Nutrición Hospitalaria

Nutr Hosp. 2015;32(1):182-188
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original/*Síndrome metabólico*

Obesity phenotypes in urban middle-class cohorts; the PRIT-Lindavista merging evidence in Mexico: the OPUS PRIME study

Guillermo Fanghänel-Salmón[1], Gabriela Gutiérrez-Salmeán[3], Virginia Samaniego[2], Alejandra Meaney[2], Leticia Sánchez-Reyes[1], Ulises Navarrete[3], Luis Alcocer[4], Ivonne Olivares-Corichi[3], Nayeli Najera[3], Guillermo Ceballos[3] and Eduardo Meaney[3]

[1]Unidad de Factores de Riesgo Cardiovascular del Servicio de Cardiología del Hospital General de México, Secretaría de Salud, México, D.F. [2]Unidad Cardiovascular, Hospital Regional "Primero de Octubre" del ISSSTE, México, D.F. [3]Laboratorio de Investigación Integral Cardiometabólica, Sección de Estudios de Posgrado e Investigación de la Escuela Superior de Medicina del Instituto Politécnico Nacional, México, D.F. [4]Cátedra Ignacio Chávez. Hospital General de México. Universidad Nacional Autónoma de México, México, DF. México.

Abstract

Background and aims: **even though overweight and obesity (O/O) are stated diseases, there is still a claim for a so-called "healthy obese" phenotype. Only few reports have explored the presence of different metabolic phenotypes along the body mass index (BMI) range and their corresponding associations to cardiovascular risks.**

Methods: **as of BMI, and according to the presence of metabolic syndrome (MS) features (waist circumference, blood pressure, fasting glycemia, and lipid profile), phenotypes were determined. Cardiovascular risk was estimated with atherogenic quotients: total cholesterol/HDL-c, LDL-c/HDL-c and the triglycerides (TG)/HDL-c index.**

Results: **in 8405 mexican adults, 36% lean, 43% overweighed and 21% obese, nine phenotypes were identified: for each weight category there were subjects with normal metabolism (none MS factors), intermediate (≤2) and dysmetabolic (≥3). Only 10.8% of O/O had normal metabolism, and 5.8% of the lean persons were dysmetabolic. Atherogenic risk was higher in dysmetabolic obese persons, but the risk was high among all dysmetabolic people, independently of the weight status. TG/HDL-c showed the same trend.**

Conclusions: **elevated cardiometabolic risk derives from the high prevalence of O/O. A great proportion of non-obese people have intermediate dysmetabolism. A genetic predisposition to obesity, insulin resistance, diabetes and dyslipidemia in Mexican population is blended**

Correspondence: Eduardo Meaney.
Laboratorio de Investigación Integral Cardiometabólica.
Sección de Estudios de Posgrado e Investigación.
Escuela Superior de Medicina del Instituto Politécnico Nacional.
Plan de San Luis y Díaz Mirón s/n. Colonia Casco de Santo Tomás,
Delegación Miguel Hidalgo. C.P. 11340, México, D. F.
E-mail: lalitomini@prodigy.net.mx

Recibido: 8-I-2015.
1.ª Revisión: 9-III-2015.
Aceptado: 19-IV-2015.

FENOTIPOS DE OBESIDAD EN COHORTES URBANAS DE CLASE MEDIA; EVIDENCIA CONJUNTA PRIT-LINDAVISTA EN MÉXICO: EL ESTUDIO OPUS PRIME

Resumen

Antecedentes y metas: **aun cuando el sobrepeso y la obesidad (S/O) son enfermedades reconocidas, hay un reclamo por la existencia de un fenotipo llamado "obeso sano". Pocos estudios han explorado la presencia de diferentes fenotipos metabólicos en los rangos del índice de masa corporal (IMC) y su asociación con riesgo cardiovascular.**

Métodos: **se determinaron fenotipos de acuerdo al IMC y a la presencia de marcadores del síndrome metabólico (SM) (circunferencia abdominal, presión sanguínea, glucemia en ayunas y perfil de lípidos). El riesgo cardiovascular fue estimado con los índices aterogénicos: colesterol total/HDL-c, LDL-c/HDL-c y triglicéridos(TG)/HDL-c.**

Resultados: **en 8.405 adultos mexicanos, 36% delgados, 43% con sobrepeso y 21% obesos, se identificaron 9 fenotipos. Por cada categoría de peso se encontraron sujetos con metabolismo normal (ningún factor de SM), intermedios (≤2) y dismetabólicos (≥3). Solo el 10.8% de los sujetos con S/O tuvieron metabolismo normal y el 5.8% de los sujetos delgados fueron dismetabólicos. El riesgo aterogénico fue mayor en los sujetos obesos dismetabólicos. El riesgo fue alto entre todos los sujetos dismetabólicos independientemente del peso. El índice TG/HDL-c mostró las mismas tendencias.**

Conclusiones: **el riesgo cardiometabólico incrementado deriva de la alta prevalencia de S/O. Una gran proporción de sujetos no obesos tiene dismetabolismo intermedio. Una predisposición genética a la obesidad, la resistencia a la insulina, la diabetes y la dislipidémia en la población mexicana, junto con un estilo de vida no sa-**

to an unhealthy lifestyle, yielding to a catastrophic epidemic of diabetes, and cardiovascular diseases.

(*Nutr Hosp*. 2015;32:182-188)

DOI:10.3305/nh.2015.32.1.8646

Key words: *Obesity. Overweight. Metabolic syndrome. Cardiovascular risk. Metabolic phenotypes.*

ludable da como consecuencia una epidemia catastrófica de diabetes y enfermedades cardiovasculares.

(*Nutr Hosp*. 2015;32:182-188)

DOI:10.3305/nh.2015.32.1.8646

Palabras clave: *Obesidad. Sobrepeso. Síndrome metabólico. Riesgo cardiovascular. Fenotipos metabólicos.*

Background

Mexico faces an evolving epidemic of overweight and obesity (O/O)[1,2] resulting from changes in population habits, leading to a hypercaloric diet alongside with a sedentary lifestyle, added to a genetic predisposition to fat accumulation and development of diabetes[3].

Recently, evidence showing that O/O are neither homogenous conditions nor impose similar cardiometabolic risk to all individuals has emerged. Four well-defined phenotypes have been so far identified: lean healthy (LH), obese unhealthy (OU), the metabolically healthy obese (MHO), and the metabolically obese but with normal weight (MONW)[4,5]. The pathogenic phenotypes impose different therapeutic and/or preventive approach. Patients with MHO and MONW individuals are in a higher risk for cardiovascular outcomes or diabetes.

Although a clear-cut picture of the epidemiology of O/O in Mexico has been established a short time ago[1,2,6], no study has been addressed to identifying the prevalence of the above described phenotypes. The PRIT and the Lindavista studies[7,8], whose partial or early results have been already published, are independent observations focused towards the prevalence of essential vascular risk factors in middle-class samples of Mexico City inhabitants. The main purpose of the OPUS PRIME (*Obesity Phenotypes in Urban Middle-Class CohortS. The PRIT-Lindavista Merging Evidence in MExico*) study was to estimate the frequency of the different metabolic phenotypes in a combined cohort of the contemporary population of Mexico City, and the cardiometabolic risk inherent to each phenotype.

Methods

Study population. The basic methodology of the two base studies has been published previosly[7,8]. Briefly, the PRIT (*Prevalence of Cardiovascular Risk Factors in Hospital General de México Workers*) study assembled a sample of more than 5,000 workers of a Mexican hospital (physicians, nurses, administrative employees, janitors and maintenance employees), who were assessed in order to establish the frequency of cardiovascular and metabolic risk factors: diabetes, overweight or obesity, hypertension smoking habits, and dyslipidemias. For its side, the Lindavista study was originally an intervention trial on cardiovascular risk factors, using also a cohort of urban middle-class Mexico City inhabitants (a cohort of 2602 subjects ≥35 years, free of clinical cardiovascular or life-threatening chronic diseases), with two parallel arms: one in which therapeutic interventions were done intensively by cardiologists at the Hospital Regional "Primero de Octubre", and a control group where standard preventive interventions were conducted by primary care physicians. In the present combined analysis, baseline data from both studies were merged.

Ethics. Both studies were approved by their Ethics and Research Institutional Committees and conducted according with the Declaration of Helsinki, Good Clinical Practices and Mexican Federal Regulations; informed consent was approved by each institutional review committee and was signed before any measurements were taken.

Anthropometric and cardiometabolic assessment. Body weight was measured in kg; height was obtained in meters with a wall-stadiometer and body mass index (BMI; kg/m^2) was calculated. Abdominal circumference was measured in cm. Blood pressure was determined by means of mercurial sphygmomanometers. Fasting serum glucose, total cholesterol (TC; mg/dL); cholesterol of the high-density lipoproteins (HDL-c; mg/dL) and triglycerides (TG; mg/dL) were determined using colorimetric assay kits, following the manufacturer's instructions. Low-density lipoprotein cholesterol (LDL-c; mg/dL) was calculated using the Friedewald formula,[9] Cut-off points of all variables were established according with the current national and international guidelines on hypertension[10] (systolic and diastolic blood pressures ≥130/85 mmHg for the diagnosis of the MS); dyslipidemia[11] (hypertriglyceridemia ≥150 mg/dL and hypoalphalipoproteinemia if HDL-c <40 mg/dL in men and <50 mg/dL in women) and dysglycemia[12] (normal if fasting glycemia was <100 mg/dL, impaired fasting glycemia when fasting blood glucose was between 100 and 125 mg/dL, and downright diabetes mellitus if glycaemia was ≥126 mg/dL). According with the World Health Organization[13], the subjects were divided in three weight categories: normal weight (BMI <25), overweight (25-29.99) and obesity (≥30). A waist circumference ≥90 cm in men and ≥80 cm in women[14] was considered as indicator of abdominal adiposity.

MS was diagnosed with at least three of five traits[15]: abdominal obesity, hypertriglyceridemia, hypoalphalipoproteinemia, dysglycemia, and systolic and diastolic blood pressures ≥130/85 mmHg.

Table I
Proportion of normal weight, overweight and obesity

Categories	*Men*	*Women*	*Total*
Normal weight			
n	931	2085	3016
(proportion)	*(34.7%)*	*(36.4%)*	*(35.9%)*
Overweight			
n	1232	2369	3601
(proportion)	*(46%)*	*(41.4%)*	*(42.8%)*
Obesity			
n	517	1271	1788
(proportion)	*(19.3%)*	*(22.2%)*	*(21.3%)*
Total			
n	2680	5725	8405
(proportion)	*(100%)*	*(100%)*	*(100%)*

Total and relative frequencies (for men and women) of nutritional status according to body mass index (BMI), i.e., normal, overweight or obese, are shown.

Estimation of risks. In order to characterize the metabolic and cardiovascular risk of the studied subjects we ruled out both, the Framingham[16] and the newer Pool Cohort Equations[17] algorithms because neither of them account BMI and TG as a risk criteria, and because smoking (not considered in this analysis focused on O/O) adds considerable risk predominantly in young people, independently of their metabolic status. Instead, we used the atherogenic indexes TC/HDL[18] and LDL/HDL[19], quotients displaying the balance among the atherogenic lipid fractions and the "good" cholesterol tissue removing fraction (HDL-c). These indexes have been extensively used to predict cardiovascular disease due to the imbalance between pro-atherogenic and protective lipoproteins, leading to –as their name states- atherosclerosis and further contributing to the development of coronary artery disease (CAD). In addition, the TG/HDL[20] was also assessed as it has been associated with the risk for developing insulin resistance and it has also been proposed as the most powerful independent predictor of CAD when it is>4.

Statistical analysis. Phenotype frequencies (i.e., proportions) were calculated and then divided according to BMI and gender. Afterwards, the relative frequencies of MS abnormalities (e.g., dysglycemia, hypertension, etc.) and of the atherogenic indexes thus cardiovascular risk, were calculated in relation to each phenotype. Finally, we calculated the relative risks Finally, after applying a chi-squared test that showed significantly association among variables, we calculated the relative risk of obese and overweighed individuals with higher cardiovascular risk (according with elevated TG/HDL ratio) in comparison with participants with normal BMI. GraphPad Prism v.5 was used to performed statistical analysis; $p<0.05$ value was considered as significant in all tests.

Results

The databases combined 8,405 subjects, 68.1% of them women. Table I shows the proportion of individuals according to BMI. In both genders, the frequency of weight categories was similar, but women had a slightly greater proportion of obesity and, in correspondence, a lesser number of overweighed individuals.

Table II shows the relative frequency of the nine phenotypes encompassed in the three weight catego-

Table II
Proportion of o/o phenotypes

BMI Categories	*Metabolic phenotype*	*Men*	*Women*	*Total*
		n = 931	n = 2085	n = 3016
Lean	Normometabolic	318 (34.2%)	505 (24.2%)	823 (27%)
	Intermediate	574 (61.6%)	1444 (69.3%)	2018 (65.9%)
	Dysmetabolic	39 (4.2%)	136 (6.55)	175 (5.8%)
		n = 1232	n = 2369	n = 3601
Overweight	Normometabolic	125 (10%)	308 (13%)	433 (12%)
	Intermediate	849 (69%)	1655 (70%)	2504 (56%)
	Dysmetabolic	258 (21%)	406 (17%)	664 (18.4%)
		n = 517	n = 1271	n = 1788
Obese	Normometabolic	31 (6%)	66 (5%)	97 (5.4%)
	Intermediate	304 (59%)	723 (57%)	1027 (57.4%)
	Dysmetabolic	182 (53%)	482 (38%)	664 (37.1%)

Total and relative frequencies (for each gender) of the metabolic phenotypes according to body mass index (BMI), i.e., lean (normal), overweight or obese, are shown.

ries (normal, overweight and obesity); each having three different metabolic statuses according with the number of MS traits: normometabolic (none), intermediate (one or two) or dysmetabolic (three or more). Data show that many lean individuals were not entirely normometabolic, but had one or two features of the MS, mainly hypoalphalipoproteinemia and/or hypertriglyceridemia. In the same manner, many overweighed or obese subjects were not entirely dysmetabolic, but had just one or two MS abnormalities, or even, none. The proportion of the "healthy obese" phenotype was rather low in our sample.

Figure 1 gathers the data regarding the relationship among O/O status and the frequency of the MS traits in men (A) and women (B). There are differences among genders: the proportion of low HDL and hypertriglyceridemia was greater in women than in men in lean, but showed no differences in the other weight categories. Notwithstanding, although subjects with dysmetabolic obesity had the greater proportion of MS factors, there were not statistical differences among these persons and those with dysmetabolic overweight. Subjects pertaining to the intermediate normal weight group had the lesser proportions of hypertension and dysglycaemia. Although there was a statistical difference among intermediate and full-blown dysmetabolic phenotypes in each weigh category, no difference was found among groups. It was detected a tight (r=0.99) correlation between blood pressure ≥130/85 mmHg and weight category in the intermediate and dysmetabolic phenotypes. Concerning glycaemia, the high correlation was seen only in the intermediate phenotypes and no in the dysmetabolic, because almost 70% of the individuals pertaining to the latter category had abnormal fasting glycaemia (*graphs not shown*). The proportion of subjects with hypoalphalipoproteinemia and hypertriglyceridemia in both genders was remarkable. Dysmetabolic women had greater proportion of both dyslipidemias than men of the same categories. Men and women with normal weight had a sizable proportion of low HDL, indicating that these abnormalities are not exclusively related to overweight or obesity.

Table III shows the distribution of atherogenic indexes LDL/HDL and TC/HDL. Obese dysmetabolic subjects exhibited the highest values of both indexes, denoting the most elevated atherogenic risk. Nevertheless, dysmetabolic phenotypes of the three weight categories, had also relatively high risk values, pointing out that lean but dysmetabolic individuals have also a substantially elevated atherogenic risk. The TC/HDL

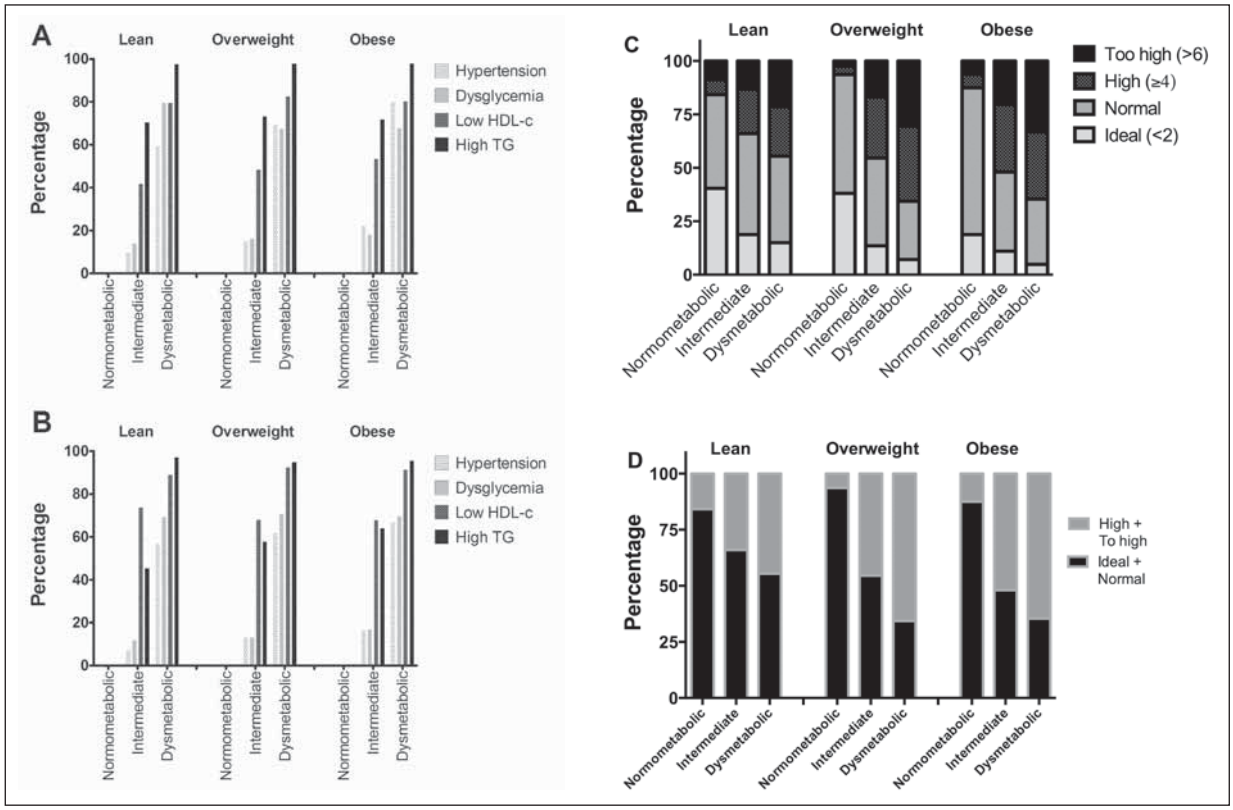

Fig. 1.—Percentage of subjects with no metabolic syndrome (MS) factors (normometabolic); ≤ 2 MS factors (Intermediate) and ≥3 MS factors (Dysmetabolic) in lean, overweight and obese Body Mass Index categories in a sample of 8,405 Mexican adults, A) *Men;* B) *Women.* C) *Triglyceride/HDL ratio levels in subjects with no metabolic syndrome (MS) factors (normometabolic); ≤ 2 MS factors (Intermediate) and ≥3 MS factors (Dysmetabolic) in lean, overweight and obese Body Mass Index categories in a sample of 8,405 Mexican adults*. D) *Triglyceride/HDL ratio levels grouped as Ideal+ Normal (<4) and High + to High (≥4) in Lean, Overweight and Obese subjects*.

Table III
Atherogenic lipid indexes

Category and phenotypes	*LDL/HDL values*		
Lean	<2.5	2.5-3.4	≥3.5
Normometabolic (%)	64.5	26.7	8.8
Intermediate (%)	49.3	27.4	22.8
Dysmetabolic (%)	33.6	27.2	38.6
Overweight			
Normometabolic (%)	59.2	26.5	14
Intermediate (%)	28.9	31.5	39.4
Dysmetabolic (%)	15.9	27.9	55.9
Obesity			
Normometabolic (%)	30.2	38.8	30.5
Intermediate (%)	33	27.7	38
Dysmetabolic (%)	19.8	30.4	49.5
Category and phenotypes	*TC/HDL values*		
Lean	<3.5	3.5-4.9	≥5
Normometabolic (%)	43.9	46.1	9.8
Intermediate	26.2	44.5	29.1
Dysmetabolic	15.9	34.5	49.5
Overweight			
Normometabolic (%)	40.5	42.2	17.1
Intermediate (%)	12.2	38.8	48.8
Dysmetabolic (%)	5.2	22.7	72
Obesity			
Normometabolic (%)	14.4	42	43.5
Intermediate (%)	15	36.3	48.5
Dysmetabolic (%)	6.7	26.6	66.6

Relative frequencies (for each BMI category and metabolic phenotype) of the atherogenic indexes are shown.

quotient, probably a better atherosclerosis risk marker for populations affected by high incidence of insulin resistant[21], showed the same trend.

Regarding the TG/HDL ratio, which establishes metabolic and cardiovascular risk, the normal-weight but dysmetabolic subjects had a similar risk profile to those with dysmetabolic O/O. In general, as seen in Figure 1C the risk according to the TG/HDL ratio increased as BMI did and moreover, after grouping low-risk (i.e., normal+ideal) and high-risk (i.e., high+too high) categories, as shown in figure 1D, it became more evident that the overall cardiometabolic risk increased within weight categories as the number of MS features did. We statistically evaluated such phenomenon by calculating relative risks (RR). Table IV shows that there is a significant increase in the relative risk of being at high cardiometabolic risk (i.e., high+too high TG/HDL risk category) as BMI increases despite that the metabolic phenotype is the same (e.g., a dysmetabolic subject has a higher probability (156%) of being at high cardiometabolic risk if he/she is obese than if he/she has a normal body weight).

Table IV

	Relative Risk	*p*
	Intermediate	
Lean vs Overweight	1.224	< 0.05
Lean vs Obese	1.3	< 0.05
Overweight vs Obese	1.136	< 0.05
	Dysmetabolic	
Lean vs Overweight	1.63	< 0.05
Lean vs Obese	1.567	< 0.05
Overweight vs Obese	0.97	0.74

Relative risk and their corresponding p-value are shown of TG/HDL ratios grouping normal+ideal ranges and high+very high categories . Only metabolically altered subjects (i.e., intermediate and dysmetabolic) were included and analysis was performed within BMI categories.

Discussion

Results found in this work delineate the metabolic status affecting a sample of the contemporary urban population of Mexico. Indirectly, the data give account of the high prevalence of not only obesity and diabetes, but also of a wider metabolic disarrangement, including hypoalphalipoproteinemia and hypertriglyceridemia.

The simplest approach to O/O, making these adiposity abnormalities a synonym of the so-called "metabolic syndrome" has a lot of shortcomings and deceitful conclusions. In order to clarify this tangled question it can be say that, in the majority of the cases of abdominal obesity, insulin resistance is a measurable phenomenon, and the secondary hyperinsulinism is a pathogenic factor responsible of comorbidities accompanying the O/O condition. Nevertheless, recent observations[22-24] have disclosed that not in all the obese or overweighed subjects are dysmetabolic yielding a "healthy obese" phenotype. However, a recent meta-analysis proved that, in comparison with metabolically healthy normal-weight individuals, obese or overweighed persons have a greater risk for outcomes and complications[25]. In the other hand, there are normal-weight persons with some or all the comorbidities of the MS, except weight excess[31]. Again, some terms that have been used to designate these phenotypes are not, in our judgment, very convenient. The phrase "metabolically obese but with normal weight (MONW)" seems inappropriate because is too long and rather confusing.

We instead propose the three classical weight categories: normal weight, overweight and obesity, adding the sub-phenotype characteristic: normometabolic, intermediate or dysmetabolic. Our data show a broad continuum in the expression of the binomial weight-metabolism, in which in one pole there is the weight excess, mainly abdominal adiposity, while in the other extreme lays an abnormal metabolism, due presumably to insulin resistance and reactive hyperinsulinism.

It is apparent that in contemporary Mexicans, both factors play important roles in the genesis of O/O. One third of the population of the combined cohorts had normal weight, and three fifths, overweight or obesity.

Our study also shows that for each weight category the more sizable proportion corresponded to intermediate phenotypes, i.e., persons with one or two traits of MS: more than two thirds of the normal-weight subjects, and more that the half of those with overweight or obesity. Only 1353 participants (16% of the entire population, 27% of the normal-weight subjects and 9.8% of the O/O population) were metabolically healthy people, with a normal glucose and lipid metabolism, and absence of blood pressure ≥130/85 mm Hg.

More relevant is the fact showing that the abnormal dysmetabolic phenotypes bring up a higher metabolic and cardiovascular risk. Measuring these risks in the way we did (through lipid quotients), it is clear that both, excess weight and a dysmetabolic state, impose a threatening risk to the bearers of these anthropometric or metabolic derangements. The TG/HDL quotient has been used frequently to predict diabetes or cardiovascular outcomes[26]. For example, in the WISE[27] study this index was a strong predictor of all-cause mortality and cardiovascular events in women with suspected ischemic heart disease. The recent study of Murguía-Romero[28] in 2244 apparently healthy college students, demonstrated that the TG/HDL ratio cutoff points used in middle-aged Caucasian of both genders can be used in our population to identify insulin resistant individuals with elevated cardiometabolic risk.

Limitations of the study. There are several limitations in this study. Firstly, both merging cohorts' samples were not probabilistic, and so there are more women than men. Secondly, samples were assembled with persons living in Mexico City, so, this fact impedes to extend the conclusions of the study to the rest of the country that has a lot of regional different peculiarities. Third, we assume that TG/HDL quotient reflects insulin resistance, but we do not measure it directly. It is known that the index does not reflect insulin resistance at least in obese women of African descent[29], although indeed indicate that metabolic state in Mexicans[28].

Conclusions

Mexican population, a truly genetic "melting pot" but with a dominant Amerindian ancestry, has a genomic composition prone to obesity, diabetes, hypertriglyceridemia and hypoalphalipoproteinemia. In addition, a cluster of nutritional and lifestyle modifications has yielded to a very fast epidemiological transition, with a skyrocketing increase of cardiometabolic diseases, to the point that nowadays, diabetes, ischemic heart disease and stroke are the leading causes of general mortality in our population.

Our data show that the majority of normal-weight subjects had already a subtle metabolic abnormality, just waiting for the bursting of the full-blown hemodynamic and metabolic shamble of the overweighed or obese dysmetabolism. The usefulness and low-cost of the TG/HDL quotient allows singling out those individuals with insulin resistance and upraised cardiometabolic risk, in order to implement the therapeutic and preventive measures.

A sustained and well-funded nation-wide campaign with the decisive support of the medical community and the entire society, against malnourishment and obesity is now mandatory in order to reduce drastically, in a relatively short period of time, the magnitude of the O/O epidemic and all its catastrophic consequences.

Conflict of interest statement

All authors declare no actual or potential conflict of interest

Acknowledgements

GFS, GGS, EM, and GC conceived the general study, performed statistical analysis and wrote, revised and approved the submitted version. VS, AM, LSR, UN, LA, and IOC participated in the collection, data gathering, construction of data bases, analysis and writing of the base-studies herein merged (i.e., Prit & Lindavista).

This work was supported by Conacyt (# 129889) and IPN grants to GC and EM.

References

1. Sánchez-Castillo CP, Velázquez-Monroy O, Lara-Esqueda A, Berber A, Sepúlveda J, Tapia-Conyer R, et al. Diabetes and hypertension increases in a society with abdominal obesity: results of the Mexican National Health Survey 2000. *Pub Health Nutr* 2004;8:53-60.
2. Rivera JA, Barquera S, Campirano F, Campos I, Safdie M, Tovar V. Epidemiological and nutritional transition in México: Rapid increase of non-communicable chronic diseases and obesity. *Pub Health Nutr* 2002;5:113-122.
3. Stern MP, Gonzalez C, Mitchell BD, Villalpando E, Haffner SM, Hazuda HP, et al. Genetic and environmental determinants of type II diabetes in Mexico City and San Antonio. *Diabetes* 1992;14:484-492.
4. Wildman RP, Muntner P, Reynolds K, McGinn AP, Rajpathak S, Wylie-Rosett J, et al. The obese without cardiometabolic risk factor clustering and the normal weight with cardiome-

tabolic risk factor clustering: prevalence and correlates of 2 phenotypes among the US population (NHANES 1999-2004). *Arch Intern Med* 2008;168:1617-1624.
5. Pajunen P, Kotronen A, Korpi-Hyövälti E, Keinänen-Kiukaaniemi S, Oksa H, Niskanen L, et al. Metabolically healthy and unhealthy obesity phenotypes in the general population: the FIN-D2D Survey. *BMC Pub Health* 2011, 11:754.
6. Gutiérrez JP, Rivera-Dommarco J, Shamah-Levy T, Villalpando-Hernández S, Franco A, Cuevas-Nasu L, et al. Encuesta Nacional de Salud y Nutrición 2012. Resultados Nacionales. Cuernavaca, México: Instituto Nacional de Salud Pública (MX), 2012.
7. Fanghänel-Salmón G, Padilla-Retana J, Sánchez-Reyes L, Torres-Acosta EM, Cortinas-López L, Espinosa-Campos J. Prevalence of coronary artery disease risk factors in workers at the General Hospital of Mexico of the ministry of health. *Endocrine Practice* 1997;3:313-319.
8. Meaney A, Ceballos-Reyes G, Gutiérrez-Salmean G, Samaniego-Méndez V, Vela-Huerta A, Alcocer L et al. Cardiovascular risk factors in a Mexican middle-class urban population. The Lindavista Study. Baseline data. *Arch Cardiol Mex* 2013;83:249-256.
9. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972;18:499-502.
10. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *J Am Med Assoc*. 2003;289:2560-2572.
11. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III) *JAMA*. 2001;285:2486–2497.
12. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2012;35:S64-S71.
13. World Health Organization (2006). BMI Classification. Global Database on Body Mass Index. [WWW document]. URL: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html
14. Sanchez-Castillo CP, Velazquez-Monroy O, Berber A, Lara-Esqueda A, Tapia-Conyer R, James WPT, et al. Anthropometric cutoff points for predicting chronic diseases in the Mexican National Health Survey 2000. *Obes Res*. 2003;11:442-451.
15. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120:1640-1645.
16. D'Agostino RB Sr, Grundy S, Sullivan LM, Wilson P. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. *JAMA* 2001;286:180-187.
17. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D´Agostino RB Sr, Gibbons R, et al. (2013). ACC/AHA Guidelines on the Assessment of Cardiovascular Risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. [WWW document]. URL: http://circ.ahajournals.org
18. Real JT, Chaves FJ, Martínez-Usó I, García-García AB, Ascaso JF, Carmena R. Importance of HDL cholesterol levels and the total/HDL cholesterol ratio as a risk factor for coronary heart disease in molecularly defined heterozygous familial hypercholesterolaemia. *Eur Heart J* 2001;22:465-471.
19. Castelli WP, Garrison RJ, Wilson PWF, Abbott RD, Kalousdian S, Kannel WB et al. Incidence of coronary heart disease and lipoprotein cholesterol levels. The Framingham Study. *JAMA* 1986;256:2835-2838.
20. Gaziano JM1, Hennekens CH, O'Donnell CJ, Breslow JL, Buring JE. Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction. *Circulation* 1997;96:2520-2525.
21. Jeppesen J, Facchini FS, Reaven GM. Individuals with high total cholesterol/HDL cholesterol ratios are insulin resistant. *J Intern Med* 1998;243:293-298
22. SIGMA Type 2 Diabetes Consortium, Williams AL, Jacobs SBR, Moreno-García H, Huerta-Chagoya A, Churchhouse C, Márquez-Luna C, et al. Sequence variants in SLC16A11 are a common risk factor for type 2 diabetes in Mexico. *Nature* 2013; 506:98-100.
23. Conus F, Rabasa-Lhoret R, Peronnet F: Characteristics of metabolically obese normal-weight (MONW) subjects. *Appl Physiol Nutr Metab* 2007;32:4–12.
24. Wildman RP, Muntner P, Reynolds K, McGinn AP, Rajpathak S, Wylie-Rosett J, et al. The obese without cardiometabolic risk factor clustering and the normal weight with cardiometabolic risk factor clustering: prevalence and correlates of 2 phenotypes among the US population (NHANES 1999–2004). *Arch Intern Med* 2008;168:1617–1624.
25. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: A systematic review and meta-analysis. *Ann Intern Med*. 2013;159:758-769.
26. He S1, Wang S, Chen X, Jiang L, Peng Y, Li L, Wan L, Cui K. Higher ratio of triglyceride to high-density lipoprotein cholesterol may predispose to diabetes mellitus: 15-year prospective study in a general population. *Metabolism* 2012;61:30-36.
27. Bittner V, Johnson D, Zineh I, Rogers WJ, Vido D, Marroquin OC, et al. The TG/HDL cholesterol ratio predicts all cause mortality in women with suspected myocardial ischemia. A report from the Women's Ischemia Syndrome Evaluation (WISE). *Am Heart J* 2009;157: 548–555.
28. Murguía-Romero M, Jiménez-Flores JR, Sigrist-Flores SC, Espinoza-Camacho MA, Jiménez-Morales M, Piña E, et al. Plasma triglyceride/HDL-cholesterol ratio, insulin resistance, and cardiometabolic risk in young adults. *J Lipid Res* 2013;54:2795-2799.
29. Knight MG, Goedecke JH, Ricks M, Evans J, Levitt NS, Tulloch-Reid MK, et al. The TG/HDL-C ratio does not predict insulin resistance in overweight women of African descent: a study of South African, African American and West African women.Ethn Dis 2011;21(4):490-4.