Prevalence of Prehypertension in Mexico and Its Association With Hypomagnesemia

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BACKGROUND
Prehypertension (preHTN) increases the risk of developing hypertension. The objectives of this study were to estimate the prevalence of preHTN in the Mexican adult population and evaluate the association between hypomagnesemia and preHTN.

METHODS
This study was a 2-phase, population-based study. In the first phase, 4,272 Mexican adults (aged 20–65 years) were enrolled to determine the prevalence of preHTN. In the second phase, a cross-sectional analysis was performed to evaluate the association between hypomagnesemia and preHTN. The exclusion criteria were chronic diarrhea, malignancy, hepatic and renal diseases, chronic inflammatory disease, and the intake of magnesium supplements. PreHTN was defined as a systolic blood pressure (BP) of 120–139 mm Hg and/or diastolic BP of 80–89 mm Hg, and hypomagnesemia was defined as a serum magnesium concentration <1.8 mg/dL.

RESULTS
The prevalence of preHTN was 37.5% (95% confidence interval [CI]: 36.0–39.0): 46.7% were men (95% CI: 44.1–49.4) and 33.2% (95% CI: 31.5–35.0) were women. The serum magnesium data were available for 921 participants. Hypomagnesemia was identified in 276 (30.0%; 95% CI: 27.1–33.0) subjects; of them, 176 (63.8%; 95% CI: 58.3–69.6) had preHTN. Individuals with preHTN exhibited lower magnesium levels than individuals without preHTN (1.78 ± 0.36 vs. 1.95 ± 0.37, P = 0.0005). A multiple logistic regression analysis (adjusted for age, sex, smoking, body mass index, waist circumference, fasting glucose, total cholesterol, high-density lipoprotein cholesterol, and triglycerides levels) indicated a significant association between hypomagnesemia and preHTN (odds ratio = 1.78; 95% CI: 1.5–4.0, P < 0.0005).

CONCLUSIONS
The prevalence of preHTN in the Mexican population is 37.5%, and hypomagnesemia is strongly associated with preHTN.

Keywords: blood pressure; hypertension; magnesium; Mexico; prehypertension; prevalence.

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According to reports by the World Health Organization, cardiovascular diseases are the main cause of death worldwide,1 and high blood pressure (BP) is the most important risk factor for the development of cardiovascular disease.2 In the year 2003, The Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure introduced the category of prehypertension (preHTN), which included systolic BP (SBP) values between 120 and 139 mm Hg and/or diastolic BP (DBP) values between 80 and 89 mm Hg. This condition clearly increases the risk of developing hypertension and cardiovascular morbidity.1

Several studies conducted worldwide have reported the prevalence of preHTN in adults; the results are very variable, from 14.5% in Turkey4 to 53.9% in Brazil.5 In México, reports regarding the prevalence of preHTN are scarce and regional. The results range from 26.5% in Chilpancingo, Gro.,6 33.8% in Veracruz, Ver.,7 to 34.8% in the general population of Mexico City.8

Given that magnesium is involved in tone modulation and vascular smooth muscle reactivity, reduction of angiotensin II action, inhibition of norepinephrine release, and acts as a calcium antagonist,9 it is possible that magnesium plays an important role in the pathogenesis of high BP. The results from epidemiological and interventional studies suggest that low serum magnesium levels may play a modest role in the development of hypertension10 and that oral magnesium intake and magnesium supplementation may play a role in BP regulation in hypertensive individuals.11–13 However, data about the role of magnesium in the pathogenesis of pre-HTN are scarce.14

This issue could have a public health importance because a substantial number of the US population fails to consume an adequate amount of magnesium in their diet.15 Dietary
magnesium intake is inadequate in adults from India (43.6%),\textsuperscript{16} Brazil (70% of women; 94% of men),\textsuperscript{17,18} Mexico (64.2% of females; 25.5% of males),\textsuperscript{19} and Spain (32.31%).\textsuperscript{20} In addition, the prevalence of hypomagnesemia in adults is 14.5%–33.7% in Germany,\textsuperscript{21,22} 26.3% and 31.0% in Mexican women and men,\textsuperscript{19} 20% among ambulatory urban African Americans,\textsuperscript{23} and 42% in Brazil.\textsuperscript{17} Although little is known about the magnesium status, these data suggest that dietary magnesium intake is inadequate and that low serum magnesium levels are frequent in adults irrespective of ethnic background.

Because high BP is a worldwide challenge, understanding the issues involved in the pathophysiology of preHTN could be useful in the planning and implementation of an effective approach to reduce the burden of chronic disease and the improvement of primary care. Therefore, the objectives of this study were to estimate the prevalence of preHTN in the Mexican adult population and evaluate the association between hypomagnesemia and preHTN.

**METHODS**

The protocol was approved by the Scientific Research Committee of the Mexican Social Security Institute. Written informed consent was obtained from the participants. According to the Declaration of Helsinki, a 2-phase, population-based study was conducted.

In the first phase, a population-based, cross-sectional, descriptive study was conducted to determine prevalence of preHTN. The eligible subjects were men and nonpregnant women aged 20–65 years from the general population in the cities of Oregón, Durango, Torreon, Guadalajara, Puebla, and Yucatan from northern, middle, and southern Mexico.

The study was designed to be representative for sex and age of apparently healthy Mexican individuals. The sampling strategy was based on a random systematic sample. For this purpose, the inhabitants and institutionalized Mexican individuals at the Mexican Social Security Institute from the above-mentioned Mexican cities were invited through public media to participate in the study. The targeted population was classified as lower and middle income.

The individuals who chose to participate were interviewed in the Clinical Centers and Medical Research Units of the Multidisciplinary Research Group on Diabetes. The questionnaires covered demographic characteristics and medical conditions. The measurements included BP, weight, height, waist circumference (WC), and biochemical parameters, such as fasting glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-c), and triglycerides levels.\textsuperscript{24}

In the second phase, a cross-sectional, comparative analysis was performed to evaluate the association between hypomagnesemia and preHTN. Individuals with preHTN were compared with a control group without preHTN. Due to financial issues, serum magnesium measurements were performed in 21.5% of the participants. To maintain the sample representativeness, serum magnesium measurements were performed with a random systematic sampling method on the individuals enrolled in the first phase of the study.

Therefore, the eligible subjects were men and nonpregnant women from the first phase of the study who had serum magnesium measurements performed.

The exclusion criteria were chronic diarrhea, malignancy, hepatic and renal diseases, chronic inflammatory disease, and the intake of magnesium supplements during the previous 6 months.

**Measurements**

Weight and height were measured with the subjects in a standing position in light clothing without shoes using a fixed scale with stadiometer (Tanita TBF-215, Tokyo, Japan). The increments of weight and height measurements were 0.1 kg and 0.01 m, respectively. Body mass index (BMI) was calculated as weight (kilograms) divided by height (meters) squared. The WC was measured as the minimum circumference at the umbilical level.\textsuperscript{24}

The BP was measured according to the recommended technique in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.\textsuperscript{3} In brief, the brachial artery BP was measured after at least 5 minutes of rest with the subjects seated and their arms bared and supported at heart level with the use of a baumanometer (Microlife AG, Heerbrugg Switzerland) and stethoscope (3M Littman Classic II, Neuss, Germany). An appropriately sized cuff was placed on the left arm (right arm for left-handed individuals), and the pulse occlusion pressure was determined. The cuff was inflated to 20 mm Hg above the occlusion pressure. The SBP was defined as the first appearance of sound (Korotkoff phase 1), and the DBP was defined by the disappearance of sound (Korotkoff phase 5). The data were collected as the average of 3 readings separated by 2 minutes. The standardization of techniques and personnel training was performed before the start of the study to reduce the interobserver variations to less than 0.05.

Venous blood samples were collected after overnight fasting. The subjects were not allowed to have caloric or fat intake for at least 10 hours before the venous blood draw.

**Definitions**

PreHTN was defined as a SBP of 120–139 mm Hg and/or DBP of 80–89 mm Hg.\textsuperscript{3} Hypomagnesemia was defined as a serum magnesium concentration lower than 1.8 mg/dl (<0.74 mmol/l).\textsuperscript{25}

**Assays**

The serum magnesium and potassium concentrations were measured using colorimetric methods; the respective intra- and interassay variation coefficients were 1.3% and 1.8% for magnesium and 1.2% and 1.5% for potassium.

The serum glucose was measured using the glucose oxidase method with intra- and interassay variation coefficients of 1.1% and 1.1%. Triglycerides and total cholesterol levels were measured enzymatically, and the HDL-c fraction was obtained after precipitation by a phosphotungstic reagent.

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The respective intra- and interassay coefficients of variation were 1.4% and 2.1% for triglycerides, 1.8% and 2.6% for total cholesterol, 1.2% and 1.6% for HDL-c.

All measurements were performed in the Central Laboratory of The Multidisciplinary Research Group on Diabetes of the Mexican Social Security Institute with the Synchron CX4 System of the Beckman Coulter using a timed endpoint method (Beckman Coulter, Fullerton, CA).

Statistical analysis

Prevalence is expressed as a percentage (95% confidence interval (CI)). We estimated the age- and sex-adjusted rates for the prevalence of preHTN.

The unpaired Student's t test and chi-square test were used to test for differences of numerical and nominal variables.

The Pearson rank correlation test was used to evaluate the correlation between serum magnesium with both SBP and DBP.

Multiple logistic regression analysis (adjusted according to the significant variables from the bivariate analysis and by the well-known risk factors for preHTN) was used to compute the association between hypomagnesemia (independent variable) and preHTN (dependent variable).

Additionally, an adjusted multiple linear regression analysis was conducted to evaluate the association between serum magnesium levels (independent variable) and SBP and DBP (dependent variables).

A P value <0.05 was defined as significant. The data analysis was performed using the SPSS 15.0 statistical package (SPSS, Chicago, IL; 1998).

RESULTS

A total of 4,272 individuals were enrolled: 2,921 (68.4%) women and 1,351 (31.6%) men. Women exhibited a higher BMI but lower WC than men; smoking, SBP, DBP, fasting glucose, and triglyceride levels were higher and HDL-c was lower in men than women, Table 1.

The prevalence of preHTN and hypertension was 37.5% and 13.2%; prevalence that was significantly higher in men than in women, Table 1.

A total of 1,917 (44.8%), 1,579 (37.0%), and 776 (18.2%) individuals were obese, overweight, and normal weight, respectively. The prevalence of preHTN according to the BMI was 44.0% (95% CI: 41.8–46.2), 34.6% (32.3–37.1), and 27.4% (24.3–30.6) for the obese, overweight, and normal weight individuals.

A diagnosis of type 2 diabetes was established in 615 participants (14.4%; 95% CI: 13.3–15.5): 386 women (62.8%) and 229 men (37.2%). The prevalence of preHTN among diabetic women was 39.4% (95% CI: 34.6–44.4) and 30.8% (95% CI: 26.3–35.6) in diabetic men.

The serum magnesium levels were available for 921 participants; hypomagnesemia was identified in 276 (30.0%; 95% CI: 26.3–35.6) subjects; of them, 176 (63.8%; 95% CI: 58.3–69.6) had preHTN.

The frequency of smoking, BMI, WC, fasting glucose, total cholesterol, and triglyceride levels were higher and the serum magnesium levels were lower in the individuals with preHTN than in individuals without preHTN. Men with preHTN showed higher frequency of smoking, WC, fasting glucose and lower age than women with preHTN. Furthermore, men without preHTN exhibited higher frequency of smoking, WC, and triglycerides levels and lower HDL-c levels compared with women without preHTN (Table 2).

Table 3 shows the analysis of the target population, according to magnesium status and preHTN. Hypomagnesemic individuals without preHTN exhibited higher fasting glucose and lower HDL-c levels than normomagnesemic individuals without preHTN. Moreover, normomagnesemic individuals

Table 1. Characteristics of the target population

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Men</th>
<th>Women</th>
<th>P valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>4,272</td>
<td>1,351</td>
<td>2,921</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>43.9 ± 10.4</td>
<td>44.1 ± 10.1</td>
<td>43.6 ± 11.3</td>
<td>0.13</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>519 (12.4)</td>
<td>222 (16.4)</td>
<td>297 (10.2)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Prevalence of prehypertensionb</td>
<td>37.5 (36.0–39.0)</td>
<td>46.7 (44.1–49.4)</td>
<td>33.2 (31.5–35.0)</td>
<td>&gt;0.005</td>
</tr>
<tr>
<td>Prevalence of hypertensionc</td>
<td>13.6 (12.2–14.2)</td>
<td>18.3 (16.2–20.4)</td>
<td>11.6 (10.4–12.7)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29.9 ± 5.8</td>
<td>30.2 ± 5.8</td>
<td>29.6 ± 5.6</td>
<td>0.002</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>98.1 ± 13.9</td>
<td>101.6 ± 13.6</td>
<td>96.8 ± 13.8</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>120.2 ± 18.7</td>
<td>125.0 ± 18.2</td>
<td>117.7 ± 18.5</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>74.6 ± 18.2</td>
<td>77.5 ± 12.7</td>
<td>73.3 ± 15.7</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Fasting glucose, mg/dl</td>
<td>107.9 ± 42.0</td>
<td>111.1 ± 45.8</td>
<td>106.4 ± 40.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>202.1 ± 56.2</td>
<td>201.7 ± 75.6</td>
<td>208.7 ± 44.2</td>
<td>0.64</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dl</td>
<td>43.6 ± 13.2</td>
<td>39.2 ± 11.3</td>
<td>45.7 ± 13.4</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Triglycerides, mg/dl</td>
<td>172.6 ± 134.7</td>
<td>200.2 ± 160.7</td>
<td>160.2 ± 118.6</td>
<td>&lt;0.0005</td>
</tr>
</tbody>
</table>

Data are mean ± SD, otherwise is indicated.

Abbreviation: HDL, high-density lipoprotein.

aP value between men and women.

bData are % (95% confidence interval).
with preHTN exhibited a higher frequency of smoking and higher WC, cholesterol, and triglyceride levels than individuals with hypomagnesemia and preHTN (Table 3).

There was a significant negative Pearson correlation rank between serum magnesium levels and SBP ($r = -0.152$, $P < 0.0005$) and DBP ($r = -0.164, P < 0.005$).
The multiple logistic regression analysis (adjusted for age, sex, smoking, BMI, WC, fasting glucose, total cholesterol, HDL-c, triglyceride, and serum magnesium levels) indicated a significant association between hypomagnesemia and preHTN (odds ratio = 1.77; 95% CI: 1.3–4.4, \( P < 0.0005 \)).

Finally, the adjusted multiple linear regression analysis demonstrated that serum magnesium levels are significantly associated with SBP (\( B = −6.39; 95\% \) CI: \(-9.8 \) to \(-1.5 \)) and DBP (\( B = −2.6; 95\% \) CI: \(-2.9 \) to \(-1.3 \)) in the subjects with preHTN, but not in normotensive individuals (\( B = 0.66; 95\% \) CI: \(-1.7 \) to \(3.0 \) and \( B = −0.93; 95\% \) CI: \(-3.1 \) to \(1.1 \), for the SBP and DBP, respectively).

**DISCUSSION**

The results of this study demonstrate that preHTN exhibits a prevalence of 37.5% in Mexican adults. In addition, irrespective of the well-known risk factors related to preHTN, our results indicate that serum magnesium levels lower than 1.8 mg/dl are associated with preHTN.

To the best of our knowledge, this is the first study that estimates the prevalence of preHTN in a representative National Mexican population. Our results are slightly higher (36.8%) than reported by Chávez-Negrete et al.\(^7\) and Jiménez-Corona et al.\(^8\) who studied representative samples from the general populations of Veracruz Ver. and Mexico city (cities in middle Mexico) and reported the prevalence of preHTN to be 33.8% and 34.8%, respectively. However, the prevalence of preHTN reported by Gómez-Guzmán et al.\(^6\) in a Mexican population from Chilpancingo Gro. (a city in southern Mexico) was lower (26.5%).

Although ethnicity most likely plays a role in the pathogenesis of preHTN, the current reports about prevalence of preHTN do not support the hypothesis that differences could be attributable to ethnicity per se. The prevalence of preHTN in the population from Shandong China (37.1%), northern Ethiopia (37.2%),\(^2\) and Mainland China (37%)\(^2\) is similar to the prevalence in the Mexican population in our study (37.5%). In addition, the prevalence of preHTN in the United States (31%),\(^2\) Korea (31.6%),\(^2\) and Japan (32%)\(^2\) is similar to the prevalence in African Surinamese, Hindustani Surinamese, and White Dutch individuals living in Amsterdam (32.8%),\(^2\) and in Veracruz Ver., Mexico (33.8%).\(^7\) Furthermore, the highest prevalence of preHTN has been reported in populations from China (59.8%), Malaysia (68.9%), India (57.7%),\(^3\) Brazil (53.9%),\(^5\) and Vietnam (41.8%).\(^4\) The lowest prevalence has been reported in Chinese adults from urban and rural areas (21.9%)\(^3\) and in Turkish adults (14.5%).\(^4\) These results do not indicate an ethnic pattern.

Given that the risk of hypertension is associated with BP in the range of preHTN,\(^6\) the variability of preHTN prevalence emphasizes that in addition to ethnicity, other risk factors play an important role in the development of preHTN.\(^3\) There is an urgent need to develop strategies for early detection, prevention, and treatment of preHTN.

Cross-sectional studies conducted to establish the associated risk factors for developing preHTN demonstrate that aging, sex, low education level, smoking, alcohol consumption, anthropometric indices of obesity (BMI, WC, and body fat), diabetes, elevated fasting plasma glucose, triglycerides, cholesterol levels, and low HDL-c levels are significantly associated with preHTN\(^5,6,7,26,28,33,34,36–39\). In agreement with these reports, our results show that individuals with normomagnesemia and prehypertension exhibited a high frequency of cardiovascular risk factors (Table 3) that could explain the development of preHTN.

Studies that analyzed the association between serum magnesium levels or dietary magnesium intake with preHTN are scarce.\(^4,40–41\) Recently, based on a cross-sectional study with a small sample size (\( N = 107 \)) and using a multivariate logistic conditional forward analysis adjusted for age, sex, alcohol consumption, BMI, fasting glucose levels, and triglyceride levels, we reported that hypomagnesemia is significantly associated with preHTN (odds ratio = 1.98; 95% CI: 1.11–4.20, \( P = 0.04 \)) in otherwise healthy subjects.\(^4\) In the present study, based on a representative sample of the Mexican adult population (\( N = 921 \)), the multiple logistic regression analysis adjusted for the well-known risk factors for developing preHTN demonstrated that hypomagnesemia is significantly associated with preHTN. This finding strongly supports the hypothesis that low serum magnesium levels play an important role in the pathogenesis of preHTN. The subjects with preHTN in this study had lower serum magnesium levels than individuals without preHTN, and among individuals with hypomagnesemia (\( N = 276 \)), the prevalence of preHTN was 63.8%.

Results from an 18-month behavioral lifestyle intervention study that included the “Dietary Approaches to Stop Hypertension (DASH),” a dietary pattern based on increased intake of fruits, vegetables, dairy, fiber, calcium, potassium, and magnesium, demonstrated that the DASH was effective in helping participants with preHTN or stage 1 hypertension reach the established recommendations to control BP.\(^4\) Similarly, a cross-sectional epidemiologic study that included 17 population samples from Japan, China, United Kingdom, and the United States indicated that intakes of phosphorus, calcium, and magnesium above the country specific medians were inversely associated with BP.\(^40\) These results support the hypothesis that healthier eating patterns with magnesium and other micronutrients could be useful for the prevention of preHTN.

Although evidence regarding the regulation of BP by magnesium has been previously reported,\(^42,43\) there have not been interventional studies to demonstrate the benefits of magnesium for preHTN. Thus, in addition to the early detection of preHTN, advice for practicing a healthy lifestyle and consuming the recommended amount of magnesium could be useful strategies to prevent hypertension.

Finally, plasma aldosterone secretion, which can be stimulated by a rise in serum potassium,\(^44\) fall in serum sodium, and/or body fat mass,\(^45\) leads to increased sodium and decreased potassium levels. However, the feedback regulation mechanism of aldosterone eventually fails and can lead to hypertension through events such as water retention, accumulation of extracellular fluid volume, and increased cardiac output.\(^46\) In the target population of our study, the serum potassium concentration was within the normal range and was similarly distributed in the analyzed groups. In addition, after adjusting the multiple regression analyses
for serum potassium levels, hypomagnesemia remained significantly associated with preHTN. We did not measure urinary potassium or aldosterone levels; thus, further research is needed in this field.

Several limitations of this study should be mentioned. First, due to the cross-sectional design, causality between hypomagnesemia and preHTN cannot be established. Second, alcohol consumption, education level, and serum calcium, which are well-known risk factors for developing preHTN, were not evaluated. Third, we did not measure serum magnesium in all individuals; however, because the magnesium measurements were performed with a random systematic sample method and the appropriate sample size was analyzed, this limitation was minimized. Finally, we cannot exclude the presence of white coat high BP; however, a diagnosis of preHTN was established after several measurements of BP to minimize the possible bias.

The main strengths of the study were the sampling strategy and the large sample size representative of the Mexican adult population.

In conclusion, our results demonstrate that the prevalence of preHTN in the Mexican population is 37.5% and that hypomagnesemia is strongly associated with preHTN.

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DISCLOSURE

The authors declared no conflict of interest.

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