The impact of body mass index on blood pressure measured with a mercury sphygmomanometer in children and adolescents with type 1 diabetes mellitus

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Abstract

Background: Patients with type 1 diabetes mellitus (T1DM) and overweight have more risk to develop changes in blood pressure that increase cardiovascular morbidity and mortality. In this study, the relationship between blood pressure (BP) with the body mass index (BMI) and the average of the last three measurements of glycated hemoglobin (HbA1c) in patients with T1DM was determined. Methods: A cross-sectional analytical study was conducted in children and adolescents with T1DM with over a year since diagnosis. The dependent variables were systolic and diastolic BP, measured with a mercury sphygmomanometer. The independent variables were BMI and average of the last three measurements of HbA1c. A linear regression with a 95% confidence interval was used. Results: Seventy-five patients with T1DM were studied. The median of disease duration was 3.5 years (min 1-max 14.8 years), BMI 19.5 ± 3.1 kg/m² and HbA1c 8.3 ± 2.4%. Sixty-six patients showed BP < percentile 90 and 9 BP ≥ percentile 90 (12%). Two models of linear regression were constructed, with systolic and diastolic BP as dependent variables. The possible predictor variables were suggested by theoretical context and statistical analysis. The predictive variable of high BP was zBMI (body mass index expressed in z-score) for systolic and diastolic BP. Also, the models suggested that for an increase of one unit of zBMI, corresponded a rise of 5.1 and 3.6 mmHg in systolic and diastolic BP, respectively. Conclusions: A positive correlation between systolic and diastolic BP with zBMI was observed.

**Introduction**

Patients with type 1 diabetes mellitus (T1DM) develop chronic complications that significantly increase their cardiovascular morbidity and mortality: two of the most frequent are hypertension (HTN) and chronic kidney disease.\(^1,^2\)

Because of the two-fold risk of HT on children and adolescents, especially with a long time of progression of T1DM\(^3\), blood pressure (BP) measurement with a strict technique is a mandatory procedure in the evaluation of this metabolic alteration.

In the pediatric clinical environment, and more frequently in the field of research, automated BP measurement has replaced the traditional measurement with the auscultatory method using mercury sphygmomanometer, mainly due to problems of mercury toxicity and increased availability of electronic devices that require less training to use. However, in general, BP readings obtained with electronic devices are significantly higher than those recorded by the auscultatory method, with the risk of overestimating the HTN diagnosis.\(^4\) Also, it should be noted that the reference values to consider high BP in children and adolescents were initially obtained using the auscultatory method with a mercury sphygmomanometer.\(^5\)

In the different studies in which the relationship between T1DM and high BP has been investigated,\(^2,^3,^5\) electronic or aneroid devices have been used more frequently, whereas mercury sphygmomanometers have been used occasionally.\(^4,^6\)

The association between HTA and T1DM has been explained, in large part, by the higher degree of adiposity and poor metabolic control of the individuals.\(^5,^9\) This association can be influenced by local factors and by the BP measurement technique, for which the objective of this study was to determine the relationship between BP with body mass index (BMI) and the mean of the last three measurements of glycosylated hemoglobin (HbA1c) in pediatric patients with T1DM.

**Methods**

**Study population**

An analytical cross-sectional study\(^10\) was conducted in children and adolescents with T1DM of the Pediatric Endocrinology Service, Nuevo Hospital Civil de Guadalajara Dr. Juan I. Menchaca, from November 2014 to February 2016. The Ethics and Research Committees of the institution approved this research, and written consent was obtained from the parents or tutors.

Diabetic patients with a minimum of one year of disease progression were consecutively included and divided into two groups, one with BP < percentile 90 and one with BP ≥ 90 percentile.\(^11\) Individuals who presented an HbA1c value > 7.5% were considered as “exposed”.

A sample with 0.05% alpha error, 20% beta error, a ratio of 1 between subjects with normotension and hypertension was calculated: 44% of subjects with T1DM, HTN and HbA1c > 7.5%, 15% of subjects with T1DM, no HTN and HbA1c ≥ 7.5%. The prevalence of exposure (HbA1c ≥ 7.5 in 15 and 44%) was obtained from patients with T1DM treated in the Endocrinology department of the institution. The minimum odds ratio (OR) detected was 4.4. The suggested sample size was 76 subjects.

Patients with genetic diseases, secondary hypertension, active treatment with drugs that modify BP, with smoking habit and who used illicit drugs, in addition to patients with incomplete data or those who requested their withdrawal from the study were not included in the study.
**Variables**

The dependent variables were systolic BP (SBP) and diastolic BP (DBP), expressed in mmHg for age, sex, and height, in addition to the diagnosis of normotension and prehypertension.11

The independent variables were metabolic control, determined by the mean of the last three HbA1c values, and adiposity, measured through the BMI. T1DM was considered when two or more fasting blood glucose determinations were $\geq 126$ mg/dl or random blood glucose $\geq 200$ mg/dl with symptoms of hyperglycemia, and values of HbA1c $\geq 6.5\%$ were detected.12 Also, the presence of an abrupt clinical picture of ketosis and the absence of acanthosis nigricans were considered as clinical evidence of insulin resistance.

Metabolic control was defined as the mean of the last three HbA1c determinations, measured within four months. The values $\leq 7.5\%$ were considered as adequate glycemic control and $> 7.5\%$ as poor glycemic control for statistical analysis.

BMI was used as an indirect measure of the degree of adiposity, according to the World Health Organization (WHO), which is classified as low ($\leq 1$ standard deviation [SD]); normal ($\pm 1$ SD); overweight (from $> 1$ SD to $\leq 2$ SD) and obesity ($> 2$ SD).13

**Procedures**

The informed consent and assent were obtained after explaining the investigation to the tutors and patients. Patients with T1DM who met the inclusion criteria attended a direct interview for data collection and the determination of anthropometric parameters using the Habicht method.13

Individuals were evaluated in the hypertension clinic by an observer explicitly trained in the correct technique of BP measurement, according to the criteria established by international organizations.11,14 This person measured the BP of the individuals three times in each of the two visits, with an interval of two to six weeks between both appointments. The BP was measured between 10:00 h and 13:00 h with a non-foldable desktop mercurial sphygmomanometer (Tycos® Instrument, North Carolina, USA). The procedure was explained to each child, and they were told not to speak during the measurement. The patients remained seated, with their back supported and their feet placed on a flat surface, in a comfortable environment, and at rest for five minutes. The arm was uncovered to the shoulder and supported on a horizontal surface at the level of the heart. Previously, the arm circumference was measured to meet the requirement of using the most appropriate arm cuff, with a width of 40% and a length of 80-100%. The arm cuff was centered on the brachial artery, without excessively tightening it, or leaving it too loose; the lower edge was 3 cm above the antecubital fossa. Subsequently, the maximum inflation level was determined by the Osler maneuver, which consists of palpating the radial artery and concomitantly inflating the arm cuff 30 mmHg above the point of disappearance of the pulse corresponding to the SBP, to avoid pain or discomfort during measurement. The cuff was deflated; the stethoscope was placed over the brachial artery with the entire surface in contact with the skin, the arm cuff was quickly and steadily inflated to the predetermined level, releasing the air from the chamber at a speed of 2 mmHg per heartbeat. The cuff was not re-inflated after having started deflation to confirm SBP or DBP. SBP was determined when two continuous beats appeared (Korotkoff phase I) and DBP at the moment where the noises disappeared (Korotkoff phase V). An additional 10 mmHg after the last noise was examined to confirm the disappearance of the noises.

**Statistical analysis**

The mean and standard deviation of the quantitative variables were calculated. In the case of a normal distribution, the means were compared with the Student’s t-test for two independent variables. When the distribution was asymmetric, the median was determined and compared using the Mann-Whitney U test. Qualitative variables were expressed in proportions and compared using the $\chi^2$ or Fisher’s exact tests. The association of qualitative variables with the BP $\geq 90$ percentile was determined with OR.

A multiple linear regression analysis was performed to study the relationship between SBP and DBP with BMI, the mean of the last three HbA1c measurements, and the time of progression. In all calculations, the confidence interval was 95% (95% CI). The analyses were performed with the statistical program for social sciences (SPSS Statistics for Macintosh, Version 22.0. Armonk, NY: IBM Corp.).

**Results**

Seventy-five children and adolescents with T1DM, with an average age of $14.3 \pm 2$ years (range of 10 to 19 years), 56% males and a male/female ratio of 1:3 were studied. The average weight was $48.2 \pm 12.3$ kg (range 25.6
to 87.7 kg), and the BMI was 19.5 ± 3.1 kg/m²: low weight in 13.3%, normal weight in 68%, and overweight in 18.6%. No obesity was detected in any case. The progression of T1DM was 4.6 ± 3.6 years, with a median of 3.5 years, a minimum of 1 and a maximum of 14.8 years. The progression period of T1DM was < 5 years in 66.7% and ≥ 5 in 33.3% of the cases.

The total insulin dose per day was 49 ± 18 IU. HbA1c was determined in 74 patients, with an average percentage of 8.3 ± 2.4%; HbA1c was < 6.5 in 12.2%; 6.5 to < 8 in 32.4%; ≥ 8 to < 10 in 29.7%; ≥ 10 to < 12 in 13.5%, and ≥ 12 in 12.2%.

The last three HbA1c measurements mean was > 7.5% in seven individuals with BP ≥ percentile 90 (78%) and in 41 subjects with BP < percentile 90 (62%).

The frequency of the quantitative variables was normal, given that the values of the typical error of the asymmetry index and kurtosis index were close to 0.5 and <1, respectively.

SBP and DBP levels were 103.7 ± 9.4 mmHg and 68.8 ± 7 mmHg, respectively. Sixty-six individuals showed BP < percentile 90 and nine BP ≥ percentile 90 (12%). Of these, high SBP was observed in 4%, high DBP in 6.6%, and both SBP and DBP in 1.3%.

When comparing the quantitative variables of patients with BP ≥ percentile 90 and with normal BP, the averages for age, birth weight, current weight, progression time, total insulin dose, and HbA1c were similar in both study groups. Moreover, the mean BMI and waist circumference were higher in the group of patients with BP ≥ percentile 90 (Table 1).

From the comparison of the qualitative variables, it was found that the family history of HTN and obesity, being preterm at birth, weight gain > 15 kg of the mother during pregnancy, percentage of progression ≥ 5 years and HbA1c > 7.5% were distributed similarly in both study groups.

Moreover, female gender and higher BMI and waist ratio were more frequent in patients with prehypertension (Table 2).

Two multiple linear regression models were constructed to analyze the correlation between quantitative variables and BP, with SBP and DBP as dependent variables. The possible predictor variables were those that the theoretical context and the previous statistical analysis suggested. After checking the ANOVA summary with a significant linear relationship (p <0.001) and the independent residues with each other (Durbin-Watson statistic of 1.94 for SBP and 2.1 for DBP and mean of residuals of zero), the only predictor variable of BP ≥ percentile 90 was the BMI for both SBP (β = 0.54; p <0.001) and DBP (β = 0.51; p <0.001).

Regression models also suggested a 5.1 mmHg increase in SBP (Table 3) and 3.02 mmHg DBP (Table 4) for each increment of a zBMI unit (BMI expressed in zeta scores).
**Discussion**

Children and adolescents have an increased risk of vascular and renal complications during the evolution of T1DM. Gröber-Grätz et al. found a higher prevalence of other risk factors, such as overweight and obesity, which may be associated with increased cardiovascular morbidity in children with no diabetes. Flores-Huerta et al. also documented a positive association of overweight and obesity with BP levels (obtained with different measurement techniques) in children and adolescents with no diabetes, in whom a higher BMI correlated with higher systolic and diastolic BP. However, none of these studies performed a correlation analysis between BMI with SBP and DBP. Furthermore, higher association and prediction of cardiovascular damage has been demonstrated with the method known as 24-hour Ambulatory BP Monitoring (ABPM) compared to the measurement in the medical office.

Children and adolescents with diabetes and a high degree of adiposity, apart from their frequent lack of glycemic control, have a significant risk of presenting higher BP levels and, consequently, a greater cardiovascular risk. Although some studies have addressed this relationship in different ethnic populations of diabetic children worldwide, the effect of increased adiposity on the BP level in the mestizo Mexican population or other Latin American populations is unknown.

In this study, BMI was used as an indirect measure to estimate the degree of adiposity, since it was
reported to be a useful marker of body fat. The relationship between BMI and BP was also studied.\textsuperscript{19} The results obtained showed a relationship between BMI and SBP ($\beta = 0.54$) and DBP ($\beta = 0.51$). It was also found that each increase of a zBMI score unit in children with diabetes corresponded to a 5.1 mmHg increase in SBP and 3.6 mmHg in DBP. After evaluating 164 patients with T1DM in Poland, whose BP was measured with an electronic device, Pietrzak et al. also found a correlation between BMI and SBP ($\beta = 0.37$) and DBP ($\beta = 0.28$).\textsuperscript{3}

Other authors, such as Guimaraes et al.\textsuperscript{6} in Brazil, who measured BP with a mercury device and a strict measurement technique in a large sample of 536 non-diabetic children and adolescents, and Van Vliet et al.\textsuperscript{8}, in the Netherlands, who measure it in 283 children with T1DM, found a frequency of high SBP and DBP in subjects with high BMI. Unfortunately, no correlation analysis was performed in either of these studies. In the latter study, nearly 40% of subjects presented overweight or obesity and a higher prehypertension frequency. In contrast, in a small sample of 60 adolescents with T1DM whose BP was measured in the medical office with a validated electronic device, de Oliveira et al.\textsuperscript{2} in Brazil, found no significant correlation between the increase in BMI and BP; however, a statistical trend was observed between overweight and a higher DBP.

In the present work, 12% of individuals were found with BP $\geq$ percentile 90, but none with BP $\geq$ percentile 95 most likely because of the small sample size, since Margeirsdottir et al., after studying a population of 1,658 patients with T1DM in Norway, found BP $\geq$ percentile 95 in 4% of the children and a percentage with BP $\geq$ percentile 90 but BP $<$ percentile 95,\textsuperscript{1} similar to the frequency of the present study.

Different biological mechanisms have been identified as an explanation for this relationship between higher BMI and higher BP. For example, with more adipose tissue, insulin resistance increases, and more inflammatory cytokines are released, with the consequent rise in oxidative stress. Furthermore, the renin-angiotensin-aldosterone system is activated, vascular dysfunction and sodium retention are increased, and more activity of the sympathetic nervous system is observed in association with increased renal dysfunction, which is usually more intense in the presence of albuminuria and contributes to increased cardiovascular risk.\textsuperscript{20}

Another variable that has been associated with a higher level of BP in children with T1DM is poor glycemic control. In this sense, de Oliveira et al.\textsuperscript{2} observed that children and adolescents with significant uncontrolled glycemia (11.6% HbA1c) showed higher levels of systolic and diastolic BP. Also, they found a positive correlation with diastolic BP, showing an increase of 1.73 mmHg for every 1% increase in HbA1c.

In a retrospective study, Torchinsky et al.\textsuperscript{21} evaluated 148 children with T1DM in the US and found a higher average level of DBP and heart rate with higher HbA1c levels. Moreover, a correlation with insulin doses was even observed. In another study, in which BP was measured in 106 North American children with T1DM using ABPM with bivariate analysis, Chatterjee et al.\textsuperscript{7} also found a higher frequency of lack of glycemic control in subjects with prehypertension and hypertension. In contrast, no positive correlation between HbA1c and BP by linear regression was demonstrated by Pietrzak et al.\textsuperscript{3}

### Table 4. Multiple linear regression with diastolic blood pressure as a dependent variable

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Non-standardized coefficients</th>
<th>Typified coefficients</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>68.381</td>
<td>2.391</td>
<td>63.61-73.15</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>zBMI</td>
<td>3.597</td>
<td>0.779</td>
<td>0.511</td>
<td>2.04-5.15</td>
</tr>
<tr>
<td>Female gender</td>
<td>−0.854</td>
<td>1.487</td>
<td>−0.061</td>
<td>−3.82-2.1</td>
</tr>
<tr>
<td>Progression time</td>
<td>0.170</td>
<td>1.576</td>
<td>0.012</td>
<td>−2.97-3.31</td>
</tr>
<tr>
<td>HbA1c</td>
<td>−0.356</td>
<td>1.534</td>
<td>−0.024</td>
<td>−3.42-2.70</td>
</tr>
<tr>
<td>Insulin dose per kg of weight</td>
<td>1.041</td>
<td>2.268</td>
<td>0.052</td>
<td>−3.48-5.56</td>
</tr>
</tbody>
</table>

ANOVA of the model. Significance $\leq$ 0.001; adjusted $R^2 = 0.204$. Diabetes mellitus progression time $> 3.5$ years. Each increase in a zBMI unit corresponds to an increase of 3.6 mmHg of diastolic blood pressure.

HbA1c, the average of the last three measurements of glycosylated hemoglobin; CI, confidence interval; zBMI, body mass index expressed as zeta score.

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In this study, no correlation was found between glycemic control and BP, although there was a higher frequency of elevated HbA1c in subjects with prehypertension in the bivariate analysis. However, it was not statistically significant. It should be noted that the average HbA1c levels in this study were similar to those reported by other authors.\textsuperscript{3,7}

Regarding the time of progression of T1DM, a relationship with BP was not observed. However, Pietrzak et al.\textsuperscript{3} documented a positive correlation between the time of progression and the DBP. Also, de Oliveira et al.\textsuperscript{2} reported a higher frequency of prehypertension with a longer time of progression of the T1DM1, only in the bivariate analysis.

It is worth mentioning that individuals with BP \( \geq \) percentile 90 showed a longer time of disease progression, higher HbA1c levels, and a higher proportion of inadequate glycemic control. However, despite being clinically significant values, they showed no statistical significance. Similarly, weight gain >15 kg during pregnancy was not relevant.

A limitation of the present study was the small sample size, since with a prevalence of 12% of BP \( \geq \) percentile 90, assuming the prevalence of exposure to HbA1c of 15% and 44%, the power of the study is close to 60% to identify an OR of 4.5. However, in this investigation, the OR of exposure to HbA1c of 15% and 44% was close to 2 and the power to 20%. Regardless, the sample size was satisfactory to test the relationship between BMI and BP. Another limitation would be that adiposity was estimated through the BMI and not with other forms of evaluation. Regarding the above, WHO suggests that adiposity can be estimated with the BMI since there is an adequate correlation between BP with the mean of the last three HbA1c measurements, probably due to the small sample size.

Therefore, it is essential to achieve a balance between income and energy expenditure in clinical practice through an adequate diet, physical activity, and satisfactory use of insulin to avoid exaggerated adiposity gain. Also, the monitoring and screening of macrovascular and microvascular complications is essential in patients with T1DM, according to the ISPAD 2018 guidelines.\textsuperscript{22}

### Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

### Conflicts of interest

The authors declare that they have no conflicts of interest.

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### References


