

PRESENCE OF INSULIN RESISTANCE SYNDROME IN MEXICAN CHILDREN OF SAN LUIS POTOSI (MEXICO).

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Introduction



The metabolic syndrome, also called insulin resistance syndrome, is a cluster of metabolic anomalies including hyperinsulinemia, glucose intolerance, low-density lipoproteins (VLDL) and triglycerides (Tg) increase, high-density lipoproteins (HDL) decrease and hypertension. This syndrome plays an important role in the origin of cardiovascular disease (CVD) (1-6). Definitions for the diagnosis of the metabolic syndrome are focused on adult populations. (7-10),

Actually specific criteria for its early diagnosis has been defined for children and adolescents from northern Mexico (11). However, in this study we did not considered the presence hiperinsulim and Insulin resistance (IR) seems to be the primary anomaly in this syndrome, as reported in epidemiological studies performed in adults (12,13,14), and is a fundamental component of CVD and diabetes mellitus type 2 (DM), while syndrome insulin resistance is associated with IR and obesity in 85% of the cases (15). Moreover, there is evidence of compensatory hyperinsulinemia and IR in absence of clinical disorders among young people and in non-obese children, even decades before blood glucose levels increase (16). In recent reports, Haffner and collaborators demonstrated a decrease of insulin sensitivity in young Mexican-American adults, non obese and normoglycemic, compared with white non-Hispanic subjects. These studies suggest that IR starts early among Mexican-American subjects (17,18,19).

Few studies have been performed in children attempting to found associations among IR, body composition and serum lipoprotein levels. Of these, most studies were carried out in Caucasian, Afro-American, Hispanic, pima Indians and Japanese children (20, 21, 22). In addition, the analysis were performed in obese subjects, which limited the sample size (23-26). Nevertheless, these studies are extremely important given the diabetes and CVD epidemics that Latin-American countries will soon face up, due to the genetic predisposition of our population (27-30). In a recent pilot study performed in San Luis Potosí, Mexico, we found anomalies such as HDLc decrease, triglycerides increased and hyperinsulinism, that suggest the presence of metabolic syndrome in infantile population (31,32).

In light of this antecedent, we hypothesized that insulin resistance syndrome-associated parameters could be identified early in Mexican children in order to prevent the onset of DM in adults and decrease its prevalence and incidence in our country. For this purpose, we analyzed the relationships among IR, plasma lipid levels and anthropometrical measurements in children aged from 6 to 13 years old.

Materials and Methods

Subjects: Six hundred children (6-13 years old) were recruited from elementary schools in San Luis Potosí, Mexico. According to a list of schools provided by the Education Ministry, (from 273 public schools, 13 schools were selected by random to participate in this study). At each school 5 to 10 children were selected by random per grade. The inclusion criteria were the absence of any disease or medical treatment, and from the 600 children that fulfilled this conditions, 494 were included in this study. The project was approved by the Bioethics Committee of the Faculty of Medicine of the University of San Luis Potosí. Before providing and informed signed consent, the parents received detailed information about the purpose and methodology of the study. In one session, the clinical history was obtained, a previously validated questionnaire about life style (physical activity, sedentary, hours watching television) and alimentary habits was applied, weight, height and blood pressure (BP) were measured. The venous blood sample was withdrawn after 12 hour fasting overnight.

Biochemical analysis: Analytical determinations were performed in serum. Glucose was quantified by means of the glucose oxidasa method (Roche Diagnostics), cholesterol through the technique described by Stahler and collaborators (33), triglycerides according to Wahlefeld (34) and HDL following the technique of Burstein and collaborators (35). All determinations were carried out instrumentally (Reflotrón, Roche-Syntex, ciudad) and LDL were calculated using the Friedwald equation (36). Insulin was determined by radioimmunoassay using the technique Coat-A-Count-Insulin DPC in serum (37), while IR was evaluated according to the HOMA methodology proposed by Matthews (38). Control serum were analyzed in each batch quantifications for each one of the parameters analyzed, the variation coefficients were lower than 5%.

Statistics: Raw data of insulin, cholesterol and HDL concentrations were log transformed in order to satisfy normality criteria all other variables followed a normal distribution. Comparisons between clinical and biochemical parameters by gender were done by Student t-test. To analyze the relationship between insulin and HDL, systolic and diastolic blood pressure, cholesterol and triglycerides Pearson correlation coefficients were calculated. The significance value was fixed at 0.05. All analysis were done with the SPSS version 10.

Results

The questionnaire showed a mean of 3.5 hours daily watching TV, and less than 20 minutes of physical activity by day. In addition, inadequate diet and high soda consumption were repeatedly reported. The clinical and biochemical characteristics of the studied population are presented in table 1, separated by gender. We found statistically significant differences in boy and girls between systolic blood pressure, cholesterol, triglycerides, DL, insulin and insulin resistance index ($p < 0.01$) (Observe Table 1).

Table 1. Comparison between clinical and biochemical characteristics by gender in 494 children living in the city of San Luis Potosi, Mexico.

	<i>Girls (n = 173) Mean ± SD</i>	<i>Boys (n=321) Mean ± SD</i>
<i>Weight</i>	34.6 ± 11.4	35.6 ± 10.8
<i>Height</i>	1.3 ± 0.1	1.4 ± 0.1
<i>Age</i>	9.6 ± 1.9	9.5 ± 1.8
<i>Systolic blood pressure^b</i>	97.6 ± 12.4	92.7 ± 12.0
<i>Diastolic blood pressure</i>	58.5 ± 10.5	57.9 ± 9.6
<i>Glucose mg/dL</i>	83.2 ± 8.6	84.4 ± 8.3
<i>Cholesterol mg/dL^{a, b}</i>	158.3 ± 1.2	164.7 ± 1.2
<i>Tryglicerids mg/dL^b</i>	98.4 ± 43.5	89.2 ± 39.1
<i>HDL mg/dL^{a, b}</i>	41.2 ± 1.3	46.2 ± 1.3
<i>LDL mg/dL</i>	98.0 ± 23.9	102.3 ± 31.3
<i>Insulin µU/mL^{a, b}</i>	11.9 ± 1.8	9.1 ± 1.8
<i>Insulin Resistance Index by HOMA^{a, b}</i>	1.9 ± 1.8	2.4 ± 1.8

^a Geometric mean , ^b Student t-test $p < 0.01$

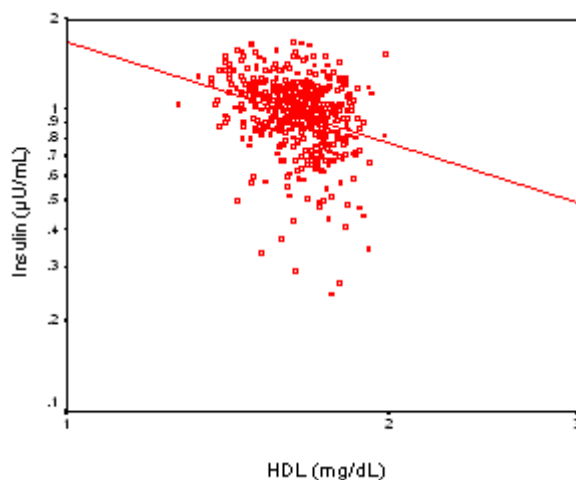
Age was divided in two groups younger and older than 10 years old. Values for index of insulin resistance were calculated for each quartile. Twenty-five of children in the older group had insulin resistance values above 3.36 (Observe Table 2).

Table 2. Values for Index of Insulin Resistance by HOMA by quartiles in two age groups in 494 children living in the city of San Luis Potosi, Mexico.

<i>Age group</i>	<i>Q₁</i>	<i>Q₂</i>	<i>Q₃</i>
6 – 10 (n=326)	1.25	1.84	2.72
> 10 – 13 (n=168)	1.91	2.78	3.36

The relationship between insulin and HDL is presented (Observe Figure 1). As expected a significant negative correlation was found between both values ($r = -0.31$, $p < 0.001$).

Figure 1. Relationship between HDL values (mg/dL) and insulin values (μ U/mL) in 494 children children living in the city of San Luis Potosi, Mexico ($r=-0.31$, $p<0.001$)



The correlations between insulin and blood pressure are presented in Figure 2 and 3 (systolic, $r = 0.34$, $p < 0.001$; diastolic, $r = 0.23$, $p < 0.001$).

Figure 2. Relationship between diastolic blood pressure (mmHg) and insulin values (μ U/mL) in 494 children children living in the city of San Luis Potosi, Mexico ($r=0.23$, $p<0.001$).

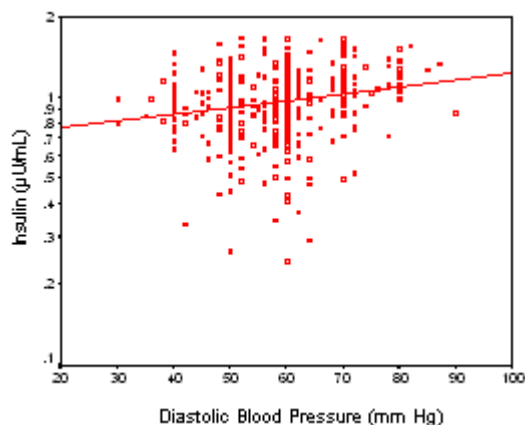
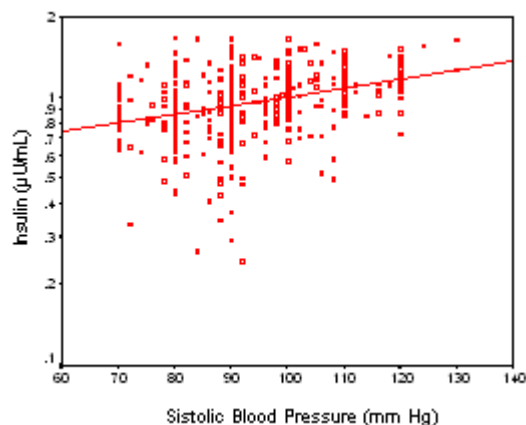


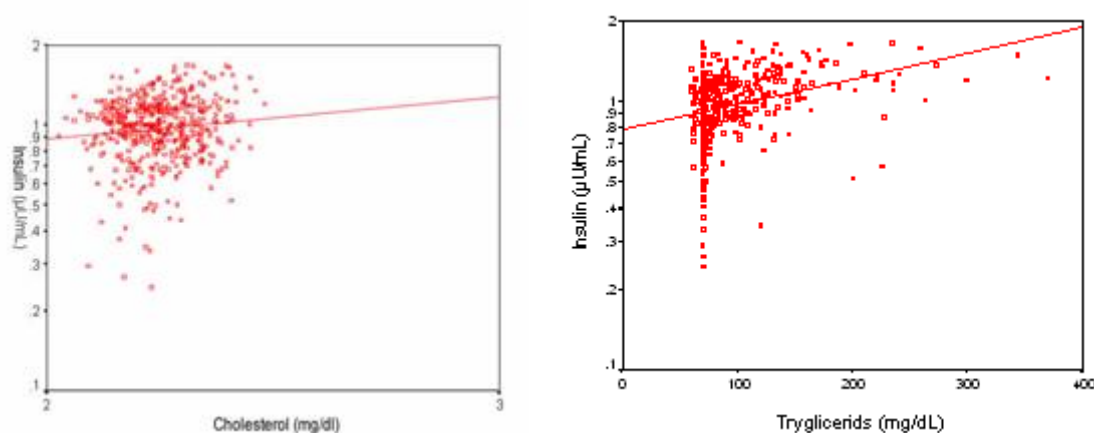
Figure 3. Relationship between systolic blood pressure (mmHg) and insulin values (μ U/mL) in 494 children children living in the city of San Luis Potosi, Mexico ($r=0.34$, $p<0.001$).



Positive and significant correlations were found between insulin and cholesterol ($r = 0.11$, $p = 0.01$) (Observe Figure 4) and between insulin and triglycerides ($r = 0.39$, $p < 0.001$) (Observe Figure 5).

Figure 4. Relationship between cholesterol values (mg/dL) and insulin values (μ U/mL) in 494 children children living in the city of San Luis Potosi, Mexico ($r=0.11$, $p=0.01$).

Figure 5. Relationship between tryglicerids values (mg/dL) and insulin values (μ U/mL) in 494 children children living in the city of San Luis Potosi, Mexico ($r=0.39$, $p<0.001$).



Discussion

It has been mentioned since 1988 that variations of insulin-stimulated glucose entry to the cell are determinants of premature atherosclerosis disease (39), given that the cluster of syndrome insulin resistance anomalies (hyperinsulinism, glucose intolerance, VLDL increase (TG), decrease of HDL cholesterol and hypertension) appear as consequence of insulin resistance (40). As mentioned above, there are reports that this syndrome is present in young, normogluceic and non-obese individuals from other ethnic groups, and children start presenting it as well (41-44).

Our purpose was to search for characteristic of this syndrome among Mexican children, given the high risk of our population due to genetic predisposition. Our results demonstrate that : 1) Blood glucose levels are normal in the studied population, both in girls and boys. 2) We found 11.5% children with insulin resistance among the group younger than 11 years old and 23.3% insulin resistant cases in the group of pubescent children, between 11 and 13 years old. Although it is reported that during puberty there is a "normal" increase of insulin resistance (45), we found here that the phenomenon is also present in pre-pubescent individuals. 3) Insulin resistance was higher in girls than in boys. It would be interesting to elucidate whether this fact is linked to the higher incidence of obesity among women than in men (46,47). 4) We obtained a positive, significant correlation between insulin and triglycerides, blood pressure and total cholesterol, which is in accordance with the expression of the plurimetabolic syndrome in adults (48,49). Also a similar correlation was observed between insulin and LDL (data not shown). Many studies have already demonstrated the inverse correlation between insulin and HDLc, as a component of the anomalies present in syndrome of insulin resistance, which was also found in our study (50,51). Moreover, the higher risk of cardiovascular disease by low levels of HDLc is well known, and we obtained a mean value that was just slightly higher than the lowest acceptable level in adults, which is 39.0 mg/dL. This finding is also in accordance with the predominantly sedentary life style reported in the clinical history and in the questionnaire (the average time that children spent watching television was 4 hours, also they did not practiced any sports activity).

The association between obesity and dyslipidemia and hyperinsulinism is widely know, even in pediatric population (52-55), nevertheless our findings are from a non-obese population, in children with a body mass index below 25, to accord the "International cut off points for body mass index for overweight and obesity by sex between 2 and 18 years, defined to pass through body mass index of 25 and 30 Kg/m² at age 18, obtained by averaging data from Brazil, Great Britain, Hong Kong, Netherlands, Singapore and

United States" (56), this indicating that biochemical changes and hyperinsulinism precede obesity? Independently of the answer to this question, our populations is in risk and this findings strongly suggest that the metabolic syndrome is present since childhood in our geographical region.

Conclusions

This study in San Luis Potosí, México analyzes the presence of insulin resistance syndrome among pediatric population. Our results indicate that preventive strategies must be implemented, such as programs of physical activity for the children, better alimentary habits and frequent monitoring of children at higher risk. These measures should be directed to ameliorate the quality of life from young adults, as well as to decrease the high costs that the complications associated to the metabolic syndrome represent for our health care institutions. Without underestimating the importance of the programs that the Health Ministry develops for the education of diabetic patients, we consider that it is even more important to prevent this disease. Prevention will lead to a decrease of its incidence and prevalence, since our population presents a high genetic predisposition for diabetes. It should be advised to increased the curricular hours oriented to practice sports in the publics schools, as a strategy for reducing the risk to develop obesity. Finally, is an obligation of the Mexicans to prevent the diabetes of our own people.

Abstract

There are some studies reporting a reduction in the insulin sensitivity in Mexican-American young people with normal levels of glucose compared with White persons suggesting that insulin resistance began at early ages in this group. Studies oriented to evaluate insulin sensitivity and lipoproteins levels are scarce and the majorities have been conducted in adults, mainly in Caucasian, African-American, Pima (group of Native Americans) and Japanese. In children, only obese population has been studied. Another shortcoming is the small simple size of the studies. Because some parameters associated with insulin resistance can be detected since childhood. The objective of this study was to quantify the levels of lipids in blood and anthropometric measurements associated with insulin resistance in Mexican children aged 6 to 13 years (n=494). The sample was selected by random from children attending public elementary schools. Blood samples were obtained to analyze glucose, cholesterol, triglycerides, insulin and low and high density lipoproteins (LDL and HDL respectively). Also blood pressure and anthropometric measurements were taken. All the biochemical measurements were done by enzymatic methods, only for insulin radioimmunoanalysis was conducted. Insensitivity to insulin was measured by HOMA, the mean value of HOMA was higher in girls compared with boys ($p < 0.01$). For boys the proportion of insuline resistance index with values above 3.36 was 25% in the age group of 10 to 13 years. An inverse correlation between insulin and HDL was observed ($r = -0.31$, $p < 0.001$). And positive associations between insulin and systolic blood pressure ($r = 0.35$, $p < 0.001$), diastolic blood pressure ($r = 0.23$, $p < 0.001$), triglycerides ($r = 0.39$, $p < 0.001$) and total cholesterol ($r = 0.11$, $p = 0.01$). Our results shown the early presence of parameters associated with the insulin resistance syndrome in children as observed in adults.

Key words: glucose intolerance, insulin resistance, diabetes, children

Resumen

Algunos estudios reportan la sensibilidad disminuida a la insulina en México- Americanos jóvenes, normoglucémicos, comparados con blancos no hispanos, evidenciando que la resistencia a la insulina comienza a una edad temprana en esta población. Estudios enfocados a la evaluación de la sensibilidad a la insulina y niveles de lipoproteínas son escasos y la mayoría han sido realizados en adultos, principalmente en población Caucásica, Áfrico-americanos, Indios Pima y Japoneses. En niños, solo población obesa ha sido estudiada y la mayoría de las investigaciones tienen un tamaño de muestra pequeño. Debido a que algunos parámetros asociados con la resistencia a la insulina pueden detectarse en la infancia, el objetivo de este estudio fue cuantificar los niveles de lípidos en sangre y evaluar los parámetros antropométricos asociados con resistencia a la insulina en niños Mexicanos de 6 a 13 años de edad (n=494). La muestra fue seleccionada de manera aleatoria de niños que asistían a las escuelas públicas. Se obtuvieron muestras de sangre para analizar glucosa, colesterol, triglicéridos, insulina y lipoproteínas de baja y alta densidad (LDL y HDL respectivamente). También se midió la presión arterial y se evaluaron las medidas antropométricas. Las determinaciones se hicieron por métodos enzimáticos excepto la insulina la cual se determinó por radio inmunoanálisis. La insensibilidad a la insulina se midió por HOMA, el valor promedio de HOMA fue mayor en las niñas que en los niños ($p < 0.01$). En el grupo de edad entre 10 - 13 años el 25% de los niños tuvo valores de índice de resistencia a la insulina mayores a 3.36. Obtuvimos una correlación negativa entre insulina y HDL ($r = -0.31$, $p < 0.001$), positiva con: la presión sanguínea sistólica ($r = 0.35$, $p < 0.001$), diastólica ($r = 0.23$, $p < 0.001$), con triglicéridos ($r = 0.39$, $p < 0.001$) y colesterol total ($r = 0.11$, $p = 0.01$). Nuestros resultados demuestran la aparición temprana de parámetros asociados con el síndrome de resistencia a la insulina que se observa en adultos.

Palabras clave: intolerancia a la glucosa, resistencia a la insulina, diabetes, niños

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