, such as case-control studies,

<sup>☆</sup> Please cite this article as: Velazquez-Bautista M, López-Sandoval JJ, González-Hita M, Vázquez-Valls E, Cabrera-Valencia IZ, Torres-Mendoza BM. Respuesta al comentario a nuestro artículo titulado: «Asociación del síndrome metabólico con bajo peso al nacimiento, consumo de dietas hipercalóricas y acantosis nigricans en escolares y adolescentes con sobrepeso y obesidad». *Endocrinol Diabetes Nutr.* 2017;64:568-569.