EDITORIAL COMMENT

The terrible epidemic that devastates Mexico. A national crusade against atherosclerosis is urgently needed[+]

La terrible epidemia que devasta México. Urge una cruzada nacional contra la aterosclerosis[+]

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The socioeconomic, political, and cultural changes that Mexico experienced over recent decades substantially modified its population's nutritional, anthropometric, and epidemiological profiles to give rise to a rapid and regionally uneven epidemiological transition. Without completely disappearing, the old epidemics of previous times, rooted in extreme poverty, malnutrition, ignorance, and lack of basic hygiene, such as malaria, diarrheal diseases, tuberculosis, and others, have given way to a wave of chronic degenerative epidemics, such as obesity, type 2 diabetes mellitus, atherosclerotic diseases, and malignancies, in part originate from an unhealthy lifestyle and which are now the leading public health problems in Mexico. In 2023, 774,110 deaths occurred in the country, of which 50.5% corresponded to the sum of deceases due to heart diseases (24.4%),

diabetes mellitus (14.2%), and cancerous diseases (11.8%). Ischemic heart disease (mainly myocardial infarction) accounted for 75.5% of all cases of heart disease.[1] A prominent fact that must be noted first is that, currently, people with diabetes do not die from this disease but instead largely from cardiovascular complications, mainly myocardial infarction.[2,3] In this way, to the number of deaths due to ischemic heart disease, we would have to add an unknown but presumably significant number of deceases reported due to diabetes in the outdated death certificates still in use. Of similar relevance is the fact that a pathogenic phenomenon underlying atherosclerotic diseases, diabetes, and a vast proportion of cancerous diseases is obesity. According to the 2022 version of the National Health and Nutrition Survey (*Encuesta Nacional de Salud y Nutrición 2022* [Ensanut 2022]), 38.3% of the subjects surveyed were overweight, and 36.9% were obese, meaning that four-fifths of the adult population had an unhealthy weight.[4] Meanwhile, in school-age children and adolescents, the proportion of overweight was 19.2 and 23.9%, and obesity was 18.1 and 17.2%, respectively.[5] Those figures showed that nearly one-fifth of these young age groups have a weight problem. The exponential growth of obesity in our society is appalling, indicating that neither the Mexican state, the medical corporations, nor civil society, in general, have undertaken solid corrective actions to reduce the intensity of this epidemic flagellum. To make matters worse, if cardiovascular and cardiometabolic primary prevention is poorly and incompletely carried out, the clinical management (diagnosis and treatment) of both ischemic heart disease and diabetes is, in general, dreadfully performed.[6,7] The direct and indirect costs of ischemic heart disease and diabetes have not been fully estimated in Mexico in terms of clinical attention expenses, loss of years of life, early disability, and work absenteeism, but presumably must be very high.

An immovable medical paradigm is that lipid abnormalities are crucial in the genesis of atherosclerotic lesions.[8,9] The role of all lipid particles containing apoB100 has been well established,[10] particularly the more atherogenic lipid particle, the low-density lipoprotein (LDL).[11] Less universally accepted is the atherogenic effect of both hypertriglyceridemia and low concentrations of high-density lipoprotein (HDL), the so-called hypoalphalipoproteinemia. However, there is a robust body of evidence about the role of the increased concentration of triglycerides as a risk factor for atherosclerotic cardiovascular diseases (ASCVD).[12-15] The role of low HDL concentration is more elusive because, on the one hand, the protective effect of HDL depends not only on its plasma concentration but also on the tissue cholesterol extraction capacity of some genetic variants of its principal apolipoprotein ApoA-1.[16] Equally important is the fact that HDL sometimes behaves as a Janic molecule, being pro-inflammatory and atherogenic instead of protective.[17] Also, most of the once very promising CETP (cholesteryl ester transfer protein) inhibitor drugs (trapibs) have failed to show cardiovascular protection (CV) despite the remarkable increment of HDL concentrations. Only in the REVEAL study did one of these drugs, anacetrapib, show a moderate protective benefit.[18]

A set of dyslipidemic phenotypes assails the contemporary Mexican population: between 40% and 66% of the adult population is hypercholesterolemic, two-thirds have hypoalphalipoproteinemia, and more than 50% have hypertriglyceridemia.[19-21] As overweight and obesity are associated in a large proportion of the cases with insulin resistance syndrome and secondary hyperinsulinism, the Mexican overweight/obese and diabetic populations frequently present a consequence of these metabolic disarrays, a dyslipidemic complex named «atherogenic dyslipidemia» or «lipid triad». It is characterized by hypertriglyceridemia, hypoalphalipoproteinemia, and an increase of small and dense LDL lipoproteins,[22,23] and it is associated with a remarkable atherogenic power.[24] Some indications need to be corroborated in further studies that this type of dyslipidemia is a significant determinant of myocardial infarction in our population.[25] Finally, the role of lipoprotein(a) [Lp(a)]has been established as a relevant risk factor for ASCVD, aortic stenosis, and thrombosis.[26,27] As it is known, there are considerable interethnic differences in Lp(a) concentrations, which

depend fundamentally on genetic influence. To our knowledge, only one group of Mexican researchers has studied this lipid in our population, showing an inverse correlation with the so-called metabolic syndrome and two alleles directly associated with coronary and aortic valve calcification.[28-30] More studies are necessary to confirm the influence of this lipoprotein on the ASCVD epidemic in Mexico.

Of the most significant importance is that various studies using different risk scales showed an ominous reality and a somber prognosis of Mexico's public health. The study REMECAR[31] comprehended subjects from a private registry with known or suspected cardiovascular diseases or carriers of cardiovascular risk factors. Using European risk scales (SCORE-2 and SCORE-OP),[32,33] it was estimated that 95% of these patients had high or very high risk. Despite this, around two-thirds of the participants were not on any lipid-lowering therapy, and only 12.4% received treatment with a high-intensity statin. Unsurprisingly, less than 20% of patients with established CV disease have goal LDL-c values less than 55 mg/dL.

Additionally, only a quarter of the patients with diabetes and 14% of subjects with other CV risk factors and high CV risk attained the LDL-c goals. In the primary prevention Lindavista study,[20] participants were not medicated with cholesterol-lowering drugs at the time of recruitment. In this study, the American College of Cardiology/American Heart Association ASCVD Risk Estimator system[34] and the GLOBORISK[35] tool showed that half of the cohort population had intermediate or high risk. However, both scales grossly underestimate the risk when their results were compared with the quotient TG/HDL (as a marker of insulin resistance and an index of CV forecasting).[12,36] The data from these studies reveal that in our country, in both sceneries of primary and secondary prevention, LDL-c goals are not achieved in most of the patients, because the diagnosis is not carried out, or statins are not used, inclusively in those conditions where they are mandatory, or because high-intensity statins are not used at the appropriate doses.

Despite everything described above, the Mexican national health system, fragmented as it is, devoid for political reasons of clear leadership at the national level, suffering a chronic shortage of financial resources, and in the absence of long-range preventive programs and solid public policies, has not identified the problem of dyslipidemia as a priority for the country's public health.[19]

To point out just a few of the severe limitations that make it difficult the primary and secondary prevention of ASCVD, mainly ischemic heart disease, we enlist the following problems:

1. **Mexico needs to spend more and better on health.** Mexican health spending (the sum of medical care goods and the cost of all services of clinical attention and prevention)[37] is one of the lowest not only among the 38 market-oriented economies encompassed in the OECD (Organization for Economic Cooperation and Development) but also among Latin American countries. For example, describing total health expenses as a percentage of the Gross Domestic Product (GDP, an index expressing the national wealth), Cuba spends 14%, Argentina, Brazil, Uruguay, El Salvador, Nicaragua, and Panama above or around 10%, and 8% Costa Rica.[38] In comparison, in 2022, Mexican health spending represented 5.1% of the national GDP,[39] at any rate, far from the 6% recommended by international organizations.[40] Still, even worse, only 2.93% came from the government (the rest went out of the citizen's pockets). In this context, health spending in Mexico is comparable to the poorest sub-Saharan African countries. With this scarcity of economic resources, achieving an efficient, universal, and modern level of clinical care is impossible, and neither is it possible to achieve effective cardiovascular prevention. That amount of health expenses is inadmissible for a country with the 12 or 14th world[41] economy (at the same level as Spain, Australia, and Korea).

2. **Control of the overweight and obesity epidemic, facing powerful resistance, is still far away.** Although some estimable advances have been made against the epidemics of overweight/obesity (for

example, the new labeling of food products different from the old one, designed and imposed by the food industry),[42] we are still far from implementing a series of public policies that limit on the one hand the mass consumption of ultra-processed junk food, sweetened beverages, and other poisonous products. On the other hand, the nation does not effectively encourage the achievement of cardiovascular and cardiometabolic health in our society, promoting, especially in childhood and adolescence, the frequent practice of physical exercise, a healthy diet, and the abstention from the consumption of tobacco products and other addictive substances. There is overwhelming evidence about the benefit of weight loss diminishing several atherogenic variables and mortality from CV outcomes.[43,44] Unfortunately, the frontal fight against this epidemic naturally faces opposition from powerful economic and political interests.[42]

3. **The country does not have the regulatory and legislative framework to establish public policies to reduce the ASCVD epidemic's force.** The nation lacks both legal framework and solid public policies, scientifically based, long-lasting, well-funded, and extensively publicized to reduce the incidence and lethality of ASCVD risk factors, mainly obesity, high blood pressure, lipid abnormalities, and smoking in our population. Before the era of statins, the North Karelia Project (then extended to all of Finland)[45] could reduce cardiovascular mortality (65% in men and 70% in women) in a brief lapse, simply convincing the Finnish society to reduce the consumption of saturated fat and salt, better control of blood pressure, and less smoking. These remarkable results were achieved by utilizing community interventions, public policies, and pertinent legislation, with the joint actions of the state organs, the industry, communications media, health personnel, and civil society.

4. **Clinical diagnosis of ASCVD risk factors, drug treatment, and therapeutic lifestyle modifications of dyslipidemias and other atherogenic determinants are generally not well carried out, especially at the first level of care, public and private.** This problem begins in primary medical education, as the curricula of almost all the 168 medical schools nationwide need to prioritize the prevention, diagnosis, and treatment of the nation's leading health problems. Neither, in general, the postgraduate residencies dedicate a special effort to increase in this field, with due depth and extent, future specialists' clinical and preventive skills. To make this problem even worse, the continuing medical education provided by the state to the physicians serving in public health institutions is scarce and occasional. The critical mission of raising and maintaining the knowledge and skills of physicians is mainly carried out by respected medical societies and congregations, sometimes with the economic assistance and help of the health industry. However, it is not always free of commercial intentions and distortions. As a result, in our most important health institutions, especially at the first level of care, as a general phenomenon (and, of course, with admirable exceptions), the clinical management of the most important CV risks is not the most appropriate, nor the closest to the current state of the art. Some data that backed up this last statement are addressed by several studies (some of them contradictories) on the control of different ASCVD determinants in Mexico. These results show a rate of dyslipidemia control of 30%, rates of control of high blood pressure from 21 to 50%, and adequate glycemic control in patients with diabetes at about 40%.[46-49] Health institutions do not regularly provide the diagnostic and therapeutic tools necessary for correctly managing ASCVD risk factors, mainly in the first and second levels of medical care. For example, the lipids usually measured in first-contact clinics are only total cholesterol and triglycerides. Without the measurement of HDL, it is impossible to estimate (with all the known limitations) LDL nor the non-HDL cholesterol and lipid triad, which are essential goals in a population like ours. Usually, dyslipidemia is diagnosed very late,

generally when there is already a clinical episode of ASCVD. The recommendation to determine the complete lipid profile of the entire population, starting at 18 years of age, is not followed.[50]

5. **In primary prevention, recognition of new cases of CV risk factors and estimation of risk are equally important.** In this respect, the nation does not have its own risk score, which properly considers certain frequent traits of the Mexican population. To tailor the intensity of treatment according to the level of risk, it is necessary to have a proper risk score that considers the anthropometric and metabolic traits of the Mexican population, mainly abdominal circumference and triglyceride concentrations, that are set out apart in all the most risk score systems done in other populations (the United States and Europe) very different to ours.[12,29-31] It is time to carry out our score system derived from a long-running, nationwide study of the main CV risk factors.

With all the above background, a group of academic-oriented physicians and scientists deeply involved in lipidology and cardiovascular prevention are interested in presenting a strategic plan to the new health authorities that would be simple, practical, and advantageous in cost-benefit relations. Although the other ASCVD risk factors (diabetes, hypertension, smoking, and obesity) have similar importance, our group called GERETRA-HCL (an acronym for the Spanish name of *Grupo de Expertos para la Recomendación Estratégica del TRAtamiento de la HiperColesteroLemia en* México, i.e., Group of Experts for the Strategic Recommendation of the Treatment of Hypercholesterolemia in Mexico) would focus its main interest in the reduction of the blood lipid disorders.

Ours is an entirely apolitical, heterogeneous group formed by persons coming from different institutions and associations: Hospitals of the social security institutions (IMSS, ISSSTE), from the Federal health hospitals (IMSS-Bienestar), cardiology and cardiovascular preventive national associations, several National Health Institutes, the Army, the National Academy of Medicine, and superior education institutions as the National Autonomous University of Mexico

and the National Polytechnic Institute. The group does not have another purpose besides the wish to combat the ASCVD epidemic. We respectfully invite other basic, epidemiology, nutrition, or clinical scientists to join us in this crusade against one of the main ASCVD risk factors to alleviate the intensity and extension of the epidemic.

In a second future communication, the group will present to the new Secretary of Health, Dr. David Kershenobich, whose excellent academic accreditations are recognized by everyone, a project of strategic approach funded on international experiences.[51] The crusade that we propose is only possible under the auspices of the state but also requires the decisive involvement and compromise of all of us.

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