



Hypertension and dyslipidemia

Hipertensión y dislipidemia

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Cardiovascular diseases (CVD) are the leading cause of death, both in Mexico and in the rest of the world. Cardiovascular (CV) risk factors are not only etiopathogenic agents of CVD, but also, their presence worsens their outcomes, including mortality. High blood pressure (HBP) is one of the main leading cardiovascular (CV) risk factors next to dyslipidemia, diabetes mellitus, obesity, smoking, and physical inactivity.

The main objectives of this text are to discuss the relationship between HBP and dyslipidemia, and their pathogenic mechanisms, which increase the underlying vascular damage in the development of CVD. Also, some epidemiologic aspects of CVD in Mexico will be discussed, to better understand the proper way to get control of the disease and how the combination of both pathologies, HBP and dyslipidemia, increment their potential damage due to the addition of multiple pathophysiological mechanisms.

HBP is one of the leading CV risk factors in Mexico, as the national surveys on health and nutrition, organized by the Mexican Federal Secretary of Health and the National Institute of Public Health have revealed.^{1,2} After HBP, diabetes, tobacco smoking, and dyslipidemias are the most relevant risk factors.³ The rate increases as the population ages.

In Mexico the underreporting, undertreatment and poor cipher control of HBP are of great concern, explaining in part the steady increase of atherosclerotic cardiovascular diseases (ASCVD) in our country. Ischemic heart disease was the leading cause of general mortality and stroke, the sixth, in 2019.⁴ The so called «rule of the halves»⁵ establishes

that of the entire universe of patients with HBP, only half of them is aware that are hypertensive, only half of these informed patients receive antihypertensive treatment, while among those treated, only half are controlled.⁶ This rule is a measure of the health authority's efficacy, the medical community's attitude and knowledge, and the general society information level. In time, in the most advanced countries this rule had been changed, increasing the number of awareness, treatment and control rates. This has not happened in Mexico. Different governmental and independent studies have shown dissimilar total control rates (the proportion of all hypertensive universe that are controlled, not only the control rate of treated patients), varying from 5% to 20%.⁷⁻⁹

HBP is a condition that has serious health repercussions, damaging the arterial vessels and the parenchyma of organs of vital importance as the brain, eye, heart, and kidney. In patients aged 40-89 years, starting from blood pressure figures of 115/70, every 20 mmHg increase of systolic pressure or 10 mmHg of diastolic pressure doubles the mortality risk due to ischemic heart disease or stroke.^{10,11}

National Health and Nutrition Survey in the last four lustra have shown that in Mexico, HBP ranks high among the nine most common causes of death, to the point that in 2015 was responsible of 18.1% of the preventable deaths.¹² A form of estimating the burden of a particular disease in a nation or subnational region is the calculation of DALYs (disability-adjusted life years), an indicator which unites premature mortality with disability. HBP in our country ranks fifth place among the risk factors responsible for the national disease burden.¹³

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Received:
11/06/2021
Accepted:
28/06/2021

How to cite: Guerra-López A. Hypertension and dyslipidemia. *Cardiovasc Metab Sci.* 2021; 32 (s3): s273-s276. <https://dx.doi.org/10.35366/100811>

Different sources (national surveys carried out in 2000, 2006 and 2012 and academic independent studies)^{1,7-9,14} confirm that depending on the characteristics of the sample and the blood pressure measure technique, prevalence of hypertension varies from 25 to 32%.^{1-3,7-9,12} Although from 2000 to 2006, there was a slight increase in HBP prevalence, from the latter year to now, HBP prevalence has remained stable. We do not consider the findings of the so-called Half-way National Health and Nutrition Survey,² because the technique to measure blood pressure was changed. According to various studies, HBP rises with age, until more than half of people over 70 years of age are hypertensive. Most Mexican hypertension investigators agree that men are more affected than women in younger ages. But upon reaching the menopause, prevalence tends to be similar in both genders, and in older age groups, there are more hypertensive women, probably because more men have already died.

Moreover, dyslipidemia is another risk factor of great importance in Mexican population. The 2006 National Health and Nutrition Survey (ENSANUT 2006) showed that in the Mexican population aged 20 to 69 years, the prevalence of several types of lipid abnormalities was as follows. Total cholesterol (TC) ≥ 200 mg/dL, was 43.6%. Hypertriglyceridemia (triglycerides [TG] ≥ 150 mg/dL) was found in 31.5% of participants, while prevalence of hypoalphalipoproteinemia (HDL-c < 40 mg/dL) was 60%, and that of combined dyslipidemia (TC ≥ 200 mg/dL plus TG ≥ 150 mg/dL) was 18.2%.¹⁵ Hypertriglyceridemia was found more elevated in the RENATHA study:¹⁶ which showed a prevalence between 25-65% in diverse states of the republic, with a national mean value about 50%, while the Lindavista study⁹ found 62% of hypoalphalipoproteinemia in the cohort, and hypertriglyceridemia in half the women and nearly two-thirds of the male respondents. This lipid combination is probably the consequence of abnormal Amerindian genes plus a recent drastic change in eating habits, and lack of physical exercise. For those reasons, our population is prone to abdominal obesity, the so-called «metabolic syndrome» (dysmetabolic obesity), dysglycemia, diabetes, and atherogenic dyslipidemia.

The combination of HBP and dyslipidemia increases four times the risk of CVD, as was demonstrated by Yusuf's INTERHEART study.¹⁷ This combination of risk factors is frequently found in Mexican population, concerningly associated to obesity and diabetes mellitus. In the FRIMEX study⁸ of 140,017 persons, it was demonstrated that to a higher total cholesterol value, corresponded a greater prevalence of HBP (19.9% when TC was < 200 mg/dL, 27,8% with TC between 200-239 mg/dL, and up to 33% when TC was ≥ 240 mg/dL).

The relationship between HBP and dyslipidemia is signaled by several pathophysiological mechanisms including, but not limited to endothelial dysfunction, oxidation, inflammation, and the role of the renin-angiotensin-aldosterone system (RAAS), among other processes, all of them having a paramount participation in the genesis of both risk factors and their vascular and organ consequences.

A healthy endothelium should respond to increased pressure, to shear, and to perpendicular stress, producing vasodilating substances. A healthy endothelium must maintain the equilibrium between the vasodilating substances nitric oxide, prostacyclin, bradykinin, and acetylcholine, among others; and the vasoconstrictor substances, like angiotensin II, endothelin, thromboxane A₂, and others. Risk factors such as HBP and dyslipidemia potentiate each other, altering the normal endothelium function.

In this context, the RAAS plays a primary role in this homeostatic equilibrium when it is overexpressed. Angiotensin II has been named the proinflammatory «honorary cytokine» causing through various mechanisms endothelial dysfunction, decreasing nitric oxide availability, increasing PAI-1 production, promoting platelet aggregation, causing vasoconstriction, and producing overactivity of the membrane NADPH oxidase, one of the main producers of reactive oxygen species (ROS). Among the consequences of the increase of ROS are the start-up of the nitroxidation cascade, the increment of low-density lipoprotein (LDL-c) peroxidation and damage to all biomolecules. These processes disrupt vascular permeability, generate more infiltration of leukocytes, and

activate transcription factors like the nuclear factor-kappa B (NF- κ B), which is also activated by angiotensin II. NF- κ B^{18,19} is a crucial promoter of a variety of cellular responses, including tissue growth, inflammation, autophagy, apoptosis, production of adhesion molecules (as vascular cell adhesion molecule-1, VCAM-1), release of chemokines (as the monocyte chemoattractant protein-1 (MCP-1), and interleukins 1, 6 and 8 (IL1, 6 and 8), among others. All these substances lead to atherogenic mechanisms, as are tissue cholesterol entrapment, inflammation, vascular tissue remodeling, proliferation of smooth muscle cells, activation of metalloproteinases, debilitation of the fibromuscular atheroma cap, etc.

The main target in the treatment of dyslipidemias is the LDL-c. The desirable value of the concentration of total cholesterol, LDL-c and triglycerides to be reached by treatment depends on the risk profile of each patient. But in the patient with both conditions, a primordial therapeutic target is also attaining recommended blood pressure ciphers.

In conclusion, HBP is one of the most important cardiovascular conditions in Mexico. A combination of HBP and dyslipidemia increases the pathogenic power of each on the cardiovascular system. The mechanisms that link both HBP and dyslipidemia, from a pathophysiological point of view are complex, but the RAAS has a primary role, and its inhibition is part of the integral treatment. Inflammation, oxidation, and endothelial dysfunction, as well as coagulation disorders, are some of its deleterious consequences.

As physicians, we must commit our efforts to detect hypertension and dyslipidemias in time and give the appropriate treatment to the patients.

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