

Cardiovascular and Diabetes Risk in Preschoolers

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Abstract: *Objective:* To perform an exploratory analysis of possible alterations in clinical markers of cardiovascular risk and type 2 diabetes in preschoolers living in urban and suburban areas of the municipality of Hermosillo, Sonora, Northwest Mexico. *Methods:* An observational and cross-sectional study was carried out on children from urban and suburban areas. Their weight, height, waist circumference, body fat percentage, and blood pressure were measured, and their lipid profile, glucose, and insulin concentrations were evaluated. *Results:* Eighty-two children with an average age of five were included in the study; 48 from the conurbation and 34 from the urban area. We found that malnutrition, overweight, and high body fat percentage (27 ± 0.52) coexist. In the suburban area, there was a higher percentage of children with pre-hypertension and alterations in lipids: elevated triglycerides (35%) and low HDL-c (25%) ($p < 0.01$). In the urban area, there was a higher percentage of children with altered glucose (12%), elevated insulin concentrations, and insulin resistance. *Conclusion:* The findings of this study show that cardiovascular risk factors and type 2 diabetes are prevalent in children aged three to six living in urban and conurbation areas of Hermosillo, Sonora.

Keywords: Preschool children; Malnutrition; Lipids; Glucose; Insulin; Risk factors; Cardiovascular disease; Obesity; Type 2 diabetes; Mexico

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1. Background

The obesity epidemic has reached the child population worldwide, thus necessitating the evaluation of risk factors for non-communicable diseases, such as type 2 diabetes and cardiovascular diseases, in school children. Thus far, investigations have shown that school children exhibit physical and metabolic changes associated with obesity, including alterations in blood lipid and markers of glucose metabolism^[1]. Genetics, diet, and physical inactivity are implicated in its early onset^[2].

Some studies suggest that excess weight gained before the age of five may persist into adulthood (“persistent obesity”)^[3,4]. Although obesity is uncommon in children or adolescents with cardiovascular disease, the risk factors that precipitate atherosclerosis can be observed in children as young as four^[5].

Serum lipid and lipoprotein concentrations increase during early childhood at approximately two years of age and reach those observed in young adults^[6-8]. Epidemiological studies have shown that if blood lipid concentrations are altered in childhood, there is a high risk of atherosclerotic lesions in adulthood^[9]. Other

research has established that blood lipids in children are correlated with obesity and insulin resistance ^[10].

Previous studies by our working group carried out in the Sonora population have confirmed overweight and obesity in children aged six to nine, as well as metabolic syndrome in urban (7%) and rural (5%) areas. Diet and physical inactivity are the two main factors involved ^[11].

In Mexico, the problem does not seem to be confined to school children. According to the National Health and Nutrition Survey ^[12], 14.1% of children under five years of age are overweight and obese, and alterations in cardiovascular risk markers, such as lipid profile, can be observed, suggesting that cardiovascular diseases begin at an earlier age in this population.

The objective of this study was to perform an exploratory analysis of possible alterations in the clinical markers of cardiovascular risk and type 2 diabetes in preschoolers living in urban and conurbation areas of the municipality of Hermosillo, Sonora, northwestern Mexico.

2. Materials and methods

An observational and cross-sectional study was carried out on children from urban and suburban areas of Hermosillo, Sonora. This research is part of the Follow-up Studies of the School Breakfast Program in Sonora that is carried out every year at the Research Center for Food and Development A.C. Participating schools were randomly selected from a census of preschools belonging to the School Breakfast Program.

Inclusion criteria: children between three and six years of age, without respiratory disease, fever, or diarrhea; having taken all the measurements and informed consent signed by parents or legal representatives who agreed to participate (the objective of the study and the inherent benefits and risks of their children's participation were clearly detailed in accordance with what was stated and approved by the interinstitutional ethics committee of CIAD A.C.). Children who did not meet these criteria were excluded from the study.

2.1. Anthropometry, body fat, and blood pressure

Body weight and height were measured according to the procedure described by Jeliffe *et al.* ^[13]. The World Health Organization's Anthro software, version 3.2.2, was used to calculate the BMI z-score for age (z-BMI/E) ^[14]. Waist circumference was measured with a fiberglass tape measure (Lafayette Instrument, USA), considering the midpoint between the last rib and the iliac crest. Central obesity was considered to be a value more than or equal to the 90th percentile, according to sex and age, for the Mexican-American population ^[15]. Body fat was measured by electrical bioimpedance, with the IMP5TM equipment (Impedimed IMP5TM Impedimed Pty. Ltd., Australia). Body fat mass was calculated using the equation generated by Ramirez and his co-authors ^[16]. Blood pressure was measured with a mercury baumanometer (Desk Model Mercurial Sphygmomanometer, Model 100, USA), following the criteria of the National High Blood Pressure Education Program (NHBPEP) for children and adolescents ^[17].

2.2. Plasma lipid, glucose, and insulin

After fasting for 12 hours, 5 ml of blood was drawn from the median cubital vein. Plasma and red blood cells were separated by 2400 x g centrifugation. Total cholesterol and triglycerides were measured with commercial CHOD-PAP (Roche Diagnostics) and GPO-PAP (Roche Diagnostics) kits, respectively. High-density lipoprotein cholesterol (HDL-c) was determined in the supernatant after lipoprotein precipitation with Apo B (Roche Diagnostics); low-density lipoprotein (LDL-c) was calculated using the equation described by Friedewald and others ^[18]. Daniels and Greer's percentiles and cut-off points were used to classify lipid profile values ^[19]. Fasting glucose was measured by using the GOD-PAP glucose oxidase method (Roche Diagnostics), in which a value greater than 100 mg/dL was considered impaired fasting ^[20]. Insulin was determined by sandwich immunoassay (ELISA) with a commercial reagent kit (ALPO Insulin Diagnostics, NH, USA), using the reference values proposed by García-Cuartero and his group ^[21].

In order to reveal the characteristics of the population, the normality of the data was verified (19 quantitative variables using Kolmogorov-Smirnov, Shapiro-Wilks W, Anderson-Darling, D'Agostino tests), and descriptive statistics were performed, grouped by urban and conurbation areas. The data were presented as mean \pm standard deviation and as median and interquartile ranges, respectively. Student's t-test for independent samples was used to test the differences between groups, and the Mann Whitney U test was used for non-normal variables. In order to test the differences by body fat content (normal, moderate, and high), an analysis of variance (ANOVA) was used. In both analyses, the differences were considered significant with $p \leq 0.05$. The data were analyzed by using the statistical program NCSS 2007 (Number Cruncher Statistical System for Windows, Kaysville, Utah, USA).

3. Results

Eighty-two preschoolers aged three to six were evaluated from two different geographical areas of Hermosillo, Sonora; 34 from different neighborhoods in the urban area (13 girls and 21 boys), and 48 from the suburban area, including Poblado Miguel Alemán and the town of El Tazajal (25 girls and 23 boys).

Table 1 shows the data obtained on physical growth and metabolic profile, according to the study area. Preschoolers in the urban area had significantly higher concentrations of total cholesterol, glucose, insulin, and homeostatic model assessment for insulin resistance (HOMA-IR) ($p < 0.05$). In contrast, the mean age and waist circumference were higher in preschoolers from the conurbation area ($p < 0.05$).

Table 1. Physical characteristics, body composition, and biochemical-clinical variables of preschool children from urban and conurbation areas of Hermosillo, Sonora, Mexico

Parameter	Total (n=82)	UA (n=34)	CUA (n=48)	p
Age** (years)	5.07 (4.6–5.2)	4.9 (4.0–5.2)	5.1 (4.7–5.4)	0.05
Weight** (kg)	16.7 (15.6–18.6)	16.4 (15.7–18.6)	16.8 (15.2–18.9)	0.75
Height* (cm)	105.5 \pm 5.0 (93.9–118.6)	105.5 \pm 5.2 (97–118.6)	105.6 \pm 5.0 (93.9–116.6)	0.93
Z-P/E*	-0.4 \pm 0.9 (2.4–2.2)	-0.3 \pm 0.8 (-2.4–1.8)	-0.5 \pm 1 (-2.4–2.2)	0.28
Z-T/E*	-0.7 \pm 1 (-3.0–2.1)	-0.5 \pm 0.9 (2.6–2.1)	-0.9 \pm 1.0 (3.0–1.0)	0.07
Z-IMC	-1.6 \pm 0.8 (-1.7–2.6)	-0.0 \pm 0.7 (-1.7–1.6)	0.0 \pm 0.9 (-1.5–2.6)	0.81
Waist circumference**	50.15 (48.1–52.8)	49.1 (47.4–51.2)	51.1 (46.9–53.4)	0.03
Fat % (BIE)*	22.2 \pm 5.9 (7.1–41.1)	21.6 \pm 6.37 (7.1–34.8)	22.6 \pm 5.5 (11.7–41.1)	0.45
PAS**	80 (70–87.5)	80 (72.5–90)	80 (70–84.3)	0.18
PAD**	50 (41.8–57.5)	51.2 (42.5–60)	50 (40–55)	0.75
TG (mg/dL)**	86.7 (44–189)	85.4 (44–189)	87.2 (49.2–187.4)	0.41
CT (mg/dL)*	114.3 \pm 26.5 (64.4–196.1)	121.6 \pm 26.6 (65.4–196.1)	109 \pm 25.25 (64.4–169.2)	0.05
LDL-c (mg/dL)*	58.2 \pm 25.2 (139–127.8)	62.1 \pm 26 (18.6–127.8)	55.5 \pm 24.5 (13.9–108.4)	0.24
HDL-c (mg/dL)**	37.8 (17.2–89.1)	40.93 (30.3–53.4)	35.76 (17.2–89.1)	< 0.01
Glucose (mg/dL)*	82.3 \pm 14.0 (49–123)	87.9 \pm 15.3 (67–123)	78.4 \pm 11.2 (49–103)	< 0.01
Insulin, μ IU/L (n=63)	2.45 (0.07–28.7)	3.5 (0.05–28.7)	1.87 (0.01–18.1)	< 0.01
HOMA-IR** (n=63)	0.49 (0.01–4.7)	0.75 (0.06–4.7)	0.36 (0.01–2.1)	< 0.01

*Mean \pm standard deviation; **median (interquartile range [25–75]); UA: urban area; CUA: conurbation area; % fat (BIE): percentage fat by electrical bioimpedance; TC (mg/dL): total cholesterol; TG (mg/dL): triglycerides; HDL-c (mg/dL): high-density lipoprotein cholesterol; LDL-c (mg/dL): low-density lipoprotein cholesterol; SBP (mmHg): systolic blood pressure; DBP (mmHg): diastolic blood pressure [1]. The difference between groups was tested by using student's test for two independent samples, and Mann-Whitney U was used for non-normal data ($p < 0.05$).

3.1. Alterations in body composition and clinical indicators

In both study areas and age groups, stunted growth was observed (children aged three to five in the urban area = 5.8%; conurbation area = 5.2%; children older than five in the conurbation area = 17.2%). Only one case of impairment was found in a child under five years of age in the urban area.

In addition, “risk of overweight,” “overweight,” and elevated waist circumference were observed (**Table 2**). In the conurbation area, there was a higher proportion of children under five years of age who were overweight and with elevated waist circumference (≥ 90 percentile; Fernandez and his group) ^[15] as well as elevated body fat percentage ^[22].

Table 2. Alterations in body composition and biochemical markers in preschoolers by study area

Classification	Reference value	3-5 years		≥ 5 years	
		UA (n=19)	CUA (n=17)	UA (n=29)	CUA (n=17)
Overweight ^Δ	BMI/E > 1DE	ND	10.5%	11.7%	7.1%
Elevated waist circumference*	> 90 percentile	11.7%	21%	5.8%	6.8%
Elevated body fat**	> 26% children	ND	ND	5.8%	6.8%
	> 34% girls				
		UA (n=34)	CUA (n=48)		
High triglycerides [¥]	> 85 mg/dL	30%	35%		
High total cholesterol [¥]	> 200 mg/dL	3%	ND		
High LDL-c [¥]	110–129 mg/dL	6%	ND		
Very low HDL-c [¥]	38 mg/dL (≤ 5 percentile)	6%	25%		
Altered glucose ^δ	> 100 mg/dL	11.7%	2%		
High insulin ^δ	90 percentile/age	20%	2.6%		
HOMA-IR ^δ	90 percentile/age	16%	ND		
Pre-hypertension (diastolic) ^θ	90–94 percentile	41%	27%		
Pre-hypertension (systolic) ^θ	90–94 percentile	ND	6%		
High diastolic blood pressure ^θ	> 99 percentile	ND	4%		
High systolic blood pressure ^θ	> 99 percentile	ND	2%		

Abbreviations: CUA, conurbation area; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment for insulin resistance; LDL, low-density lipoprotein; UA, urban area.

In terms of clinical markers (**Table 2**), approximately 30% of the children had elevated triglycerides, above the 95th percentile (85 mg/dL) ^[19]. In contrast, their HDL-c levels were low (38–43 mg/dL), especially in the conurbation area, where there was a higher proportion of children with very low concentrations (≤ 5 th percentile = 38 mg/dL).

More markedly, in the urban area, glucose and insulin alterations were found with cases of insulin resistance. Blood pressure measurements showed that in both areas, there were children with elevated normal diastolic blood pressure, a clinical condition called pre-hypertension ^[17]. Joint cases of diastolic and systolic hypertension were only observed in the conurbation area.

In both areas, there were cases of hypoglycemia (urban area = 8.8%; conurbation area = 27%) and pre-diabetes (urban area = 11.8%; conurbation area = 2%). Likewise, among the preschoolers studied (n=82), 9.5% had elevated insulin levels (≥ 90 th percentile = 10.63 μ IU/mL), indicating that this condition is more prevalent in the urban area (20% versus 2.6%) ($p < 0.01$). Insulin resistance was found in 6.3% of the total population studied ^[21].

An exploratory comparison analysis revealed some significant differences between sexes. Girls in the

urban area had higher body fat percentage ($24\% \pm 6.7$ versus $20\% \pm 5.6$) ($p \leq 0.05$) and triglyceride concentration (95.8 versus 71.9 mg/dL) ($p < 0.01$) than boys. In the conurbation area, girls had higher insulin and HOMA-IR values than boys ($p < 0.05$). An analysis of association between the variables showed that there is a correlation between body fat percentage and waist circumference in both study groups (urban area, $r = 0.71$; $p < 0.01$; conurbation area, $r = 0.64$; $p < 0.01$).

The majority of children older than five years of age had normal body fat content (urban area = 64.7%; conurbation area = 72.4%) ($p < 0.01$); however, cases with moderate (urban area = 29.4%; conurbation area = 17.2%) and high (urban area = 5.8%; conurbation area = 10.3%) body fat content were also noted [22]. Using the body fat classification as a reference [22], possible changes in the biomarkers were evaluated, showing that children with moderate and high body fat percentages tend to have higher systolic and diastolic blood pressure, glucose, total cholesterol, LDL-c, as well as triglycerides.

4. Discussion

This study was carried out in the city of Hermosillo, Sonora, among preschool children living in urban and suburban areas. The global analysis of physical growth, considering P/E and T/E indicators, shows that approximately 10% of preschool children between three and five years of age and 6.8% of children older than five years of age have impaired growth. With regard to this, the WHO [23] points out that undernutrition during the first years of life can increase the risk of chronic non-communicable diseases in adulthood.

In addition, stunted growth was detected, and children at risk of overweight (conurbation area = 10.5%; urban area = no cases) and overweight (conurbation area = 15.7%; urban area = 5.8%) were observed. In their analysis of the issues of overweight and obesity in preschool children worldwide, De Onis and her colleagues reported a prevalence of overweight risk of 14.4% globally and 13.6% for developing countries [24]. The overweight risk figure observed in this study is 1.5% higher than those reported worldwide. Our findings also highlight that the area around the city of Hermosillo is the most affected by overweight issues, and it is noteworthy that no cases of obesity were found in the study areas (> 3 SD). The national report for this age group revealed that the combined prevalence of overweight plus obesity in urban areas and rural areas was 14.1% and 8.7%, respectively. Our overweight results are very similar to this report; however, a direct comparison is not feasible because the reference used employs combined prevalence.

A high proportion of children in both age groups and study areas had waist circumference values above the 90th percentile. In children older than five years of age, a concordance was found between the proportion of children with elevated waist circumference and that of children with elevated body fat percentage [22]. Considering the limitations that may exist due to the lack of percentile references for our population, it can be assumed that a portion of these children's body fats accumulates around the viscera. Excess fat accumulated before puberty is associated with increased blood lipid concentrations, and thus increased risk of chronic degenerative diseases [25].

The results obtained from the growth indicators point to a preschool population, in which undernutrition and overweight coexist, especially in the urban area; the double burden of malnutrition is evident. It has been shown that malnutrition in childhood is a marker of premature chronic diseases in adulthood, such as diabetes and cardiovascular disease [26]. It is important to consider that at this stage of life, overweight can be a factor favoring atherosclerosis that will manifest itself as cardiovascular disease in adulthood.

In accordance with the pediatric recommendations for lipid profiling suggested by Daniel and Greer [19], this study shows that the preschool population evaluated had elevated plasma triglycerides (95th percentile = 85 mg/dL) and low HDL-c concentrations (5th percentile = 38 mg/dL). Both indicators are considered independent cardiovascular risk factors, as well as being part of the metabolic syndrome. Blood lipids are influenced by genetics, diet, and physical activity.

This study did not evaluate any of these variables and hence cannot explain the influence of any of these factors on the alterations found. Epidemiological studies have shown that if blood lipid concentrations are altered during childhood, atherosclerotic lesions will eventually occur in adulthood [9].

HDL particles have antioxidative properties (PON1 enzyme) that prevent the oxidation of LDL particles, and thus atherosclerosis [27]. In this study, 25% of the children in the suburban area and 5.8% in the urban area had values below the 5th percentile of HDL-c, a condition referred to as hypoalphalipoproteinemia. It is also important to highlight that most of the children were below the 10th percentile (43 mg/dL) (conurbation area = 54%; urban area = 50%), suggesting that this population may have very low antioxidant protection against LDL-c and also less capacity to catabolize stored cholesterol, which could lead to the onset of fatty streak formation at a young age.

The clinical pattern of elevated triglycerides and low HDL-c (86.7 mg/dL and 37.8 mg/dL) agrees with that reported by Reaven and his co-authors for the Mexican-American school population (84.6 mg/dL and 47 mg/dL) [28]. Additionally, with previous studies carried out in the same region but among school children aged six to twelve, in whom the same pattern of alterations was observed, Ramirez found a similar lipid pattern, characterized by metabolic syndrome, in rural (5%) and urban (7.4%) areas [11].

The findings of this study are significant as they show that the alterations in blood lipids that had been previously reported in school children and adults in the same region can be observed in preschool age. The alterations at this age also suggest that there may be a genetic factor involved [29].

Another important risk factor for cardiovascular disease is arterial hypertension, which is associated with other factors such as overweight, obesity, physical inactivity, and high lipid concentrations [2]. In this study, only those in the conurbation area were found to have diastolic (4%) and systolic (2%) hypertension; however, according to the National High Blood Pressure Education Program Working Group 17 (NHBPEP 17), a large proportion of preschoolers have diastolic prehypertension. A previous study by our group reported 12% prevalence of hypertension in school children in this same area. The proportions reported in this study are smaller but are significant since the issue is detected at an even earlier age.

Fasting glucose and insulin concentrations, as well as the HOMA-IR values were significantly higher in the urban area ($p < 0.01$). Children with impaired glucose had a mean value of 116 mg/dL, where the highest value recorded was 123 mg/dL in the urban area, which received medical attention for a possible diagnosis of diabetes. The elevation of insulin observed in the children (urban area = 20%; conurbation area = 2.6%) suggests possible metabolic compensation in the attempt to normalize glucose concentration [30].

According to the diagnostic criteria of Garcia and his group [21], children, in the urban area, have insulin resistance with HOMA-IR values above the 90th percentile. Both, insulin and insulin resistance coincide with the findings of altered glucose, indicating possible impairments in glucose metabolism that could trigger type 2 diabetes at an earlier age [20]. Acanthosis nigricans, which is associated with hyperinsulinemia, was also looked for in this study, especially in the neck region, but no cases were found. The data for two additional variables, birth weight and type of birth (cesarean section or delivery) (conurbation area $n = 37$; urban area $n = 29$), were also recorded when possible. Of the total number of records obtained for each case, the average birth weight was as follows: conurbation area = 3417 ± 568 g; urban area = 3259 ± 579 g ($p = 0.2$). In the conurbation area, 21% of the children were macrosomic (birth weight greater than 4 kg), and 78% were delivered without complications. In contrast, in the urban area, 3.6% were macrosomic, and 58% were delivered without complications.

The results obtained from this investigation show the double burden of malnutrition, in which undernutrition and overweight issues coexist with high percentages of body fat. Cardiovascular risk factors and type 2 diabetes have also been verified to coexist in this age group. The conurbation area had a higher percentage of children with lipid abnormalities, high triglycerides (35%), low HDL-c (25%), and

prehypertension, while the urban area had a higher percentage of children with altered glucose (12%) and elevated insulin concentrations along with insulin resistance.

The dietary study carried out by Ayala-Mendivil ^[31] on school children from the same region showed that their diet is high in fat (> 30%), of which 37.6% comes from saturated fats and 5.4% from trans fats; likewise, 39% of the total carbohydrates consumed comes from simple sugars. These results suggest that preschoolers may have a similar dietary pattern that, in part, would respond to the clinical indicators observed in this study.

It is possible that other variables that have not been evaluated in this study, such as physical activity and heredity, play an important role in the occurrence of these clinical alterations, which, in addition, are risk factors of the metabolic syndrome ^[32]. In the case of children in the urban area, their birth weight seems to reflect that there may be a metabolic decompensation since pregnancy. In addition to the small sample size, we did not have adequate information to be able to prove this because we did not collect data on the mother's diet, weight gain during pregnancy, nor on the diagnosis of gestational diabetes, which are all aspects that remain as an unresolved task.

5. Conclusion

The findings of this study show that cardiovascular risk factors and type 2 diabetes are prevalent in children aged three to six living in urban and suburban areas of Hermosillo, in northwestern Mexico.

One of the limitations of this study lies in the fact that it has a small sample size, which prevented us from extrapolating the results to the rest of the preschool population. However, it is possible to demonstrate that there are indeed alterations in the clinical indicators of cardiovascular disease and diabetes in the preschool population, with significant differences between the groups evaluated. The birth weight registry gathered appears to point to a plausible explanation for the alterations at such a young age; however, further information is required to confirm it.

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Disclosure statement

The authors declare no conflict of interest.

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