RISK FACTORS ASSOCIATED WITH HYPERTENSION IN MEXICAN ADOLESCENTS

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Abstract

Introduction. High blood pressure (HBP) in children and adolescents is often an entity underdiagnosed. An increase in cardiovascular risk factors (CVRF) has been recently reported in adolescents. The objective of this study was to evaluate the frequency of hypertension and pre-hypertension and the risk factors associated to hypertension in Mexican adolescents.

Methods. A cross-sectional study was performed in adolescents, both genders between 15 and 19 years of age. The clinical variables of age, sex, weight, height, body mass index, blood pressure, family history of diabetes and hypertension, weeks of gestation at birth were obtained and blood samples were collected for measurement of cholesterol, triglycerides, low density lipoprotein, very low density lipoproteins, high density lipoproteins, uric acid and serum insulin. Data were analyzed in SPSS version 18.0.

Results. 384 adolescents between 15 and 18 years old were studied. Of those studied, 291 (75.8%) are female and 93 (24.2%) male. Hypertension was found in 6% of all adolescents, Pre-Hypertension in 9.4% and normal BP in 84.6%. The relationships between systolic blood pressure and glucose (r= 0.170; P= 0.001), TCh (r= 0.119; P= 0.020), HDL (r= -0.147; P= 0.004) and LDL (r= 0.166; P= 0.001) were realized. Male sex (RR:3.97; 95%CI:2.51-6.27), family history of hypertension (RR:3.81; 95%CI:2.39-6.05) and obesity (RR:3.29; 95%CI:2.11-5.15) were risk factors involved in the development of hypertension.

Conclusions. A 6% frequency of hypertension and 9% of Pre-hypertension were found. Male sex and family history of hypertension were risk factors associated with hypertension in adolescents. It is necessary to perform longitudinal studies with a specific methodology and laboratory studies for analyzing the impact of traditional risk factors in the development of cardiovascular disease in adolescents.

1. Introduction.

High blood pressure (HBP) in children and adolescents is often an entity underdiagnosed with its own characteristics in terms of diagnosis, etiology and management that differ from those in adults. In addition, it is well known that even slight alterations in BP in the early ages of life result in organ damage associated with hypertension in adulthood for the risk to develop cardiovascular disease (CVD) [1]. In adults, several risk factors are involved in CVD etiology such as age, hypertension, obesity, dyslipidemia and diabetes that have been clearly associated. An increase in cardiovascular risk factors (CVRF) has been recently reported in adolescents [2]. Studies of cardiovascular risk factors including hypertension in Mexico have shown that its risk profile could be different from that presented by older populations [3].

The principal risk factor for cardiovascular disease in adults is the central obesity that is associated with alterations in blood pressure (BP), lipids profile, and glucose metabolism [4]. One of the problems that have been observed in Mexico is the increased prevalence of obesity in children and adolescents; the problem is the parallel increase in complications related to their presence, which may include metabolic, psychological and orthopedic, among others. [5,6].

Lifestyles have changed in the last decades in Mexico. Physical activity and alimentation have been pointed out as principal factors for preventing obesity in adolescents [7]. It has been reported that adolescents with or without obesity, more frequently those with increased abdominal fat, may have elevated BP levels, an altered atherogenic serum lipid profile, characterized by an increase in the concentration of serum total cholesterol (TC), triglycerides (TGL) and low density lipoproteins (LDL), and by a decrease in the high density lipoproteins (HDL) (1). Currently, it is recognized that alterations in serum lipid profile in children and adolescents with obesity may be early indicators of HBP levels or part of the metabolic syndrome [8].

Potential impact on health by identifying risk factors associated to hypertension in early age is unknown.

Nevertheless, the increased incidence of obesity in adolescents could provide a significant increase in the incidence of HBP and metabolic problems at early ages. Health problems and behaviors arise during adolescence such as tobacco and alcohol use, diet and exercise patterns, overweight and obesity have a serious impact on the health and development of adolescents today, and potentially devastating effects on their health as adults tomorrow. Middle and late adolescence, are in a stage of life where food choice is especially influenced by fad diets and publicity, which can lead to inappropriate feeding. Many boys and girls enter adolescence undernourished, making them more vulnerable to disease and early death.

The objective of this study was to evaluate the frequency of hypertension and pre-hypertension and the risk factors associated to hypertension in Mexican adolescents.

2. Methods.

2.1 Participants.

Between March 2014 and February 2015, a cross-sectional study was carried out in 384 adolescents from 15 to 19 years old (middle and late adolescence) of both sexes, from whom demographic and clinical data were collected. Morelia is a city and municipality in the north central part of the state of Michoacán in central Mexico. Adolescents enrolled in this study were attended in the Family Medicine Unit (FMU) No 80 of Mexican Institute of Social Security in Morelia, Michoacán, Mexico. FMU No. 80 is localized in the urban zone of Morelia which has a total population of 222,349 patients and the adolescent population between 15-19 years old is 55,207. An invitation to participate in the study of outpatient of FMU No. 80 was realized. Those who agreed were cited in a doctor's office of the FMU accompanied by at least one parent. Adolescents with primary hyperlipidemia, hypertension, diabetes, or glucose intolerance were excluded. Any adolescent receiving pharmacological treatment was also excluded. The study was authorized by the Hospital Ethical Research Committee. All parents gave their written consent, and adolescents gave their verbal and written assent.

2.2 Anthropometric and Biochemical measurements.

Weight was measured to the nearest 0.1 kg and height to the nearest 0.1 cm. BMI was calculated as weight (kg)/height(m^2); Blood pressure was measured with a mercury sphygmomanometer after 20 minutes rest, in a supine position. Two sizes of cuff were used (11x36, and 12x41 cm); the cuff width was required to cover two thirds of the length of the adolescent's arm. Currently, the reference values being used for the PA provided in the tables of the Task Force for Blood Pressure in Children [9] state that for each age and sex percentiles set BP values in relation to height percentile. The definition of hypertension employed was BP greater than the 95th percentile (P) may be hypertension. If the BP was greater than the 95th percentile, BP was staged. Stage 1 (95th percentile to the 99th percentile plus 5 mmHg), BP measurements were repeated on two more occasions, and Stage 2 (>99th percentile plus 5 mmHg), prompt referral should be made for evaluation and therapy. Prehypertension: systolic and/or diastolic ≥P90 but <P95 (in adolescents also ≥120 / 80 mmHg, although these values are below the P90) and normal blood pressure: systolic and diastolic blood pressure <P90. If the BP was greater than the 90th percentile, the BP was repeated twice at the same office visit, and an average SBP and DBP was used.

Blood samples of all children were collected after 12 hours of fasting from a vein in the antecubital fossa, without venous occlusion. Before collecting the blood, we asked each adolescent the hour of last food for fasting confirmation. Blood samples were separated into aliquots and frozen immediately at -70°C until analysis in order to avoid interassay variability. Glucose, UA, cholesterol, triglycerides (TG), and high density lipoprotein (HDL), and low density lipoproteins LDL concentrations were measured using an automatic analyzer (Vitros 5.1 Ortho Clinical Diagnostics®).

2.3 Statistical Analysis

Data were stored and analyzed using SPSS 18.0 statistical package (SPSS Inc, Chicago, IL). Test selection was based on evaluating the variables for normal distribution using the Kolmogorov-Smirnov test. Differences between groups

were calculated using a Student's t-test for independent samples. Pearson's correlation and linear regression coefficients were used to analyze the relation between variables. A $P<0.05$ was considered statistically significant in all cases.

3. Results

384 adolescents between 15 and 18 years old were studied. Of those studied, 291 (75.8%) are female and 93 (24.2%) male.

The frequency of hypertension, Pre-hypertension and normal BP is shown in Figure 1.

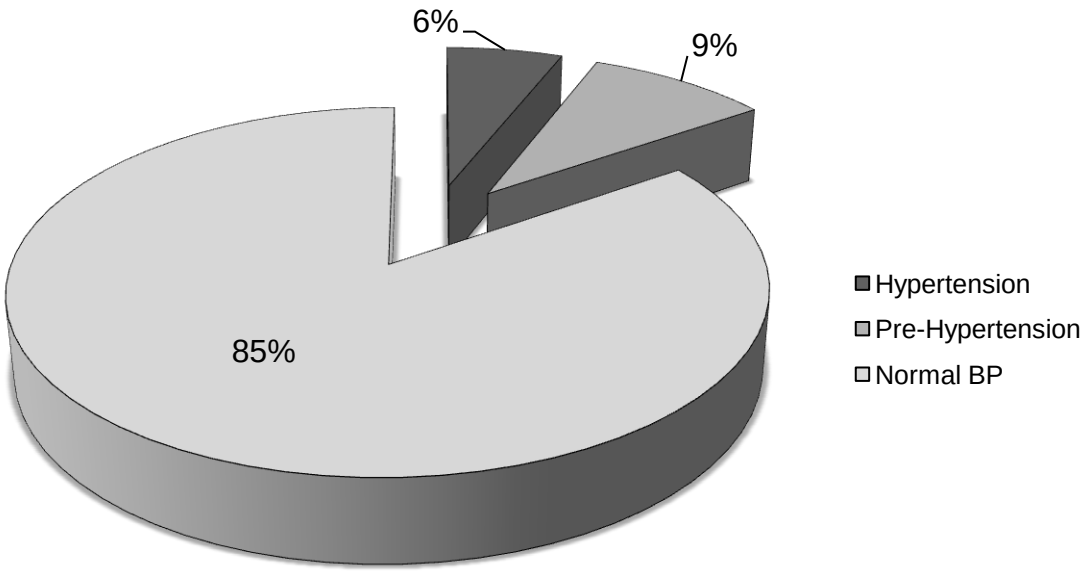

Figure 1. Frequency of Hypertension, Pre-Hypertension and Normal Blood Pressure in adolescents.

Hypertension was found in 6% of all adolescents, Pre-Hypertension in 9.4% and normal BP in 84.6%. Systolic Hypertension was found in 4.70%, systolic Pre-Hypertension in 9.40% and Normal systolic BP in 85.90%. Diastolic Hypertension: 2.3%, Diastolic Pre-Hypertension in 1.6% and Normal Diastolic BP in 96.1%. According to these data, adolescents were grouped in Hypertension group, Pre-Hypertension group and Normal BP group. Clinical and biochemical characteristics of all participants by group are presented in table 1.

Table 1. Clinical, anthropometrical and biochemical characteristics of adolescents.

Variable	Hypertension n=23	Pre-Hypertension n= 36	Normal BP n= 325	P
Age (yr)	16.43 ± 9.45	16.39 ± 1.12	16.19 ± 1.06	0.346
Weight (Kg)	70.18 ± 15.98	72.11 ± 14.46	58.05 ± 10.83	0.0001
BMI (Kg/m^2)	25.45 ± 5.74	26.70 ± 5.86	22.66 ± 3.76	0.0001
Systolic BP (mmHg)	121.65 ± 12.52	119.22 ± 5.49	99.69 ± 7.42	0.0001
Diastolic BP (mmHg)	80.13 ± 10.14	76.94 ± 5.90	67.29 ± 7.21	0.0001
Glucose (mg/dL)	93.48 ± 9.15	94.75 ± 12.75	89.40 ± 10.97	0.008
Insulin (µUI/L)	17.04 ± 10.79	19.07 ± 19.16	19.68 ± 18.20	0.785
TCh (mg/dL)	154.24 ± 36.31	149.88 ± 42.71	141.78 ± 31.75	0.102

HDL (mg/dL)	50.31 ± 10.96	49.62 ± 14.66	54.86 ± 17.31	0.112
LDL (mg/dL)	76.47 ± 40.03	71.47 ± 39.50	61.54 ± 32.75	0.041
TG (mg/dL)	137.24 ± 47.33	143.92 ± 82.86	126.87 ± 53.19	0.176
Uric Acid (mg/dL	4.32 ± 0.91	4.62 ± 1.18	4.61 ± 1.68	0.829
HOMA	4.01 ± 2.73	4.62 ± 5.33	4.44 ± 4.39	0.870

BMI: Body Mass Index; BP: Blood Pressure; WC: waist circumference; TCh: Total cholesterol; HDL: High density lipoprotein; LDL: Low density lipoprotein; TG: Triglycerides. HOMA: Homeostasis Model Assessment. Values are presented as mean ± standard deviation. *ANOVA test P<0.05*

The average age was 16 years of age, the Pre-Hypertension group had a higher BMI in comparison with Normal BP group (P= 0.0001). LDL was higher in hypertension group (P= 0.041). Total cholesterol, HDL, triglycerides and uric acid were not difference between groups (P<0.05).

We analyze the frequency of risk factors associated with hypertension in adolescents (Table 2).

Table 2. Frequency of risk factors associated with hypertension in adolescents.

Variable	**Hypertension n=23**	**Pre-Hypertension n= 36**	**Normal BP n= 325**
Male Sex	13 (56.5%)	20 (55.6%)	60 (18.5%)
Family History of DM	12 (52.2%)	21 (58.3%)	90(27.7%)

Family History of HTA	13 (56.5%)	21 (58.3%)	67 (20.6%)
Prematures	2 (8.7%)	5 (13.9%)	31 ((9.5%)
Obesity ≥ 95 Percentile	9 (39.1%)	16 (44.4%)	45 (13.8%)
Glucose ≥100mg/dL	5 (21.7%)	10 (27.8%)	52 (16%)
TG ≥150 mg/dL	20 (87%)	28 (77.8%)	253 (78.1%)
TCh ≥200mg/dL	2 (8.7%)	5 (13.9%)	11 (3.4%)
HDL < 40 mg/dL	4 (17.4%)	12 (33.3%)	57 (17.5%)
LDL ≥ 130 mg/dL	2 (8.7%)	3 (8.3%)	10 (3.1%)
Uric Acid ≥ 5.5 mg/dL	1 (8.3%)	5 (29.4%)	77 (28.4%)
IR ≥ 3.16	12 (52.2%)	16 (44.4%)	149 (45.8%)

DM2: Diabetes mellitus; HTA: Hypertension; TCh: Total cholesterol; TG: Triglycerides; HDL: High density lipoprotein; LDL: Low density lipoprotein; IR: Insulin resistance. Values are expressed in frequencies (%).

32% of adolescents reported a family history of DM2 and 26.30% of hypertension in parents or grandparents. It is noteworthy that a high frequency of Hypertriglyceridemia was found in three groups (Hypertension: 87%; Pre-Hypertension: 77.8% and normal BP: 78.1%); likewise to insulin resistance (Hypertension: 52.2%; Pre-Hypertension: 44.4% and normal BP: 45.8%). Frequency of LDL ≥130 mg/dL was lowest in three groups; Hypertension: 8.7%; Pre-

Hypertension: 8.3% and normal BP: 3.1%. The relationships between systolic blood pressure and glucose (r= 0.170; P= 0.001), TCh (r= 0.119; P= 0.020), HDL (r= -0.147; P= 0.004) and LDL (r= 0.166; P= 0.001) were realized. Diastolic blood pressure was inversely associated with weeks of gestation (r= -0.121; P= 0.017) and positively with triglycerides (r= 0.105; P= 0.040).

Relative risk analysis of factors associated with hypertension in adolescents was performed (Figure 2).

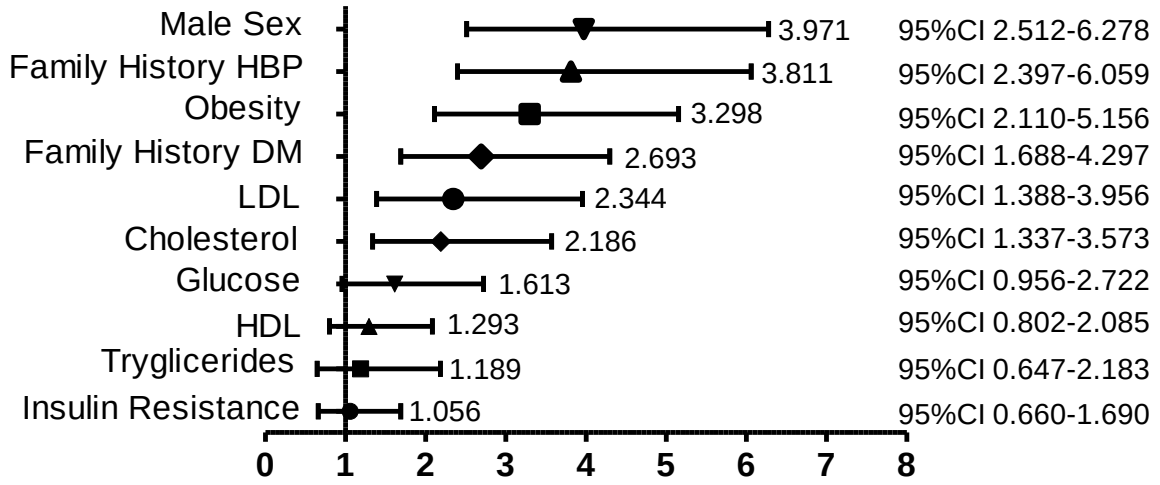

Figure 2. Relative risk with 95% confidence interval (CI) analysis of cardiovascular risk factors associated with hypertension in adolescents.

We found that male sex (RR: 3.971 95% CI: 2.512-6.278), family history of hypertension (RR: 3.811; 95% CI: 2.397-6.059) and obesity (RR: 3.298; 95% CI: 2.110-5.156) were risk factors involved in the development of hypertension. Family history of DM (RR: 2.693; 95%CI: 1.688-4.297), LDL (RR: 2.344; 95% CI: 1.388-3.956) and Cholesterol (RR: 2.186; 95% CI: 1.337-3.573) had a lesser magnitude of risk.

A logistic regression was realized to estimate the probability of hypertension based on predictor variables (Sex male, family history of hypertension, obesity, family history of diabetes, LDL, Cholesterol, Glucose, HDL, Triglycerides and insulin resistance). In table 3 we show the results of logistic regression model.

Table 3. Logit regression model to estimate the probability of hypertension in adolescents.

Variable	β	Standard error	Wald	P	β Exp	95% CI β Exp	
						lower	upper
Constant	0.275	0.407	0.456	0.500	1.316		
Male Sex	1.527	0.415	13.558	0.0001	4.604	2.042	10.379
Family History of HBP	1.346	0.423	10.104	0.001	3.842	1.675	8.810

HBP: High blood pressure.
Log Likelihood sex: -90.405; P= 0.0001;
Log Likelihood Family history hypertension: -88.390; P= 0.002

In the logit regression model only male sex and Family history of high blood pressure were the risk factors that were predictors related with the hypertension or prehypertension as dependent variable.

4. DISCUSSION

In this study, 6% of frequency of hypertension and 9% of Pre-hypertension **were found. The frequency of prehypertension or hypertension is different in comparison with other studies**. In the National Health and Nutrition Survey (NHANES) 13.6% of boys and 5.7% of girls were prehypertensive [10]; Ferrer Arocha [11] in Cuba, reports a lower frequency of hypertension of 2% and pre-hypertension of 6.9%; Salazar Vazquez [12] in the north of Mexico identified a 6.7% of high blood pressure that is consistent **with the results of this study**. It is known that blood pressure in childhood has particularities, with a tendency to increase as age advances, mainly in adolescence where a significant increase is based on growth and body development occurs. Isolated elevations of blood pressure in children can be a "signal" of essential hypertension as it is known that elevated blood pressure levels in childhood tend to persist into adulthood [13].

Some risk factors for hypertension and pre-hypertension were studied. Hypertriglyceridemia was the risk factor with more frequency in the hypertension group (87%) in comparison with the pre-hypertension (77.8%) and the normal BP (78.1%) groups; these frequencies are higher in comparison with the ERICA

study [14] that reported 7.4% of prevalence of hypertriglyceridemia in adolescents in Brazil and in other study realized by Arjona Ortegón et al [15] in Costa Rica, show a hypertriglyceridemia prevalence of 12%. Low HDL was present in low frequency in the hypertension (17.4%) and the normal BP (17.5%) groups. The combination of those metabolic alterations, low HDL, and high TG is usually present, especially in obese patients and patients with improper lifestyles [16,17]. The inadequate traditional dietary habits are considered a risk factor for hypertriglyceridemia and it is important to emphasize that in other studies. In addition, BMI was increased in the hypertension and the pre-hypertension groups. The presence of obesity was significantly associated with a high blood pressure. These trends probably occur because obesity is a common comorbid condition [18,19] that in **this** study occurred in 39.1% in the hypertension group and 44.4% in the prehypertension group.

In relative risk analysis, some factors were associated with pre-hypertension and hypertension; obese adolescents, of male sex and with family history of high blood pressure had three times more probability for developing high blood pressure. Risk factors by logit regression were analyzed and only positive family history of hypertension and male sex were the most important factors that predispose hypertension in adolescents, but these findings disagree with Hansen [20] who reports a positive family history of hypertension, but that did not increase the adjusted odds of identification for hypertension or prehypertension. In fact, a family history of CVD represents the net effect of shared genetic, biochemical, behavioral and environmental components. The association of a positive family history with increased CV risk has been confirmed for men, women, and siblings and in different racial and ethnic groups [21,22], and the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents Summary Report [23] highlights the importance of education in the importance of the accurate and complete family health information of adolescents. As genetic sophistication increases, linking family history to specific genetic abnormalities will provide

important new knowledge about the atherosclerotic process in its early stages [24,25]. This article also has limitations. First, the cross-sectional study design decreased the ability to show causality compared with longitudinal studies although the large and complex evidence base that addresses cardiovascular risk beginning in childhood, and the absence of decades long event-driven clinical trials, required consideration of substantial and consistent evidence from observational studies, developing a chain of evidence [26]. Second, it does not assess the condition of pubertal outbreak, or sex hormones so it was not possible to analyze the association of sex hormones and cardiovascular risk factors.

There is a mistaken belief that cardiovascular disease (CVD) is typical of adult life, regardless of the fact that CVD begins at an increasingly early age, missing the opportunity to intervene early and more efficiently. Other studies reported by Gomez García et al [27], support that high circulating levels of sP-selectin, leptin, PAI-1, vWF, and UA in childhood obesity are related to the presence of platelet activation and may promote early vascular abnormalities (endothelial dysfunction) potentially responsible for increased cardiovascular morbidity and mortality later in life. In medical practice, it is necessary to do early detection of risk factors for CVD from an early age [28,29].

In conclusion, in this study, a 6% frequency of hypertension and 9% of Pre-hypertension were found; male sex and family history of hypertension were the predictor risk factors for hypertension in adolescents in Morelia, Michoacán, México. It is necessary to realize longitudinal studies with a specific methodology and laboratory studies for analyzing the impact of traditional risk factors in the development of cardiovascular disease in adolescents.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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