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Genetic and environmental determinants of the susceptibility of Amerindian derived populations for having hypertriglyceridemia



Carlos A. Aguilar-Salinas^{a,*}, Teresa Tusie-Luna^b, Päivi Pajukanta^{c,d}

^a Department of Endocrinology and Metabolism, Instituto Nacional de Ciencias Médicas y Nutrición, México City, México

^b Unit of Molecular Biology and Genomic Medicine, Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México and Instituto Nacional de Ciencias Médicas y Nutrición, México City, México

^c Department of Human Genetics, David Geffen School of Medicine at UCLA, Los Angeles, USA

^d Molecular Biology Institute at UCLA, Los Angeles, USA

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ABSTRACT

Here, we discuss potential explanations for the higher prevalence of hypertriglyceridemia in populations with an Amerindian background. Although environmental factors are the triggers, the search for the ethnic related factors that explain the increased susceptibility of the Amerindians is a promising area for research. The study of the genetics of hypertriglyceridemia in Hispanic populations faces several challenges. Ethnicity could be a major confounding variable to prove genetic associations. Despite that, the study of hypertriglyceridemia in Hispanics has resulted in significant contributions. Two GWAS reports have exclusively included Mexican mestizos. Fifty percent of the associations reported in Caucasians could be generalized to the Mexicans, but in many cases the Mexican lead SNP was different than that reported in Europeans. Both reports included new associations with apo B or triglycerides concentrations. The frequency of susceptibility alleles in Mexicans is higher than that found in Europeans for several of the genes with the greatest effect on triglycerides levels. An example is the SNP rs964184 in APOA5. The same trend was observed for ANGPTL3 and TIMD4 variants. In summary, we postulate that the study of the genetic determinants of hypertriglyceridemia in Amerindian populations which have major changes in their lifestyle, may prove to be a great resource to identify new genes and pathways associated with hypertriglyceridemia.

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Abbreviations: ABCA1, ATP binding cassette protein A1; Apo B, Apolipoprotein B; BMI, Body mass index; ChREBP, Carbohydrate response element binding protein; FADS3, Type 3 fatty acid desaturase; FCHL, Familial combined hyperlipidemia; FHTG, Familial hypertriglyceridemia; GWAS, Genome wide association study; HDL-C, High density lipoprotein cholesterol; MLXIPL, Max-like protein X Interacting protein like; MODY, Maturity onset diabetes of the young; NHANES, National Health and Nutrition Examination Survey; USF1, Upstream transcription factor 1.

* Corresponding author at: Instituto Nacional de Ciencias Médicas y Nutrición, Departamento de Endocrinología y Metabolismo, Vasco de Quiroga 15, Col. Sector XVI, Tlalpan, Mexico City 14000, Mexico. Tel.: +52 55 56554523; fax: +52 55 55130002.

E-mail addresses: caguilarosalinas@yahoo.com (C.A. Aguilar-Salinas), mttusie@gmail.com (T. Tusie-Luna), ppajukanta@mednet.ucla.edu (P. Pajukanta).

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1. Introduction

The study of ethnic groups with an increased risk for having a disease has been a successful strategy to generate new knowledge [1]. The greater susceptibility of the Hispanics for having hypertriglyceridemia is a well-documented phenomenon [2], but, it has been subject of only a small set of studies. Hispanics is an admixed population [3]. A large percentage of the Hispanics living in the US or in Latin America have their origins in the Amerindian groups, the first residents of the continent. The Amerindians have suffered infections, wars and famine that have reshaped several times their environment, lifestyle and the size of the population [4]. As a consequence, it is likely that selection processes have occurred in this ethnic group. Hispanics have been poorly represented in genetic studies; for example, it is the only ethnic group not included in the lipid GWAS reports. The inclusion of individuals with other ethnic backgrounds may narrow the large loci in which associations have been detected. Furthermore, this approach increases the likelihood to detect rare variants with major effects. In this review, we discuss several approaches to identify potential explanations for the higher prevalence of hypertriglyceridemia in populations with an Amerindian background. By this mean, a better comprehension of the pathogenesis of hypertriglyceridemia may be achieved.

2. Epidemiology of hypertriglyceridemia: Focus in Hispanics

Hypertriglyceridemia is a common lipid disorder (Table 1). In the NHANES 1999–2004 survey (n = 5610 adults) almost a third of the participants (33.1% ± 0.8%) had a value above 150 mg/dl [5]. As a result, more than 63.4 million Americans had hypertriglyceridemia. Triglycerides concentrations greater than 500 mg/dl are usually caused by genetic causes and are associated with an increased risk for having pancreatitis. This abnormality was estimated to occur in close to 3.4 million Americans [6]. The prevalence of hypertriglyceridemia was proportional to the age and it is greater in men (36.7% vs 29.6%, p < 0.001). Smoking, scant physical activity, diabetes and a body mass index greater than 25 kg/m² were conditions more commonly seen in hypertriglyceridemic individuals compared against the rest of the population.

Hispanics are the ethnic group in the US with the highest prevalence of hypertriglyceridemia (40.4% for men and 34.9% for women). This abnormality is less common in Caucasians (39% for men and 31.6% for women) and in African Americans (19.5% for men and 13.6% for women). Moderate (200– < 500 mg/dl) and severe (500–2000 mg/dl) forms of hypertriglyceridemia were also more frequent in Hispanics; 19% fall in any of these two categories [2,5,7]. Contrary to that observed in Caucasian males, the mean triglycerides did not

Table 1 – Mean plasma lipid concentration in adults in Amerindian-derived populations and its comparison against other ethnic groups.

NHANES ^a	LDL cholesterol			HDL cholesterol			Triglycerides		
	1988–1994	1999–2002	2007–2010	1988–1994	1999–2002	2007–2010	1988–1994	1999–2002	2007–2010
<i>Mexican Americans</i>									
Total	125	121	118*	48.7	48.9	49.4	134	139	127
Men	127	125	120*	45.2	45.0	45.4	136	142	136
Women	123	117	115*	52.3	52.9	53.7	132	135	117*
<i>Caucasians</i>									
Total	129	124	116*	50.4	51.2	52.5*	120	125	111*
Men	132	126	115*	44.8	45.5	46.7*	130	134	119*
Women	126	121	116*	55.7	56.6	58.1*	112	117	104*
<i>Afro-Americans</i>									
Total	128	121	115*	55.2	54.5	56.1	93	94	88
Men	129	121	116*	52.4	51.0	52.6	100	99	94
Women	127	121	114*	57.3	57.3	58.7	88	90	83
<i>Mexican Health Surveys</i>									
Total	1994 ^b	2000 ^c	2006 ^d	1994 ^b	2000 ^c	2006 ^d	1994 ^b	2000 ^c	2006 ^d
Total	106.4	130.1	131.5	34.2	38.4	38.9	133.0	181.7	139.6
Men	110.2	125.0	128.1	34.2	38.6	37.1	151.0	162.9	148.9
Women	106.0	120.8	136.1	38.0	38.1	40.1	124.6	199.5	131.5

Data are expressed as mg/dl. * p < 0.05 between the 1988–2004 and the 2007–2010 surveys.

Modified from:

^a Carroll M, Kit B, Lacher D, Shero S, Mussolino M. Trends in serum lipids and lipoproteins in US adults, 1988–2010. *JAMA*. 2012;308:1545–1554

^b Aguilar-Salinas Carlos A, Olaiz G, Valles V, Ríos JM, Gómez Pérez FJ, Rull JA, Rojas R, Franco A, Sepúlveda J. High prevalence of low HDL cholesterol concentrations and mixed hyperlipidemia in a Mexican nationwide survey. *J Lipid Research* 2001;42:1298–307.

^c Barquera S, Flores M, Olaiz-Fernández G, Monterrubio E, Villalpando S, González C, Rivera J, Sepúlveda J. Dyslipidemias and obesity in Mexico. *Salud Publica Mex* 2007;49 suppl 3:S338–S347.

^d Aguilar-Salinas CA, Gómez Pérez FJ, Rull JA, Villalpando S, Barquera S, Rojas R. Prevalence of dyslipidemias in the 2006 Encuesta Nacional de Salud y Nutrición. 2009 *Salud Pública Méx*. 2010;52 (supl1) S44–S53.

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