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ORIGINAL ARTICLE

The triglycerides and glucose index is associated with elevated blood pressure in apparently healthy children and adolescents

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Abstract

Prevalence of elevated blood pressure in pediatric population has been increasing worldwide. Thus, the aim of this study was to examine whether the triglycerides and glucose (TyG) index is associated with the presence of prehypertension or hypertension in children and adolescents. Apparently healthy children aged 6 to 15 years were enrolled in a population-based cross-sectional study. Participants were allocated into groups with normal blood pressure (NBP), prehypertension, and hypertension. Smoking, alcohol intake, pregnancy, previous diagnosis of diabetes, kidney, hepatic, or endocrine diseases were exclusion criteria. NBP was defined by systolic and/or diastolic blood pressure < 90th percentile, prehypertension by systolic and/or diastolic blood pressure ≥ 90th < 95th percentile, and hypertension by systolic and/or diastolic blood pressure ≥ 95th percentile, according to age, sex, and height percentiles. A total of 3589 children were enrolled, 1748 (49%) girls and 1841 (51%) boys, and allocated into groups with NBP (n = 2874), prehypertension (n = 271), and hypertension (n = 444). The multiple logistic regression analysis stratified by age and adjusted by the Z-score/SDS of body mass index and waist circumference showed that elevated TyG index was significantly associated with prehypertension (OR = 1.48; 95% CI: 1.08–2.05) and hypertension (OR = 1.63; 95% CI: 1.26–2.11).

Conclusion: The results of the present study shows that the elevated TyG index is significantly associated with the presence of prehypertension and hypertension in children and adolescents.

What is Known:
- *Prevalence of elevated blood pressure in children and adolescents has been increasing worldwide.*
- *Insulin resistance plays a key role in the pathogenesis of hypertension.*

What is New:
- *The elevated TyG index is significantly associated with the presence of prehypertension in children aged 6–9 years and adolescents aged 10–15 years.*
- *The elevated TyG index is significantly associated with the presence of hypertension in children aged 6–9 years and adolescents aged 10–15 years.*

Keywords TyG index · Triglycerides · Glucose · Blood pressure · Children

Abbreviations

TyG	triglycerides and glucose
NBP	normal blood pressure

Introduction

Prevalence of elevated blood pressure in children and adolescents has been increasing worldwide resulting in a major public health problem. In this context, the prevalence of prehypertension and hypertension in American children and adolescents aged 6 to 17 years was of 31.4% and 2.1%, respectively [8]; moreover, in apparently healthy Mexican children, the prevalence of prehypertension and hypertension was of 12.2% and 6.4% in children aged 6–10 years and 13.9 and 10.6% in those aged 11–15 years [4].

The sedentary lifestyle and, consequently, the weight gain are among the main risk factors for primary hypertension in children [2, 15]. In addition, insulin resistance also plays a key role in the pathogenesis of hypertension [25], finding that emphasizes the need of an early recognition of decreasing insulin sensitivity. With this regard, recently, it was reported that the triglycerides and glucose (TyG) index, a surrogate measurement of insulin resistance, were significantly associated with a

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higher risk of hypertension in middle-aged and elderly adults [7, 24]. However, to the best of our knowledge, there are no studies that have previously assessed the interaction between TyG index and the risk of high blood pressure in children. Hence, the aim of this study was to investigate whether the TyG index is associated with the presence of prehypertension or hypertension in apparently healthy children and adolescents.

Materials and methods

After the approval of protocol by the Mexican Social Security Institute Research Committee, in accordance with the ethical principles of the Declaration of Helsinki, a population-based cross-sectional study was carried out. A written informed consent was obtained from at least one of each participant's parents along with the informed assent from the children who were included in the study.

Eligible participants were apparently healthy children aged 6 to 15 years, from the general population of Mexico City, who were recruited in seven primary care units and from one elementary school, and from general population in Durango City, which were integrated in a cohort to evaluate cardiovascular outcomes. Smoking, alcohol intake, pregnancy, previous diagnosis of diabetes, kidney, hepatic, or endocrine diseases were exclusion criteria.

In order to control the potential sources of bias related to age, participants were stratified by age in two groups: (a) children aged 6–9 years and (b) adolescents aged 10–15 years. In addition, children of both groups were allocated into groups with normal blood pressure (NBP), prehypertension, and hypertension.

Definitions According to age, sex, and height percentiles, the NBP was defined by systolic and/or diastolic blood pressure < 90th percentile, prehypertension by systolic and/or diastolic blood pressure ≥ 90th < 95th percentile, and hypertension by systolic and/or diastolic blood pressure ≥ 95th percentile [12].

The cutoff for elevated TyG index was 4.65 and 4.72 for children aged 6–9 years and adolescents 10–15 years, respectively [21].

Measurements TyG index was calculated by the following formula: *Ln*[fasting triglycerides (mg/dl) × fasting glucose (mg/dl)]/2 [20].

In the standing position, after 8 to 10 h of fasting conditions, the weight and height were measured with participants in light clothing and without shoes. Weight and height were measured using a fixed scale with stadimeter (Tanita TBF-215, Tokyo, Japan). Waist circumference was measured to the nearest centimeter with a flexible steel tape while the participants were in standing position. The two anatomical landmarks used to determine tape placement were midway between the lowest portion of the rib cage and the superior border of the iliac crest (laterally) and the umbilicus (anteriorly) [3]. The body mass index was calculated as weight (kilograms) divided by height (meters) squared [13].

Blood pressure was measured according to the recommendations of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [1]. Briefly, blood pressure was measured in the brachial artery after 5 min of rest with the child seated and the arms bared and supported at heart level using a baumanometer (Microlife, Heerbrugg, Switzerland) and stethoscope (Littman Classic II; 3M, Neuss, Germany). An appropriate-sized cuff was placed on the left arm, pulse occlusion pressure was determined, and the cuff was inflated to 20 mmHg above that pressure. Systolic blood pressure was defined as the first appearance of sound (Korotkoff phase 1) and diastolic blood pressure by the disappearance of sound (Korotkoff phase 5). Data were collected as the average of three readings, each separated by 2 min [4].

Assays A whole blood sample was collected from an antecubital vein after 8 to 10 h of overnight fasting. The fasting period was confirmed by direct and independent interview with both the parents and participants in the study. Serum glucose was measured by the glucose-oxidase method with an intra-assay variation of 1.8% and an inter-assay variation of 2.1%. Triglycerides were enzymatically measured using spectrophotometric methods and the intra- and inter-assay coefficients of variation were 1.3% and 1.7%. Laboratory measurements were performed using a clinical chemistry autoanalyzer (A15; BioSystems, Barcelona, Spain).

Statistical analyses Differences between the groups were estimated using the two-tailed unpaired Student's *t* test for comparison of normally distributed quantitative variables, Mann-Whitney *U* test for skewed data, and χ^2 test for categorical variables. Additionally, one-way ANOVA with post hoc Bonferroni test was used to compare mean differences between more than two groups.

In order to assess the association between elevated TyG index (independent variable) and prehypertension and hypertension (dependent variables), we conducted a multiple logistic regression analysis stratified by age and adjusted by the Z-score/SDS of body mass index and waist circumference.

Data analyses were performed using the statistical package SPSS version 15.0 (SPSS Inc., Chicago IL, USA). A p value < 0.05 and 95% confidence interval (95% CI) defined statistical significance.

Results

A total of 3589 children were enrolled, 1748 (49%) girls and 1841 (51%) boys, and allocated into groups with NBP (n =

Table 1 Characteristics of the study population according to blood pressure. $n = 3589$, Durango and Mexico cities, 2018

N	NBP 2874	Prehypertension 271	Hypertension 444	*P*
Age, years	10.9 ± 2.3	11.8 ± 2.1	11.2 ± 2.1	< 0.001*,**,†
Girls, *n* (%)	1362 (47.3)	140 (51.6)	246 (55.4)	0.004
Body mass index, kg/m^2	20.5 ± 4.6	23.7 ± 5.5	23.8 ± 5.8	< 0.001*,**
Body mass index, *z*-score	0.96 ± 0.15	0.92 ± 0.22	0.94 ± 0.21	< 0.005*,**
Waist circumference, cm	72.0 ± 12.9	81.2 ± 14.2	80.4 ± 15.3	< 0.001*,**
Waist circumference, *z*-score	0.99 ± 0.01	0.99 ± 0.01	1.0 ± 0.02	0.01**
Systolic blood pressure, mmHg	97.0 ± 11.3	114.4 ± 8.7	121.6 ± 13.3	< 0.001*,**,†
Diastolic blood pressure, mmHg	59.5 ± 8.8	74.9 ± 7.4	78.8 ± 11.6	< 0.001*,**,†
Fasting glucose, mg/dl	89.3 ± 15.1	90.4 ± 11.2	89.9 ± 13.4	0.35
Triglycerides, mg/dl	98.6 ± 61.6	119.4 ± 67.1	118.8 ± 69.6	< 0.001*,**
TyG index	4.47 ± 0.25	4.57 ± 0.27	4.56 ± 0.27	< 0.001*,**

Values are mean ± SD

NBP normal blood pressure,

TyG triglycerides and glucose

p value was estimated using one-way ANOVA test with Bonferroni post hoc test

*$p < 0.05$ between NBP and prehypertension

**$p < 0.05$ between NBP and hypertension

†$p < 0.05$ between prehypertension and hypertension

2874), prehypertension ($n = 271$), and hypertension ($n = 444$). Participants with prehypertension and hypertension were older and exhibited higher body mass index, waist circumference, triglyceride concentrations, and TyG index than those with NBP (Table 1).

Table 2 shows characteristics of the study population stratified by sex. Regarding children aged 6–9 years, girls were older and had higher triglyceride levels and TyG index than boys, while in the group of adolescents aged 10–15 years, girls were older and exhibited systolic and diastolic blood pressure than boys.

In the group of children aged 6–9 years, those with prehypertension showed higher triglyceride levels compared with the NBP group, whereas those with hypertension exhibited higher body mass index, waist circumference, triglyceride concentrations, and TyG index than children with NBP.

Table 2 Characteristics of the study population stratified by sex. $n = 3589$, Durango and Mexico cities, 2018

	Children aged 6–9 years			Adolescents aged 10–15 years		
N	Girls 450	Boys 508	*P*	Girls 1298	Boys 1333	*P*
Age, years	8.1 ± 0.8	8.0 ± 0.9	0.204*	12.1 ± 1.6	11.9 ± 1.6	0.009*
Body mass index, kg/m^2	18.8 ± 4.2	18.8 ± 4.2	0.768*	22.1 ± 5.1	21.9 ± 4.9	0.224*
Body mass index, *z*-score	0.98 ± 0.11	0.97 ± 0.13	0.419	0.95 ± 0.17	0.95 ± 0.18	0.688
Waist circumference, cm	65.7 ± 10.9	65.8 ± 11.1	0.868*	76.7 ± 13.3	76.6 ± 13.7	0.904*
Waist circumference, *z*-score	1.0 ± 0.011	1.0 ± 0.08	0.717	1.0 ± 0.01	1.0 ± 0.11	0.336
Systolic blood pressure, mmHg	94.8 ± 13.6	94.1 ± 13.3	0.398*	104.9 ± 13.4	102.8 ± 14.4	< 0.001*
Diastolic blood pressure, mmHg	60.4 ± 11.2	60.0 ± 11.8	0.556*	65.0 ± 11.2	63.2 ± 11.5	< 0.001*
Fasting glucose, mg/dl	86.3 ± 10.3	86.9 ± 9.5	0.345*	90.2 ± 15.7	90.7 ± 16.2	0.408*
Triglycerides, mg/dl	99.2 ± 53.7	90.8 ± 52.7	0.01**	106.7 ± 68.0	104.3 ± 65.3	0.360**
TyG index	4.47 ± 0.23	4.42 ± 0.24	0.002*	4.51 ± 0.25	4.50 ± 0.28	0.145*

Values are mean ± SD

TyG triglycerides and glucose

**p* value estimated using Students' *t* test

***p* value estimated using the *U* de Mann-Whitney test

Regarding adolescents aged 10–15 years, participants with prehypertension and hypertension exhibited higher body mass index, waist circumference, triglyceride concentrations, and TyG index compared with the NBP group (Table 3).

The elevated TyG index was significantly associated with prehypertension and hypertension in the overall population as well as in the children aged 6–9 years and adolescents 10–15 years, Table 4.

Discussion

Our results revealed that, irrespective of age, the TyG index is associated with both prehypertension and hypertension in apparently healthy children and adolescents.

To the best of our knowledge, the present study is the first conducted in pediatric population to evaluate the association of the TyG index with elevated blood pressure. Our results are in accordance with epidemiological studies reporting that high TyG index is independently associated with an increased risk of developing hypertension in adults with [7, 17, 24] or without obesity [17]. Besides, observational studies have found that elevated triglycerides and insulin concentrations may predict the development of hypertension [5]; thus, given that the TyG index involves measurement of triglyceride levels, it could explain the positive association between TyG index and elevated blood pressure.

It is well known the association between insulin resistance and hypertension [10]. Insulin may exert an important role in the regulation of blood pressure inducing vasodilatation of the peripheral vasculature by nitric oxide release in the endothelium [18] and regulating renal sodium reabsorption [6]. Nevertheless, in insulin-resistant condition, the elevated insulin levels, through the activation of the mitogen-activated protein kinase, exhibit deleterious effects such as vasoconstriction and pathologic vascular cellular growth [19]. Furthermore, it has been proposed that impaired insulin signaling and systemic insulin resistance in peripheral tissues, including skeletal muscle, liver, cardiovascular, and renal tissues, induce the renin-angiotensin system activation [9, 23]. Also, some studies have indicated that hyperinsulinemia may cause hypertension by increasing sodium reabsorption and activation of sympathetic nervous system, which results in the release of catecholamines [14, 22]. Thus, it is expected that abnormalities in insulin metabolism may affect vascular and renal function leading to an increase in blood pressure.

Finally, in the group of children aged 6–9 years, girls exhibited higher triglyceride levels and similar glucose concentrations than boys; accordingly, TyG index was higher in girls than boys but without significant differences in blood

Table 3 Characteristics of the study population stratified by age. $n = 3589$, Durango and Mexico cities, 2018

	Children aged 6–9 years				Adolescents aged 10–15 years			
N	NBP 818	Prehypertension 36	Hypertension 104	*p*	NBP 2056	Prehypertension 235	Hypertension 340	*p*
Age, years	8.1 ± 0.9	8.0 ± 1.0	8.2 ± 0.8	0.15	12.0 ± 1.6	12.4 ± 1.5	12.1 ± 1.5	< 0.001*
Girls, *n* (%)	377 (46.0)	15 (41.6)	58 (55.7)	0.14	985 (47.9)	125 (53.1)	188 (55.2)	0.01
Body mass index, kg/m^2	18.4 ± 4.0	19.5 ± 4.4	21.4 ± 4.8	< 0.001**	21.3 ± 4.6	24.4 ± 5.4	24.5 ± 5.9	< 0.001*,**
Body mass index, *z*-score	0.94 ± 0.10	0.92 ± 0.19	0.94 ± 0.22	< 0.0005*	0.96 ± 0.17	0.92 ± 0.23	0.94 ± 0.21	0.002*
Waist circumference, cm	64.9 ± 10.5	68.6 ± 10.8	72.0 ± 12.7	< 0.001**	74.9 ± 12.7	83.2 ± 13.7	83.0 ± 15.2	< 0.001*,**
Waist circumference, *z*-score	1.0 ± 0.08	1.0 ± 0.003	1.0 ± 0.002	0.01**	1.0 ± 0.01	1.0 ± 0.02	1.0 ± 0.02	0.13
Systolic blood pressure, mmHg	91.3 ± 10.6	103.4 ± 8.6	116.0 ± 13.2	< 0.001*,**,†	99.2 ± 10.8	116.1 ± 7.4	123.3 ± 12.9	< 0.001*,**,†
Diastolic blood pressure, mmHg	57.2 ± 8.6	71.8 ± 8.2	8s0.1 ± 10.4	< 0.001*,**,†	60.4 ± 8.7	75.3 ± 7.2	78.4 ± 11.9	< 0.001*,**,†
Fasting glucose, mg/dl	86.8 ± 9.6	88.1 ± 9.3	85.1 ± 12.4	0.18	90.3 ± 16.7	90.8 ± 11.5	91.3 ± 13.4	0.48
Triglycerides, mg/dl	91.2 ± 47.8	114.9 ± 66.4	115.7 ± 78.4	< 0.001*,**	101.5 ± 66.0	120.1 ± 67.4	119.8 ± 66.8	< 0.001*,**
TyG index	4.43 ± 0.22	4.52 ± 0.30	4.50 ± 0.30	0.002**	4.48 ± 0.26	4.58 ± 0.26	4.57 ± 0.26	< 0.001*,**

Values are mean ± SD

NBP normal blood pressure,

TyG triglycerides and glucose

p value estimated using one-way ANOVA test with post hoc Bonferroni test

*$p < 0.05$ between NBP and prehypertension

**$p < 0.05$ between NBP and hypertension

†$p < 0.05$ between prehypertension and hypertension

Table 4 Logistic regression analysis that evaluates the association between elevated TyG index (independent variable) with both, prehypertension and hypertension (dependent variables), Durango and Mexico cities, 2018

	Prehypertension			Hypertension		
	OR	IC 95%	*p*	OR	IC 95%	*p*
Overall						
Crude	1.76	1.34–2.31	< 0.0001	1.70	1.36–2.13	< 0.001
Model 1	1.54	1.12–2.12	0.007	1.68	1.25–2.08	0.001
Model 2	1.48	1.08–2.05	0.01	1.63	1.26–2.11	< 0.0005
Children aged 6–9 years						
Crude	2.84	1.39–5.78	< 0.0005	1.92	1.21–3.05	0.005
Model 1	2.47	1.10–5.40	0.02	1.58	1.09–2.64	0.04
Model 2	2.06	1.05–4.71	0.04	1.57	1.05–2.68	0.04
Adolescents aged 10–15 years						
Crude	1.58	1.17–2.13	0.003	1.63	1.26–2.11	< 0.001
Model 1	1.41	1.10–2.0	0.04	1.63	1.22–2.19	0.001
Model 2	1.38	1.10–1.97	0.04	1.65	1.22–2.21	0.001

TyG triglycerides and glucose

Model 1: adjusted by *z*-score/SDS of body mass index

Model 2: adjusted by *z*-score/SDS of waist circumference

pressure. In this regard, it is necessary to take into account that both triglyceride and glucose levels as well as the TyG index were below the cutoff values.

There are some limitations that should be considered. First, causality between the TyG index and elevated blood pressure cannot be assured with certainty owing to the cross-sectional design of this study. Second, Tanner data were not obtained; however, study population was stratified by age in order to reduce the possible bias related with the pubertal status. Third, although insulin concentrations were not measured, TyG index is a reliable biomarker of insulin resistance that has been previously assessed in children and adolescents [11, 16]. Fourth, because blood pressure was measured as the average of three readings instead of 24-h ambulatory monitoring, it is probable misclassification of some participants. Finally, we did not collect information about physical activity and dietary intake; however, study population was recruited from the same sociocultural and economic background minimizing the potential source of bias.

In conclusion, the results of the present study show that the elevated TyG index is significantly associated with the presence of prehypertension and hypertension in children and adolescents.

Authors' contribution Luis E. Simental-Mendía conceptualized and designed the study, drafted the initial manuscript, and approved the final version as submitted. Gabriela Hernández-Ronquillo contributed to conception, critically reviewed the manuscript, and approved the final version as submitted. Claudia I. Gamboa-Gómez contributed to conception, critically reviewed the manuscript, and approved the final version as submitted. Rita Gómez-Díaz contributed to conception, critically reviewed the manuscript, and approved the final version as submitted. Martha Rodríguez-Morán contributed to conception, critically reviewed the manuscript, and approved the final version as submitted. Fernando Guerrero-Romero contributed to conception and study design, drafted the manuscript, critically revised the manuscript, and gave final approval.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent The written informed consent from at least one of each participant's parents and the informed assent from the participants were obtained.

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