Metabolic syndrome in Spanish adolescents and its association with birth weight, breastfeeding duration, maternal smoking, and maternal obesity: a cross-sectional study

Authors:

González-Jiménez, Emilio[1]

PhD. Department of Nursing. Faculty of Nursing

C/ Santander Nº 1 (52071). University of Granada, Melilla (Spain)

Tel.: (+34) 667051570

E-mail: emigoji@ugr.es

Montero-Alonso, Miguel A.

PhD. Department of Statistics and O.R. Faculty of Social Sciences

C/ Santander Nº 1 (52071). University of Granada, Melilla (Spain)

Tel.: (+34) 695215256

E-mail: mmontero@ugr.es

Schmidt Rio-Valle, Jacqueline

PhD. Department of Nursing. Faculty of Health Sciences.

Av/ Madrid s/n (18071). University of Granada, Granada (Spain)

Tel: (+34) 958243498

E-mail: jschmidt@ugr.es

García-García, Carmen J.

PhD. Department of Forensic Medicine, Toxicology and Physical Anthropology. Faculty of Medicine. Av/ Madrid s/n, (18071) University of Granada, Granada (Spain)

Tel.: (+34) 660122250

E-mail: cjgarcia@ugr.es

Padez, Cristina

[1] Corresponding author

PhD. Research Centre for Anthropology and Health. Department of Life Sciences.

Apartado 3046, University of Coimbra, 3001-401 Coimbra (Portugal)

Tel.: 351 239 854114

E-mail: cpadez@antrop.uc.pt

Number of words: 3492

Declaration of interest: The authors declare that there is no conflict of interest with any organization regarding the material in the manuscript.

Key words: Metabolic Syndrome, Adolescents, Related Factors.

Abstract

Context: The prevalence of metabolic syndrome (MetS) in adolescents is a growing problem, which justifies the analysis of the risk factors that can potentially lead to its development.

Objectives: The objectives of this research study were to verify the association among early predictors such as birth wight, breastfeeding, maternal weight status and smoke during pregnancy and the development of MetS.

Design: Cross-sectional study

Setting: The study was conducted in 18 primary and secondary schools in Granada and Almeria (Spain).

Participants: The sample population was composed of 1001 adolescents, 9-17 years of age (533 female subjects and 468 male subjects).

Variables measured: This study focused on the following variables: (i) physical and biochemical characteristics of the subjects; (ii) duration of maternal breastfeeding; (iii) maternal nutritional status; and (iv) maternal smoking during pregnancy.

Results: It was found that 18.38% of the female subjects and 7.26% of the male subjects in the sample population suffered from MetS. In both sexes, there was an inverse association (OR=0.77; 95% CI (0.54; 0.92)) between birth weight and positive MetS diagnosis. For both male and female subjects, there was also an inverse association (OR = 0.82; 95% CI (0.65; 0.97)) between the length of time that they had been breastfed and positive MetS diagnosis. Finally, the results of this study indicated that there was a significant association between the mothers' nutritional status (OR = 21.65; 95% CI (13.930; 33.65)) cigarette consumption during pregnancy (OR = 1.57; 95% CI (1.08; 2.13)) and the subsequent development of MetS in their children.

Conclusions:

An alarming prevalence of MetS was found, especially in female adolescents. Those subjects born with a higher than average birth weight had a greater risk of developing MetS in childhood

and adolescence. These findings suggest the need for urgent public health among the study population. The results of our study showed that breastfeeding children for longer than six months protected them from MetS in their early years as well as in their teens. Other risk factors for MetS were maternal smoking during pregnancy as well as maternal overweight and obesity.

Metabolic syndrome (MetS) is defined as a group of risk factors that, when occurring together, increase the risk of cardiovascular disease and type 2 diabetes (DM2) (1, 2). Until recently, the clustering of such factors had only been reported in adults. Nevertheless, there are now a growing number of studies that point to the presence of MetS in adolescents, probably due to the widespread increase in obesity in young people throughout the world (3).

The prevalence of MetS in children and adolescents varies, depending on the definition of risk factors and the population analyzed (4). However, generally speaking, few studies have specifically focused on population samples of young people (5). Recently, the International Diabetes Federation (IDF) published a set of guidelines for the diagnosis of MetS in children and adolescents with a view to establishing a simple unified definition (6). According to this definition, the identification of MetS in adolescents is based on a waist circumference of ≥ 94 cm in males and of ≥80 cm in females. This is evidently linked to other risk factors, such as fasting glucose levels of 100-125 mg/dl, triglyceride levels of ≥150 mg/dl, HDL-cholesterol levels lower than 40 mg/dl in males and 50 mg/dl in females, along with a blood pressure of ≥ 130/85 mmHg (7). However, it is also true that as yet, this definition has not been tested on subjects belonging to different ethnic groups (8, 9).

The identification of risk factors that lead to the development of MetS in youngsters is crucial for its prevention and rapid detection (10). Accordingly, it has been suggested that a higher than average birth weight is associated with the early development of insulin resistance as well as of MetS (11,12,13). For example, McCance et al. (14) studied a population of Pima Indians, and found a significant relation between a higher than average birth weight and the risk of metabolic disorders in childhood.

Another risk factor in the early development of MetS is an excessively short period (or the lack) of maternal breastfeeding in the first year of infancy (15). According to recent studies, maternal breastfeeding for longer than six months helps to prevent cardiovascular disorders and more specifically, MetS in the early years of childhood (16, 17). Nevertheless, the lack of significant results in other studies (18) has led to some controversy over the protective effect of maternal lactation in regards to the development of MetS in infancy.

Toxic maternal habits, such as cigarette consumption during pregnancy, also appear to be linked to the childhood development of MetS. After studying a cohort of 406 young Australians, Huang et al. (19) found that the children of women that had smoked during the gestation period had a heavier birth weight. This finding was corroborated in subsequent studies, such as Behl et al (20), who concluded that early exposure of the unborn infant to the toxic components in cigarette smoke is an important risk factor in the early development of serious disorders, such as MetS, later in childhood and adolescence.

Similarly, the nutritional status of pregnant mothers is also conducive to their children subsequently developing MetS (21). For example, studies such as Ryckman et al. (22) suggest that maternal obesity during the gestation period can lead to the early development of MetS. In the same line, Boney et al. (23) also found that children whose mothers had been obese during pregnancy were more prone to developing MetS in their childhood years.

In view of this research, the first objective of this study was to ascertain whether a higher than normal birth weight is directly related to the early development of MetS. The second was to verify the correlation between the duration of maternal breastfeeding and the early development of MetS. The third was to discover whether there was a relation between maternal nutritional status and maternal smoking during the nine months of gestation and the child's subsequent development of MetS.

Subjects and Methods

Study design and population

The sample population of this transversal study was composed of 1001 children and adolescents, 9-17 years of age, (533 females and 468 males) from the sixth grade of primary school to the third year of secondary school. The subjects attended 18 schools in the provinces of Granada and Almeria (Spain). The study had been previously approved by the Board of Education of the Andalusian Regional Government (Granada and Almeria Delegations), and also authorized by the directors of the participating schools. Moreover, the informed consent of the parents and tutors of the subjects was obtained previous to beginning the study. This research was performed in strict compliance with the international code of medical ethics established by the World Medical Association and the Declaration of Helsinki.

Measurements

Anthropometric measurements and blood pressure

Each subject underwent a complete anthropometric evaluation to ascertain his/her nutritional status. This evaluation was performed according to the recommendations of the European Pediatric Association (Body Composition Analysis Protocol). The variables assessed were weight, height, and body mass index (weight (kg)/height (m^2)). The subjects were weighed on a self-calibrating Seca® 861 Class (III) Digital Floor Scale with a precision of up to 100 grams. Their height was measured with a Seca® 214* portable stadiometer. For this purpose, each subject was asked to stand erect with back, buttocks, and heels in continuous contact with the vertical height rod of the stadiometer and head orientated in the Frankfurt plane. The horizontal headpiece was then placed on top of the subject's head to measure his/her height.

Overweight and obesity were defined according to the international standards of Cole et al. (24). Waist circumference was measured using the horizontal plane midway between the lowest rib and the upper border of the iliac crest at the end of normal inspiration expiration. Hip circumference was measured at the maximum extension of the buttocks as viewed from the right side. For both measurements, a Seca® automatic roll-up measuring tape (precision of 1 mm) was used to measure subjects in a standing position with their arms hanging at their sides in a normal anatomical position. The waist-to-hip ratio (WHR) was calculated by dividing the waist circumference by the hip circumference. Also evaluated were the triceps, biceps, subscapular, and suprailiac skinfolds, which were measured with a Holtain® skinfold calliper with a precision of 0.1-0.2 mm. The skinfold measurements were then used to calculate the percentage of body fat. Previously, however, it was necessary to determine body density for both sexes with Brook's (1971) equation.

Male subjects

Density: *1.1690–0.0788 x* Log_{10} *[triceps, biceps, subscapular, and suprailiac]*

Female subjects

Density: *1,2063–0,0999 x* Log_{10} *[triceps, biceps, subscapular, and suprailiac]*

After determining body density, the Siri (1961) equation was then used to calculate the body fat percentage:

Body fat percentage: [(4.95 / Density) – 4.5] × 100

Blood pressure levels were calculated with a previously calibrated aneroid sphygmomanometer and a Littmann® stethoscope. The subjects were asked to sit down and relax for at least ten minutes before their blood pressure was measured and recorded. They were requested to rest their back against the back of the chair. They were also asked not to cross their legs so that both of their feet were in direct contact with the floor. Their right arm, which had to be free of tight clothing, was extended, flexed at the elbow, and at heart level. All calculations were made on the right arm and compared to international reference standards. The results were interpreted based on Korotkoff phase I for the systolic blood pressure value and phase V for the diastolic blood pressure value. A blood pressure of ≥ 130/85 mmHg was regarded as a risk factor of metabolic syndrome.

Serum Biochemical Examination

At 8:00 A.M. after a 12-hour overnight fast, 10 ml of blood was extracted by venipuncture from the antecubital fossa of the right arm with a disposable vacuum blood collection tube. In the four hours after the extraction, all samples were centrifuged at 3500 rpm for 15 minutes (Z400 K, Hermle, Wehingen, Germany). The red blood cells were thus separated and the serum was finally frozen at -80°C for its subsequent analysis.

Only the glucose was measured immediately after collection. Plasma insulin was determined with an ELISA kit (27). Blood glucose (mg/dl) was measured by using the colorimetric enzymatic method (GOD-PAP Method, Human Diagnostics, Germany). The HbA1c was measured with high-performance liquid chromatography using a National Glycohemoglobin Standardization Program certified automated analyzer (model HLC-723 G7; Tosoh, Tokyo, Japan, intra-assay coefficient of variation <0.8 %, inter-assay coefficient of variation <0.5 %), and was standardized according to the Diabetes Control and Complications Trial.

The low-density lipoproteins (LDL-C) and high-density lipoproteins (HDL-C) as well as the total cholesterol and the triglycerides were calculated by means of the enzymatic colorimetric method with an Olympus analyzer.

Serum levels of homocysteine were calculated by immunoenzymatic assay (DRG Instruments) with a sensitivity of 1μmol/L. Intra-assay and inter-assay variation coefficients were 7% and 9%, respectively. Ceruloplasmin was determined by immunoturbidometric assay (Architect ci8200, Abbott, Abbott Park IL), with an intra-assay variation coefficient of 3.7%, an inter-assay precision of up to 4%, and a reference of 20-60 mg/dl.

MetS Definition

The diagnosis of metabolic syndrome in adolescents was based on the criteria established by the International Diabetes Federation (7). Accordingly, metabolic syndrome was diagnosed when waist circumference was ≥94 cm in male subjects and ≥80 cm in female subjects. Such waist circumference values were considered in combination with the following factors: fasting blood glucose levels of 100-125 mg/dl; serum triglyceride levels ≥150 mg/dl; HDL cholesterol levels < 40 mg/dl (male subjects) and < 50 mg/dl (female subjects); and blood pressure ≥ 130/85 mmHg.

Statistical procedures

Descriptive statistics are displayed as arithmetic means ± SD or percentages (%). Differences between the groups of male and female subjects were analyzed with ANOVA. The linear trend of the subjects was examined, based on their MetS status (i.e. MetS or non-MetS) using linear regression analyses for continuous outcomes. Differences in the characteristics of the subjects with positive MetS diagnosis and those with a negative MetS diagnosis were compared by using Student's *t* test and the χ^2 test, where appropriate. Logistic regression analyses were performed to examine the independent associations of potential correlates with MetS. Statistical analyses were carried out with the SPSS statistical package (version 20.0; SPSS Inc, Chicago, IL), where a P value of < 0.05 denoted statistical significance.

Results

Anthropometric characeristics are dyspaly in Table 1. The results obtained in our study showed that 18.38% of the female subjects were positively diagnosed with MetS as opposed to 7.26% of the male subjects who suffered from this disorder. Consequently, in the sample population, MetS evidently had a higher prevalence in the female population than in the male population. In the case of the weight variable, higher mean values were observed in both sexes in the group diagnosed with MetS as compared to those without MetS. Regarding birth weight, mean values were also greater for both sexes in the group with a positive MetS diagnosis. In fact, there was an inverse relation between variables (OR=0.77; 95% CI (0.54; 0.92)). Subjects diagnosed with metabolic syndrome were found to have higher scores for body mass index and percentage of body fat in comparison to the subjects without MetS. Not surprisingly, both the male and female subjects with MetS also had had higher waist circumference values as well as a greater waist-to-hip ratio though the male subjects had a greater waist-to-hip ratio than the female subjects.

All of the subjects diagnosed with MetS also had higher blood pressure levels. However, the results showed that male subjects had higher levels of both systolic and diastolic blood pressure than the female subjects. There were statistically significant differences ($P < 0.05$), based on gender in the values observed for all the physical variables between the group of subjects positively diagnosed with MetS and the group without the disorder.

INSERT TABLE 1 HERE

The clinical laboratory data of the subjects, distributed according to the positive or negative diagnosis of metabolic syndrome are shown in Table 2. Levels of basal insulin, basal glucose, glycosylated hemoglobin, LDL-C, homocysteine and ceruloplasmin were higher in subjects with MetS. In the case of total cholesterol, the differences between the group with MetS and the group without MetS were not as great. However, in reference to the HDL-C level, the group of healthy subjects had higher values. Statistically significant differences ($P < 0.05$) were found in the basal insulin, HBA1c, LDL-C, NEFA and ceruloplasmin values for both groups of subjects. However, there were no statistical differences in the values collected for basal glucemia, (P = 0.136), total cholesterol (P = 0.532), triglycerides (P = 0.142), HDL-C (P = 0.169), and homocysteine (P = 0.063) between the two groups of subjects.

INSERT TABLE 2 HERE

In reference to maternal breastfeeding, Table 3, the results showed that of the female subjects positively diagnosed with MetS (n = 98), only 0.56 % (n = 3) had been breastfed for longer than six months. However, in the group of healthy female subjects (n = 435), the tendency was precisely the opposite since 72.79% had been breastfed for six months or longer. Regarding the male subjects with MetS (n = 34) only 0.64% (n = 3) had been breastfed for longer than six months, whereas in the males without MetS (n = 434), 83.13% had been breastfed six months or longer. Consequently, these results confirm the existence of an inverse association (OR = 0.82; 95% CI (0.65; 0.97)) between the duration of maternal breastfeeding and the diagnosis of MetS, particularly for subjects of both sexes that had been breastfed for longer than six months.

INSERT TABLE 3 HERE

In reference to the nutritional status of the subjects' mothers during pregnancy, the fitting of the logistic regression model showed that there was a relation between the nutritional status of the mother during the nine-month gestation period. The fit of the logistic regression model reflects a salient relation between the nutritional status of the pregnant mothers and the early development of MetS in their children (OR = 21.65; 95% CI (13.930; 33.65)). Our results showed that the mothers of 5.81% of the female subjects with MetS (n = 31) were of normal weight during their pregnancy; 8.07% of these mothers (n = 43) were overweight; and 4.50% (n = 24) were obese. In contrast, the mothers of the female subjects without MetS generally had a better nutritional status during their pregnancy. More specifically, 80.30% (n = 428) were of normal weight whereas only 1.32% (n = 7) were overweight, and 0% were obese.

Similarly, the mothers of the male subjects diagnosed with MetS also had a worse nutritional status during their pregnancy. More specifically, only 0.43% (n = 2) of these mothers were of normal weight; 2.35% (n = 11) were overweight; and 4.49% (n = 21) were obese. Generally speaking, the mothers of the male subjects without MetS also had a better nutritional status during pregnancy with a normal weight prevalence of 83.33% (n = 390): an overweight rate of 8.33% (n = 39); and an obesity rate of 1.07% (n = 5). Figure 1 shows the results obtained.

INSERT FIGURE 1 HERE

Regarding the daily smoking habits of the mothers during pregnancy, the results showed that this variable had a direct influence on the early development of MetS in their children (OR = 1.57; 95% CI (1.08; 2.13)). In fact, only 0.94% (n = 5) of the mothers of the female subjects diagnosed with MetS had not smoked during pregnancy. In this sense, 1.50% of the mothers (n = 8) had smoked fewer than 10 cigarettes or 10-20 cigarettes per day, and 14.44% (n = 77) said that their daily consumption had been more than 20 cigarettes.

In the case of the mothers of the healthy female subjects, 65.85% (n = 351) had not smoked during their pregnancy and 7.88% (n = 42) had smoked fewer than 10 cigarettes per day, whereas 4.31% (n = 23) had smoked 10-20 cigarettes per day. Only 3.58% (n = 19) of the mothers said that they had smoked 20 cigarettes per day or more.

Regarding the mothers of the male subjects with MetS, 0.64% (n = 3) of them had not smoked at all during pregnancy, and 1.07% (n = 5) had smoked fewer than 10 cigarettes per day. In contrast, 0.43% (n = 2) of the mothers had smoked 10-20 cigarettes per day though only 5.13% (n = 24) said that they had smoked more than 20 cigarettes per day during the gestation period.

In the case of the mothers of male subjects without MetS, 75.43% (n = 353) had not smoked during pregnancy; 8.76% (n = 41) had smoked fewer than 10 cigarettes per day; and 2.99% (n =

14) had smoked 10-20 cigarettes per day. Only 5.55% (n = 26) of the mothers said that they had smoked more than 20 cigarettes per day. These data are shown in Figure 2.

INSERT FIGURE 2 HERE

Discussion

The results obtained in this study indicated a relatively high prevalence of MetS in the sample population, particularly in the female subjects (18.38%). The prevalence of MetS in the male subjects was somewhat lower (7.26%). When compared to the results of other authors who also used the definition of the International Diabetes Federation (7), our percentages were higher than those in Aguayo (28) (2.9%) as well as those obtained by the Studies to Treat or Prevent Pediatric Type 2 Diabetes (STOPP-T2D) Prevention Study Group* (29) (9.5%). However, it is worth mentioning that the results of our study agree with those in Tapia et al (1) (18.6%) for a sample population of adolescents in Spain. According to Pan and Pratt (30), the increased prevalence of MetS in the adolescent population is directly related to a rejection of traditional dietary habits and the growing tendency of young people to adopt a more sedentary lifestyle,

Among the physical characteristics, birth weight was found to be directly related to the development of metabolic syndrome, given the fact that this variable had higher than average values in both the male and female subjects with MetS. In contrast, Eriksson et al. (31) and Khuc et al. (32), who surveyed a population of 357 adolescents in Chile, did not find any association between birth weight and the early development of metabolic syndrome.

The results of our biochemical study confirmed the existence of statistically significant differences in the values obtained for basal insulin, HBA1c, LDL-C, NEFA, and ceruloplasmin in the group of male and female subjects diagnosed with MetS as compared to the group of healthy subjects. These results coincided with those of Chen et al. (33) and Want et al. (34) in a transversal study of 624 adolescents in China.

In regards to maternal lactation, our results showed that breastfeeding provided protection against the development of MetS in childhood and adolescence. Accordingly, there was a higher prevalence of MetS in the groups of male and female subjects who had not been breastfed as babies. These results are in consonance with those obtained in other studies of a similar population of children and adolescents (35, 36). As also highlighted by Ekelund et al. (37), the most important benefits of maternal breastfeeding in terms of MetS prevention were for those subjects who had been breastfed for more than six months.

Furthermore, our results highlight the importance of the nutritional status of mothers during the nine months of pregnancy, which has an impact on the potential development of MetS in their offspring. In this sense, the children of mothers who had suffered from overweight or obesity during pregnancy were more likely to develop MetS than those children whose mothers were of normal weight. These results agree with those obtained in previous research (38, 39, 40).

Finally, maternal smoking during pregnancy was also found to be a risk factor. Similarly to other research (41, 42), our study found that cigarette consumption by mothers during the gestation period increased the risk of their children developing MetS in childhood and adolescence.

In conclusion, the results of our study are indicative of a high prevalence of metabolic disorder in the sample population. The incidence of MetS was especially striking in the female subjects. Birth weight was closely related to the potential development of this disorder. In this regard, both male and female subjects with MetS had a higher than average birth weight than those without MetS. Maternal breastfeeding was found to protect newborns from subsequently developing MetS in adolescence, particularly when the duration of the lactation period was longer than six months. There was also an important relation between the nutritional status of mothers during pregnancy and the possibility of their children subsequently developing MetS. In this regard, the subjects whose mother had been overweight or obese during the gestation period were more vulnerable to metabolic syndrome. Finally, maternal smoking during pregnancy was also found to be a risk factor that increased the likelihood that these children would develop MetS in adolescence.

References

1. **Tapia Ceballos L** 2007 Síndrome metabólico en la infancia. An Pediatr (Barc) 66:159-166.

2. **Bahar A, Hosseini Esfahani F, Asghari Jafarabadi M, Mehrabi Y, Azizi F** 2013 The structure of metabolic syndrome components across follow-up survey from childhood to adolescence. Int J Endocrinol Metab 11:16-22.

3. **Montero Alonso MA, González-Jiménez E** 2013 Valoración del estado nutricional, resistencia insulínica y riesgo cardiovascular en una población de adolescentes de la ciudades de Granada y Almería. Nutr Hosp 28:802-806.

4. **Ford ES, Li C** 2008 Defining the metabolic syndrome in children and adolescents: will the real definition please stand up? J Pediatr 152:160–164.

5. **Mangge H, Summers KL, Meinitzer A, Zelzer S, Almer G, Prassl R, Schnedl WJ, Reininghaus E, Paulmichl K, Weghuber D, Fuchs D** 2013 Obesity-related disregulation of the Tryptophan-Kynurenine metabolism: Role of age and parameters of the metabolic syndrome. Obesity (Silver Spring) 26 [Epub ahead of print].

6. **Ekelund U, Anderssen S, Andersen LB, Riddoch CJ,Sardinha LB, Luan J, Froberg K, Brage S** 2009 Prevalence and correlates of the metabolic syndrome in a population-based sample of European youth. Am J Clin Nutr 89:90–96.

7. **Zimmet P, Alberti KG, Kaufman F, Tajima N, Silink M, Arslanian S, Wong G, Bennett P, Shaw J, Caprio S; IDF Consensus Group** 2007 The metabolic syndrome in children and adolescents: an IDF consensus report. Pediatr Diabetes 8:299–306.

8. **Korner A, Kratzsch J, Gausche R, Schaab M, Erbs S, Kiess W** 2007 New predictors of the metabolic syndrome in children: role of adipocytokines. Pediatr Res 61:640–645.

9. **Simmons RK, Alberti KGMM, Gale EAM** 2010 The metabolic syndrome: useful concept or clinical tool? Report of a WHO Expert Consultation. Diabetologia 53:600–605.

10. **Ahmadi A, Gharipour M, Nouri F, Sarrafzadegan N** 2013 Metabolic syndrome in Iranian youths: a population-based study on junior and high schools students in rural and urban areas. J Diabetes Res 30 [Epub ahead of print].

11. **Ekelund U, Ong KK, Linné Y, Neovius M, Brage S, Dunger DB, Wareham NJ, Rössner S** 2007 Association of weight gain in infancy and early childhood with metabolic risk in young adults. J Clin Endocrinol Metab 92:98-103.

12. **Crespo PS, Prieto Perera JA, Lodeiro FA, Azuara LA** 2007 Metabolic syndrome in childhood. Public Health Nutr 10:1121-1125.

13. **Agius R, Savona-Ventura C, Vassallo J** 2013 Transgenerational metabolic determinants of fetal birth weight. Exp Clin Endocrinol Diabetes 2013; 121:431-435.

14. **McCance D, Pettitt D, Hanson R, Jacobsson L, Knowler W, Bennett P** 1994 Birth weight and non-insulin dependent diabetes: thrifty genotype, thrifty phenotype, or surviving baby genotype? BMJ 308:942–945.

15. **Stuebe A** 2009 The risks of not breastfeeding for mothers and infants. Rev Obstet Gynecol 2:222-231.

16. **Verd S, Barriuso L, Gich I, Gutiérrez A, Nadal-Amat J, Carreras E.** Risk of early breastfeeding cessation among symmetrical, small for gestational age infants. Ann Hum Biol 2013; 40:146-151.

17. **Oddy WH** 2012 Infant feeding and obesity risk in the child. Breastfeed Rev 20:7-12.

18. **Yang Z, Huffman SL** 2013 Nutrition in pregnancy and early childhood and associations with obesity in developing countries. Matern Child Nutr 2013 9:105-119.

19. **Huang RC, Burke V, Newnham JP, Stanley FJ, Kendal GE, Landau LI, Oddy WH, Blake KV, Palmer LJ, Beilin LJ** 2007 Perinatal and childhood origins of cardiovascular disease. Int J Obesity 31:236–244.

20. **Behl M, Rao D, Aagaard K, Davidson TL, Levin ED, Slotkin TA, Srinivasan S, Wallinga D, White MF, Walker VR, Thayer KA, Holloway AC** 2013 Evaluation of the association between maternal smoking, childhood obesity, and metabolic disorders: a national toxicology program workshop review. Environ Health Perspect 121:170-180.

21. **Sánchez-Muniz FJ, Gesteiro E, Espárrago Rodilla M, Rodríguez Bernal B, Bastida S** 2013 Maternal nutrition during pregnancy conditions the fetal pancreas development, hormonal status and diabetes mellitus and metabolic syndrome biomarkers at birth. Nutr Hosp 28:250-274.

22. **Ryckman KK, Borowski KS, Parikh NI, Saftlas AF** 2013 Pregnancy complications and the risk of metabolic syndrome for the offspring. Curr Cardiovasc Risk Rep 7:217-223.

23. **Boney CM, Verma A, Tucker R, Vohr BR** 2005 Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. Pediatrics 115:290-296.

24. **Cole TJ, Bellizzi MC, Flega KM, Dietz WH** 2000 Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 320:1–6.

25. **Brook CGD** 1971 Determination of body composition of children from skinfold measurements. Arch Dis Child 46:182–184.

26. **Siri WE** 1961 Body composition from fluid spaces and density: analysis of methods. In: Brozeck J, Henschel A (Editors). Techniques for measuring body composition. Washington: National Acad Sci National Res Council.

27. **Berson S, Yellow RS** 1959 Quantitative aspects of the reaction between insulin and insulin-binding antibody. J Clin Invest 38:1996-2016.

28. **Aguayo Calcena AA** 2011 Prevalencia del síndrome metabólico en una población de niños obesos en el País Vasco, su relación con la resistencia a la insulina, las adipoquinas y ghrelina. (PhD thesis). Universidad del País Vasco.

29. **Studies to Treat or Prevent Pediatric Type 2 Diabetes (STOPP-T2D) Prevention Study Group*** 2008 Prevalence of the metabolic syndrome among a racially/ethnically diverse group of U.S. eighth-grade adolescents and associations with fasting insulin and homeostasis model assessment of insulin resistance levels. Diabetes Care 31:2020-2025.

30. **Pan Y, Pratt CA** 2008 Metabolic syndrome and its association with diet and physical activity in US adolescents. J Am Diet Assoc 108:276-286.

31. **Eriksson JG, Osmond C, Kajantie E, Forsén TJ, Barker DJP** 2006 Patterns of growth among children who later develop type 2 diabetes or its risk factors. Diabetologia 49:2853–2858.

32. **Khuc K, Blanco E, Burrows R, Reyes M, Castillo M, Lozoff B, Gahagan** 2012 Adolescent metabolic syndrome risk is increased with higher infancy weight gain and decreased with longer breastfeeding. Int J Pediatr 5:478610.

33. **Chen SK, Luo JS, Qin YF, Fan X, Tang Q, Feng Y** 2011 Epidemiological study on the association between obesity with metabolic syndrome in obese children and adolescents of Nanning city, Guangxi. Zhonghua Liu Xing Bing Xue Za Zhi 32:969-972.

34. **Wang SQ, Liu YJ, Zhan J, Liu XL, Feng Q, Gong J, Talbott EO, He QQ** 2013 Determinants of metabolic syndrome in Chinese schoolchildren. Asia Pac J Public Health 4 [Epub ahead of print].

35. **Yang Z, Huffman SL** 2013 Nutrition in pregnancy and early childhood and associations with obesity in developing countries. Matern Child Nutr 9:105-19.

36. **De Armas MG, Megías SM, Modino SC, Bolaños PI, Guardiola PD, Alvarez TM** 2009 Importance of breastfeeding in the prevalence of metabolic syndrome and degree of childhood obesity. Endocrinol Nutr 56:400-403.

37. **Ekelund U, Anderssen S, Andersen LB, Riddoch CJ, Sardinha LB, Luan J, Froberg K, Brage** 2009 Prevalence and correlates of the metabolic syndrome in a population-based sample of European youth. Am J Clin Nutr 89:90-96.

38. **Ornoy A** 2011 Prenatal origin of obesity and their complications: Gestational diabetes, maternal overweight and the paradoxical effects of fetal growth restriction and macrosomia. Reprod Toxicol 32:205-212

39. **Ley SH, O'Connor DL, Retnakaran R, Hamilton JK, Sermer M, Zinman B, Hanley AJ** 2010 Impact of maternal metabolic abnormalities in pregnancy on human milk and subsequent infant metabolic development: methodology and design. BMC Public Health 6:590.

40. **Motte E, Beauval B, Laurent M, Melki I, Schmit A, Vottier G, Mitanchez D** 2010 Programming nutritional and metabolic disorders: the diabetic environment during gestation. Arch Pediatr 17:60-70.

41. **Merritt TA, Mazela J, Adamczak A, Merritt T** 2012 The impact of second-hand tobacco smoke exposure on pregnancy outcomes, infant health, and the threat of third-hand smoke exposure to our environment and to our children. Przegl Lek 69:717-720.

42. **Noda T** 2013 Effects of tobacco smoke on fetus and children. Nihon Rinsho 71:454-458.

TABLE 1. Physical characteristics of subjects, based on sex and presence of metabolic syndrome

	Female subjects		Male subjects		
	Metabolic Syndrome	Non-Metabolic Syndrome	Metabolic Syndrome	Non-Metabolic Syndrome	*P* value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Weight (Kg)	68.64 ± 9.02	49.45 ± 7.86	85.09 ± 11.46	54.54 ± 11.82	0.000
Height (cm)	160.76 ± 5.76	157.43 ± 7.02	168.47 ± 8.47	161.48 ± 10.70	0.000
Birth weight (Kg)	3.26 ± 0.45	3.17 ± 0.47	3.30 ± 0.59	3.19 ± 0.51	0.038
Body Mass Index (kg/m^2)	26.39 ± 2.88	19.88 ± 2.45	29.97 ± 3.36	20.73 ± 3.13	0.000
Body Fat (%)	39.44 ± 4.83	27.38 ± 6.53	40.79 ± 3.60	26.24 ± 7.51	0.000
Waist Circumference (cm)	86.83 ± 6.00	67.72 ± 6.09	100.78 ± 5.42	71.33 ± 9.35	0.000
Hip Circumference (cm)	95.91 ± 5.80	80.97 ± 6.57	103.44 ± 5.63	82.39 ± 8.57	0.000
Waist-to-Hip Ratio	0.89 ± 0.10	0.83 ± 0.04	0.97 ± 0.04	0.86 ± 0.05	0.000
Systolic Blood Pressure (mmHg)	130.48 ± 14.34	113.65 ± 13.47	137.74 ± 15.98	117.89 ± 14.83	0.000
Diastolic Blood Pressure (mmHg)	69.87 ± 9.00	62.53 ± 8.15	73.00 ± 10.07	63.70 ± 8.79	0.000
N	98 (18.38%)	435 (81.61%)	34 (7.26%)	434 (92.73)	

Data are mean ± SD.

The mean values of the variables were compared for gender and the presence of metabolic syndrome by means of analysis of variance (ANOVA) and *post hoc* analysis.

TABLE 2. Biochemical characteristics of the subjects, based on sex and presence of metabolic syndrome.

	Female subjects		Male subjects		*P* value
	Metabolic Syndrome	Non-Metabolic Syndrome	Metabolic Syndrome	Non-Metabolic Syndrome	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Basal Insulin (mcU/ml)	33.20 ± 14.51	17.20 ± 1.92	47.82 ± 11.14	18.79 ± 6.17	0.000
Basal Glucose (mg/dL)	88.23 ± 32.33	84.54 ± 28.10	92.35 ± 38.77	85.69 ± 30.59	0.136
HBA1c (%)	6.24 ± 2.06	4.23 ± 0.32	9.27 ± 6.67	4.43 ± 0.74	0.000
Total Cholesterol	82.74 ± 16.97	81.01 ± 15.34	81.24 ± 14.32	81.77 ± 17.54	0.532
Triglyceride (mg/dL)	132.19 ± 63.86	123.20 ± 40.64	135.12 ± 66.19	128.38 ± 57.95	0.142
HDL-C (mg/dL)	39.92 ± 2.63	40.05 ± 3.17	39.21 ± 3.58	40.18 ± 2.73	0.169
LDL-C (mg/dL)	95.55 ± 25.36	92.30 ± 21.76	102.09 ± 31.49	92.64 ± 22.76	0.026
Homocysteine (µmol/L)	9.64 ± 3.77	8.93 ± 3.65	9.87 ± 4.58	9.16 ± 3.88	0.063
NEFA (mmol/L)	0.43 ± 0.21	0.18 ± 0.04	0.61 ± 0.19	0.21 ± 0.10	0.000
Ceruloplasmin (mg/dL)	50.64 ± 26.76	21.41 ± 2.44	75.26 ± 17.04	24.27 ± 11.54	0.000
N	98 (18.38%)	435 (81.61%)	34 (7.26%)	434 (92.73)	

Data are mean ± SD.

The mean values of the variables were compared for gender and the presence of metabolic syndrome by means of analysis of variance (ANOVA) and *post hoc* analysis.

TABLE 3. Duration of maternal breastfeeding, based on sex and presence of metabolic syndrome.

		Female subjects						Male subjects					
		Metabolic Syndrome			Non-Metabolic Syndrome			Metabolic Syndrome			Non-Metabolic Syndrome		
		n	%	%Total	n	%	%Total	n	%	%Total	n	%	%Total
Breastfeeding Duration	Never	84	85.72	15.76	10	2.30	1.88	26	76.48	5.55	23	5.30	4.91
	1 – 3 months	5	5.10	0.94	20	4.60	3.75	2	5.88	0.43	8	1.84	1.71
	4 – 6 months	6	6.12	1.13	17	3.90	3.19	3	8.82	0.64	14	3.23	2.99
	> 6 months	3	3.06	0.56	388	89.20	72.79	3	8.82	0.64	389	89.63	83.13
Maternal Smoking	0 cigarettes	5	5.10	0.94	351	80.69	65.85	3	8.82	0.64	353	81.34	75.43
	< 10 cigarettes	8	8.16	1.50	42	9.65	7.88	5	14.71	1.07	41	9.44	8.76
	10-20 cigarettes	8	8.16	1.50	23	5.29	4.31	2	5.88	0.43	14	3.23	2.99
	> 20 cigarettes	77	78.58	14.44	19	4.37	3.58	24	70.59	5.13	26	5.99	5.55
Nutritional Status	Normal weight	31	31.63	5.81	428	98.39	80.30	2	5.88	0.43	390	89.86	83.33
	Overweight	43	43.88	8.07	7	1.61	1.32	11	32.36	2.35	39	8.97	8.33
	Obesity	24	24.49	4.50	0	0	0	21	61.76	4.49	5	1.17	1.07

n: number of cases in each lactation period.

%: percentage of cases in each lactation period.

% Total: total percentage of cases in each lactation period, based on sex.

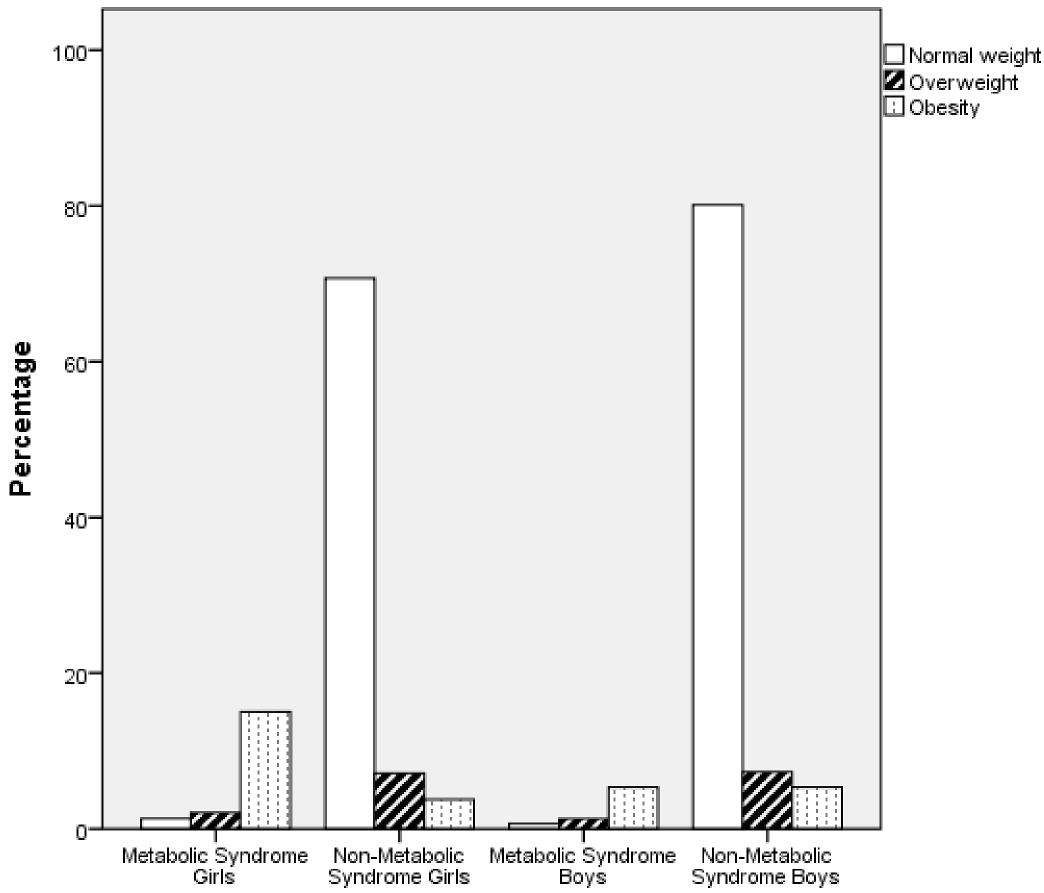

FIG. 1. Maternal nutritional status during pregnancy and the development of metabolic syndrome in their children.

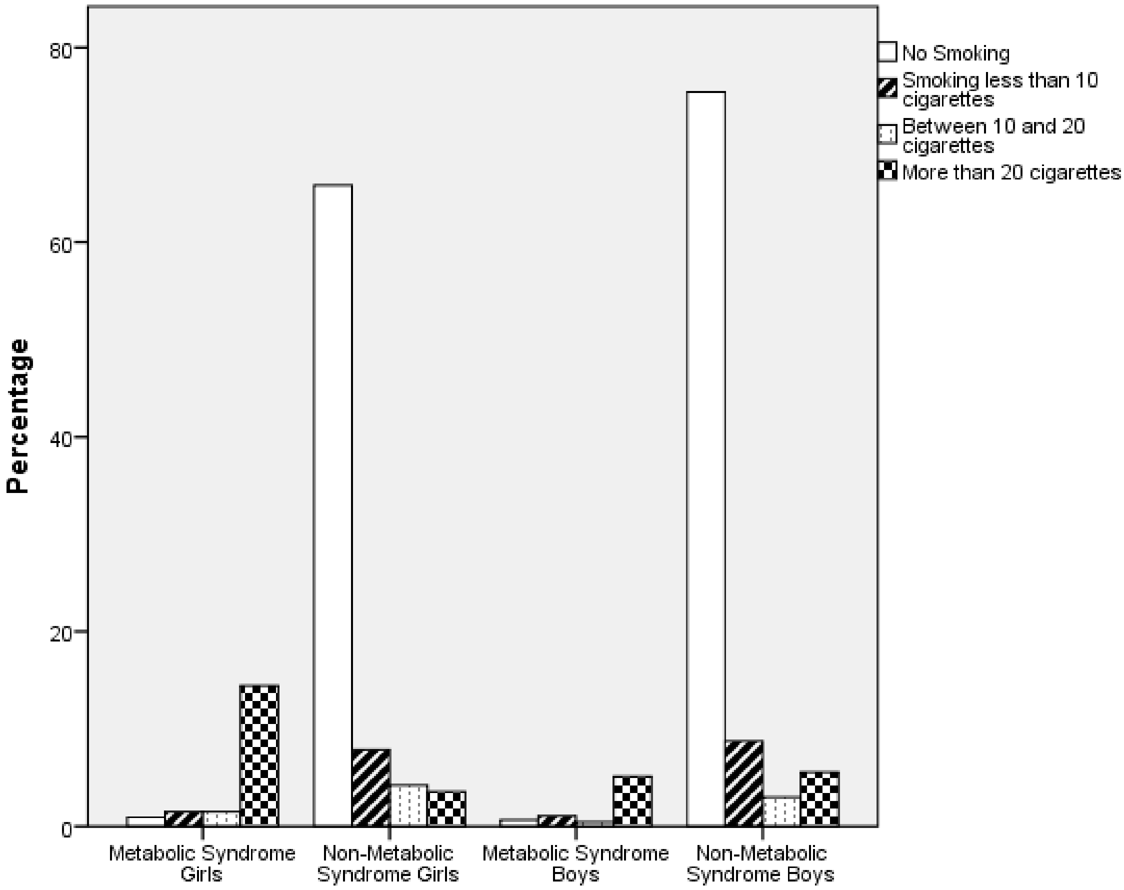

FIG. 2. Maternal smoking during pregnancy and the development of metabolic syndrome in their children.