HYPERTRIGLYCERIDEMIC-WAIST (HTGW) PHENOTYPE IN UNIVERSITY STUDENTS FROM TWO REGIONS OF MÉXICO

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ABSTRACT

Introduction*: The obesity and lipids disorders have reached epidemic proportions and are highly associated with cardiovascular disease. Hypertriglyceridemic-Waist (HTGW) index is an easy and inexpensive method to evaluate cardiovascular and type 2 diabetes risks in early way.*

Purpose*: We analyzed the prevalence and associated factors for HTGW in university (freshmen) students from two distant mexican cities.*

Methods*: The study was a cross-sectional analysis of a random sample of 13,669 subjects (17-25 years old). Blood samples were withdrawn for biochemical indicators, and blood pressure (BP) was measured. HTGW phenotype (WC) was diagnosed using anthropometric criteria for Latin American population (waist circumference, WC: for men, >90 cm; for women, >80 cm), and fasting plasma triglycerides (TG) >150 mg/dl. Bivariate analyses according to HTGW phenotype were performed by city and sex. Results. Besides of WC and TG the fasting glucose, total cholesterol and blood pressure were higher (p<0.01) in HTGW phenotype individuals in both genders. In subjects with HTGW phenotype the MetS prevalence were higher in students from México City than in those from Ciudad Juárez (p<0.01; odds ratio, 1.2-2.0).*

Conclusion*: HTGW increases the risk for several MetS and cardiovascular diseases factors in youth from these two México's regions.*

Key words*: Hypertriglyceridemic-waist phenotype, adolescents, young adults, cardiometabolic risk, abdominal obesity.*

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Introduction

Obesity (BMI≥30 kg/m2) has reached epidemic proportions in low-to-high income countries, and it is associated with several risk factors for cardiovascular disease (CVD), metabolic syndrome (MetS) and type 2 diabetes (T2DM)[1,2]. Mexico ranks second in prevalence of obesity worldwide[2] and according to the 2012 Mexican National Survey on Health and Nutrition[3], seven out of ten mexicans >20 y are overweight (BMI 25.0-29.9 kg/m2, 38.8%) or obese (32.4%) and 74% hold a morbid waist circumference (WC; (>80/>90 cm women/men), the latter considered a marker of central or visceral obesity[4,5]. Also, total body fat is related to preclinical conditions such as MetS and insulin resistance (IR) but WC is independently associated to CVD and T2DM[5]. That is why public health agencies in many countries are focusing their efforts on the early diagnosis of these chronic conditions and their biochemical and physiological markers.

From a molecular stand point, visceral adipose tissue (VAT) has an important lipolytic and proinflammatory capacity that lead to MetS. VAT releases substantial amounts o fatty acids that are captured and sterified by the liver, producing triacylglycerides (TG)-rich lipoproteins (i.e. LDL), increasing the risk for dyslipidemia, hyperglycemia, IR, and hypertension (MetS' tetrad) and cardiometabolic abnormalities[6-8]. From a clinical stand point, several indexes have been proposed for the

early diagnosis of MetS, among which BMI, WC, waist/hip ratio (WHR) and waist/height ratio (WHtR) are the most reported[4,9]. About this, BMI has been widely used to describe changes on the prevalence of obesity at a population level, but it is not valid parameter to represent obesity in all individuals[10]. Also, BMI shows poor linear correlation with intra-abdominal fat (visceral+subcutaneous) as compared to WC[1,4,11]. Nevertheless, BMI and WC are more accurate than measured body fat (BF%) by DEXA for classifying subjects with metabolic risk factors[12], being WC a better predictor for CVD, T2DM and inflammatory diseases than BMI or WHR[13,14]. WC highly correlates with visceral fat[15], but this relationship may vary when evaluating different ethnic groups[16], i.e. WC for the same BMI has increased overtime in Mexicans as a consequence of lifestyle changes[15].

In order to discriminate subcutaneous from visceral obesity, which is a better predictor for CVD, MetS and T2DM, two alternate indexes have been proposed. The first of them is the Visceral Adiposity Index (VAI), this is an empirical mathematical model, based on anthropometric (BMI and WC) and biochemical (TG and high-density lipoprotein cholesterol, HDL-C) measurements, to indicate the distribution and function of fat[17]. However, today there are still no long-term prospective studies to support the prospective power of VAI regarding cardiovascular risk. The second is based on concurrent fasting hypertriglyceridemia (HTG+; >150 mg/dl) and an increased WC (W+) known as the hypertriglyceridemic-waist (HTGW) phenotype[7,14,18-20], HTGW individuals, as compared to healthy controls, are at higher risk for CVD characterized by a deteriorated cardiometabolic risk profile: higher blood pressure and levels of apolipoprotein B and C-reactive protein but lower levels of HDL-C and apolipoprotein A-I. HTGW is also associated to a lower insulin sensitivity, prediabetes and T2DM among adults >20 y[21], and chronic kidney disease in subjects ≥40 y[22]. Both, VAI and HTGW strongly correlate with each other and with the risk for T2DM in chinese adults ≥18 y[23].

The aim of this study was to investigate the association between HTGW phenotype with other cardiometabolic and anthropometric risk factors for MetS, in two cohorts of university (freshmen) students from two regions of Mexico. To our knowledge, the prevalence of HTGW phenotype among mexican youth has not been reported to date.

Methods

Participants and survey

This cross-sectional study reports on the abdominal fat patterning and cardiometabolic profile of 13,669 (57% women, 17-25 y) freshmen university students from central (n=5,525, Mexico, City; 19°25′42″ N, 99°07′39″ W) and northern (n=8,144; Ciudad Juarez, Chihuahua; 31°43′59″ N, 106°28′59″ W) Mexico. Both cohorts were recruited from two university health studies: Healthy university (Medical Services from the Universidad Autónoma de Ciudad Juárez (UACJ)) and the Multidisciplinary Group to Investigate Health and Academic Performance (GMISARA, Universidad Nacional Autónoma de México (UNAM)). Before the study, none of the students reported any illness and no metabolic disorders were diagnosed by a physician. Study protocols met the standards of the Helsinki Declaration and were approved by institutional ethics committees. All participants gave written informed consent. Data was collected from 2006 to 2012 surveys. In both studies, perfectly trained personnel (Physicians, biochemists and anthropometrists) conducted the interviews to assure reliable demographic, socioeconomic, dietary, and health related data.

Biochemistry

Healthy University Medical Services (UACJ) and Grupo Diagnóstico Médico PROA, S.A. de C.V. (UNAM), internationally accredited laboratories, were responsible for sample collection, biochemical analysis and laboratory data handling. Students came to laboratory facilities, either UACJ or UNAM, between 7-10 AM after overnight fasting. Plasma glucose, TG and cholesterol were assayed by automatized enzymatic-colorimetric methods.

Blood pressure and anthropometry

Anthropometric data were obtained as previously described[20], following the Official Mexican Norm (NOM-008-SSA3-2010, Mexican Ministry of Health). In brief, diastolic and systolic blood pressure (BP) values were obtained after replicated measurements, i.e., after resting quietly in a sitting position for 5 min and determination of the maximum inflation level, then BP readings were obtained with a standard aneroid sphygmomanometer (Model DS44, WelchAllyn). Height and WC were recorded to the nearest 0.1 cm using a wall

stadiometer (Seca mod. 208, México City), and a metallic flexible anthropotape (Rosscraft, USA). Body weight was recorded to the nearest 0.1 kg using a digital scale (Seca 700).

Metabolic disorders & HTGW classification

Students were classified as having metabolic disorders if they had altered values in any one of the five parameters that define MetS: WC+ (>80 cm for women, >90 cm for men), HDL-C (<50 mg/dl for women, <40 mg/dl for men), TG+ (>150 mg/dl), glucose (>100 mg/dl), and blood pressure (>130/85 mmHg), or healthy if they showed none of them (6, 24). Also, students were classified as bearing the HTGW+ phenotype when both, WC and TG were higher than their threshold values[6,8]. In this work we excluded HDL-C values due to methodological difficulties.

Statistical analysis

All values were expressed as mean ± S.D. and percentage (%). Averages of MetS risk factors were compared between healthy (HTGW-) and not healthy (HTGW+) subjects and between universities, using two-way ANOVA and Sidak's multiple comparisons test. Also, differences on the prevalence (%) for MetS risk factors and HTGW phenotype between universities were determined by Chi-square and Fisher´s exact tests. To determine associations between anthropometric and biochemical variables Pearson correlation analysis was performed. To determine independence of variables on presence of HTGW and MetS logistic linear regression analysis was performed, $p<0.05$ was considered statistically significant.

Results

Tables 1 and 2 show the demographic, anthropometric and clinical characteristics of subjects, by HTGW status (healthy (HTGW-), high TG and high WC (HTGW+)) and university. All the MetS measured variables were higher ($p<0.01$) in HTGW+ vs healthy individuals in both genders (Tables 1 and 2). BMI and SBP were higher in UACJ women with HTGW+ vs healthy, DBP was higher in UNAM men (Tables 1 and 2).

It is worth to mention that prevalence of HTGW phenotype, WC, FG and TG was higher in UNAM than in UACJ students ($p<0.01$; OR, 1.06-2.13); otherwise, the prevalence of overweight and obesity (Ow/Ob, BMI≥ 25 kg/m2) and SBP was lower in UNAM than in UACJ students ($p<0.05$; OR, 0.91-0.95) (Table 3).

	UACJ		UNAM	
	HTGW -	HTGW +	HTGW -	HTGW +
n (%)	3800 (94.6)	219 (5.4)	3313 (87.8)	460 (12.2)
Age (years)	19.9 ± 3.6	23.1 ± 7.3 [a]	19.43 ± 3.0 [b]	20.8 ± 5.5 [a,b]
Weight (kg)	60.4 ± 13.2	80.7 ± 15.0 [a]	58.4 ± 10.9 [b]	70.5 ± 12.4 [a,b]
Height (cm)	159.8 ± 6.9	160.4 ± 6.1 [a]	157.4 ± 6.0 [b]	158.0 ± 6.2 [a,b]
BMI (kg/m^c)	23.6 ± 4.8	31.3 ± 5.1 [a]	23.5 ± 4.0	28.2 ± 4.3 [a,b]
Waist circumference (cm)	73.7 ± 10.8	92.5 ± 10.1 [a]	79.1 ± 9.9 [b]	91.5 ± 9.5 [a]
Glucose (mg/dL)	83.4 ± 13.6	94.0 ± 28.3 [a]	88.2 ± 7.8 [b]	93.1 ± 19.7 [a]
Total Cholesterol (mg/dL)	157.1 ± 30.7	188.1 ± 37.1 [a]	163.6 ± 28.6 [b]	192.1 ± 32.2 [a]
Triacylglycerides (mg/dL)	80.0 ± 37.1	204.1 ± 56.1 [a]	97.1 ± 34.4 [b]	206.3 ± 62.3 [a]
Systolic pressure (mmHg)	109.3 ± 12.0	113.6 ± 11.7 [a]	104.0 ± 11.1 [b]	111.0 ± 11.3 [a,b]
Diastolic pressure (mmHg)	71.2 ± 9.1	74.2 ± 10.8 [a]	70.2 ± 8.5	75.5 ± 9.8 [a]

Averages ± S.D. of MetS related parameters according to the presence/absence of HTGW phenotype, and demographic data in two regions of Mexico. Analyzed parameters showed statistical significance ($p<0.01$). [a] difference between HTGW phenotype, [b] difference between universities.

Table 1: Demographic, anthropometric and clinical characteristics of participants-Women.

	UACJ		UNAM	
	HTGW -	HTGW +	HTGW -	HTGW +
n (%)	3696 (89.6)	429 (10.4)	1536 (87.7)	216 (12.3)
Age (years)	20.6 ± 3.8	23.5 ± 6.1 [a]	19.8 ± 3.0 [b]	20.7 ± 3.8 [a,b]
Weight (kg)	71.2 ± 13.9	94.2 ± 14.8 [a]	68.2 ± 12.1 [b]	89.9 ± 13.4 [a,b]
Height (cm)	172.6 ± 6.5	173.6 ± 6.5 [a]	169.5 ± 6.3 [b]	171.6 ± 6.3 [a,b]
BMI (kg/m^c)	23.9 ± 4.3	31.2 ± 4.3 [a]	23.7 ± 3.7	30.5 ± 3.9 [a]
Waist circumference (cm)	80.7 ± 10.9	101.0 ± 9.9	82.2 ± 9.9 [b]	101.4 ± 9.6 [a]
Glucose (mg/dL)	87.1 ± 14.7	94.4 ± 19.8 [a]	90.3 ± 9.5 [b]	95.4 ± 16.8 [a]
Total Cholesterol (mg/dL)	156.7 ± 34.6	194.8 ± 37.3 [a]	162.1 ± 28.3	193.3 ± 36.9 [a]
Triacylglycerides (mg/dL)	96.9 ± 55.3	237.5 ± 85.7 [a]	107.7 ± 47.2	229.7 ± 71.5 [a]
Systolic pressure (mmHg)	115.2 ± 12.0	120.3 ± 12.7 [a]	113.4 ± 11.7	120.9 ± 11.1 [a]
Diastolic pressure (mmHg)	74.9 ± 9.1	77.5 ± 9.5 [a]	76.1 ± 8.7	81.4 ± 9.0 [a]

Averages ± S.D. of MetS related parameters according to the presence/absence of HTGW phenotype, and demographic data in two regions of Mexico. Analyzed parameters showed statistical significance ($p<0.01$). [a] difference between HTGW phenotype, [b] difference between universities.

Table 2: Demographic, anthropometric and clinical characteristics of participants-Men.

	UACJ		UNAM	
	HTGW -	HTGW +	HTGW -	HTGW +
n (%)	3696 (89.6)	429 (10.4)	1536 (87.7)	216 (12.3)
Age (years)	20.6 ± 3.8	23.5 ± 6.1 [a]	19.8 ± 3.0 [b]	20.7 ± 3.8 [a,b]
Weight (kg)	71.2 ± 13.9	94.2 ± 14.8 [a]	68.2 ± 12.1 [b]	89.9 ± 13.4 [a,b]
Height (cm)	172.6 ± 6.5	173.6 ± 6.5 [a]	169.5 ± 6.3 [b]	171.6 ± 6.3 [a,b]
BMI (kg/m^c)	23.9 ± 4.3	31.2 ± 4.3 [a]	23.7 ± 3.7	30.5 ± 3.9 [a]
Waist circumference (cm)	80.7 ± 10.9	101.0 ± 9.9	82.2 ± 9.9 [b]	101.4 ± 9.6 [a]
Glucose (mg/dL)	87.1 ± 14.7	94.4 ± 19.8 [a]	90.3 ± 9.5 [b]	95.4 ± 16.8 [a]
Total Cholesterol (mg/dL)	156.7 ± 34.6	194.8 ± 37.3 [a]	162.1 ± 28.3	193.3 ± 36.9 [a]
Triacylglycerides (mg/dL)	96.9 ± 55.3	237.5 ± 85.7 [a]	107.7 ± 47.2	229.7 ± 71.5 [a]
Systolic pressure (mmHg)	115.2 ± 12.0	120.3 ± 12.7 [a]	113.4 ± 11.7	120.9 ± 11.1 [a]
Diastolic pressure (mmHg)	74.9 ± 9.1	77.5 ± 9.5 [a]	76.1 ± 8.7	81.4 ± 9.0 [a]

Averages ± S.D. of MetS related parameters according to the presence/absence of HTGW phenotype, and demographic data in two regions of Mexico. Analyzed parameters showed statistical significance ($p<0.01$). [a] difference between HTGW phenotype, [b] difference between universities.

Table 3: Prevalence of hypertriglyceridemic-waist phenotype (HTGW+) and metabolic syndrome features among participants.

In this regard, when these variables were analyzed in HTGW+ subjects, the prevalence of all of them were higher in UNAM vs UACJ students (Figure 1), except in TC and SBP.

The logistic regression analysis did not identify any variable that was associated independently with the presence of MetS or HTGW. Furthermore, the correlations among anthropometric and biochemical variables were low (R=0.16-0.40, p<0.01), being the highest between WC and TG (R=0.40, p<0.01).

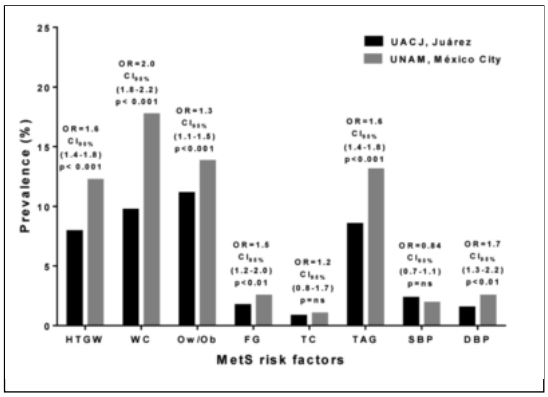

Fig. 1: Prevalence (%) of individuals with MetS risk factors. Students from both UACJ and UNAM universities were evaluated for the presence of metabolic syndrome risk factors, and for the Hypertriglyceridemic-Waist (HTGW) phenotype. WC: waist circumference; Ow/Ob: over-weight/obesity; FG: fasting glucose; TC: total cholesterol; TG: triacylglycerides; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Discussion

According to the WHO's global burden of disease, cardiovascular diseases have been raising and are the dominant diseases globally during the last decades, along with the increased contribution of obesity and the nutrition related risk factors to this burden[25]. The obesity causes lipid disorders and both are directly related to cardiovascular disease and DM2[26-28]. The most recent estimate regarding obesity averages 18% in adults of the OCDE countries; however, in México, New Zealand and the US it occurs in more than 30%, principally among low income people[2,3,29,30].The most reports examining obesity with cardiovascular risk factors are frequently based on data from high-income countries[7,8,29,30]; however more recently, studies on a variety of ethnicities have been published[18,19,21,31].

Some authors proposed that the HTGW phenotype is an alternative and inexpensive surrogate for detecting subjects at risk to develop the MetS; it is a very simple and reliable index of cardiometabolic risks associated with abdominal or central obesity, which predicts with very high probability that men may have the simultaneous presence of some cardiometabolic risk markers, such as dyslipidemia, high blood pressure, high BMI, and WC[7,8,18,19]. It is also known that the HTGW phenotype could be helpful in assessing the risk of atherosclerosis, coronary artery disease and DM2[8,18,20]. In the subjects studied here, are precisely WC and TG that best correlate with each other (R = 0.40); although low proportion of variance (R2 = 0.16), together provide the greatest amount of information in the presence of MetS.

Our data show that adolescents and young adults (17-25 years of age) with the HTGW phenotype also shown increased values for weight, BMI, glycemia, total cholesterol, triacylglycerides and blood pressure, compared to those without the HTGW, this means that HTGW is a surrogate of MetS in this population. These data agree with other reports where the studied population is middle-aged, and in some cases there are already diabetics[18,32]; in other words, we are detecting those alterations at an earlier age and probably at an earlier step, then we might have the opportunity to intervene in the young people using the HTGW index.

The most striking difference between students from both universities is that except to Ow/Ob and BP the prevalence of MetS syndrome and HTGW phenotype are higher in students from México City. We do not know why these prevalence are higher in the capital city, especially in WC (2.13 fold higher), but these epidemiological data along with the clinical characteristics of individuals with HTGW support the higher frequency of cardiovascular risk factors in young people from capital city of Mexico. However, several explanations might shade light for these findings: in the early 1990's many assembly plants were built in the border between México and the US in order to deal with a free trade agreement of North America (Canada, USA and México), which mobilized people from several states of the country to work in there, so there is more diversity in the population compared to México City; another fact is that Ciudad Juárez, among other cities in the north, is a city to cross towards US by Mexican and Central America illegal immigrants, which in many cases they stay, get married and have children who grow and get into the UACJ. It is also possible that difference in altitude, i.e., 2240 meters above sea level in México City vs 1100 meters in Ciudad Juárez, along with the contents and the servings

size in meals, being higher in México City, could account for the observed differences. It would be interesting to evaluate the HTGW phenotype in other regions of the country, where more indigenous heritage is present in the populations. Our results show that the hypertriglyceridemic-waist phenotype was associated with an increased risk for several MetS and CVD factors in youth from these two Mexican regions, which makes necessary to evaluate other epidemiological aspects of HTGW for potential intervention.

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