



Nonalcoholic Fatty Liver Disease Risk Factors in Latin American Populations: Current Scenario and Perspectives

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Nonalcoholic fatty liver disease (NAFLD) is currently the most common liver disease worldwide with an estimated global prevalence rate of 24% to 25%.¹ NAFLD burden is already significant, but due to the continuously growing rates of adult obesity and type 2 diabetes mellitus (T2DM) and population aging trends, NAFLD-related liver disease and mortality will likely increase throughout the world over the next decades.²

NAFLD is highly prevalent on all continents, but regional differences have been noted, with South America (31%) and the Middle East (32%) having the highest rates of disease and Africa exhibiting the lowest prevalence (14%).¹ In this review, we examine the existing evidence regarding

potential regional and/or racial peculiarities of NAFLD in Latin America.

IS NAFLD MORE COMMON OR MORE SEVERE IN LATIN AMERICA?

Current NAFLD prevalence estimates for Latin America are imperfect because primary data from most of the countries in this region are lacking. Available studies reporting prevalence data are from Brazil (35.2%), Chile (23%), Mexico (17%), and Colombia (26.6%) (see Younossi et al.¹ and references therein). Notably, these studies were performed more than a decade ago;

Abbreviations: NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; PNPLA, patatin-like phospholipase domain-containing protein; T2DM, type 2 diabetes mellitus; WHO, World Health Organization.

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therefore, it is likely that NAFLD prevalence is currently higher. Other indirect estimates of NAFLD prevalence in Latin America also indicate that countries of this region have indeed a high NAFLD prevalence, although the scenario is heterogeneous.³

Additional data suggesting that Latino Americans might be disproportionately affected by NAFLD have been generated in the United States. In those studies, Hispanic subjects consistently have the highest NAFLD prevalence.^{4,5} It is important to stress that the use of the ethnonyms “Hispanic” and “Latino” is not consistent in the literature. Although these two terms are often used interchangeably, “Hispanic” refers only to persons of Spanish-speaking country of origin or ancestry, whereas “Latino” is more frequently used to refer generally to anyone of Latin American origin or ancestry. Notably, Kallwitz et al.⁶ showed that NAFLD is not equally present in Hispanic/Latino subgroups, with individuals from Central American, South American, or Mexican heritage being more affected than subjects with Cuban, Puerto Rican, and Dominican backgrounds. Other studies have confirmed that NAFLD is more prevalent among Hispanic individuals, which in these studies mainly comprise Mexican Americans (reviewed by Lim and Bernstein⁵).

The severity of NAFLD also may be greater in people from Latin American origin, but no primary data regarding this are available. In a recent systematic review and meta-analysis, Rich et al.⁷ found that the risk for nonalcoholic steatohepatitis (NASH) was greater in Hispanics living in the United States, although fibrosis did not differ among the ethnic groups studied. To date, the paucity of data does not allow reaching firm conclusions regarding the severity of NAFLD in individuals of Latin American origin.

FACTORS RESPONSIBLE FOR THE HIGHER PREVALENCE OF NAFLD IN LATIN AMERICA

The increased prevalence of NAFLD in Latino Americans is likely related to genetic as well as environmental factors such as diet, exercise, and alcohol consumption. Other factors, such as the prevalence of metabolic syndrome and T2DM and access to health care, may also be at play.

Among genetic factors, several genes have been identified with be associated with NAFLD. The common

patatin-like phospholipase domain-containing protein (PNPLA) 3 nonsynonymous gene variant (rs738409 c.444 C>G p.I148M) is the most studied genetic polymorphism shown to be robustly associated with susceptibility to steatosis, steatohepatitis, and fibrosis in patients with NAFLD.⁸ Interestingly, this gene variant is twice as common in Hispanics compared with African Americans (40% versus 19%). Some data from Latin America show a high prevalence of p.I148M in the general population and even higher prevalence in individuals with Native American ancestry. A preliminary study from Chile reported an allelic frequency of the high-risk allele G of 59% in the general population,⁹ whereas in Argentina, Pontoriero et al.¹⁰ reported in a study involving 258 healthy unrelated male volunteers that the GG genotype of PNPLA3 rs738409 was present in 63.7% of individuals with maternal and paternal Native American ancestry. It is important to consider that admixture of Native Americans, Europeans, and Africans is variable throughout Latin America, which makes the genetic makeup of each country considerably heterogeneous.¹¹ Thus, a higher African genetic ancestry contribution has been found in the Brazilian population, whereas the contribution of Native American ancestry is higher in Bolivia, Peru, Mexico, Ecuador, Chile, and Colombia. Clinically, data from Mexico¹² and Brazil¹³ have confirmed the association of the PNPLA3 rs738409 variant with NAFLD in biopsy-proved patients.

With regard to other NAFLD risk factors, data from US studies show that Hispanics have a higher body mass index than several other ethnic groups and that components of metabolic syndrome (i.e. obesity, prediabetes/T2DM, arterial hypertension, visceral obesity, and dyslipidemia) are strikingly higher in this ethnic group compared with Caucasians and African Americans.⁵ Central obesity has been indicated as a potential causative factor because Hispanic persons living in the United States have high intraperitoneal and hepatic fat content when compared with Caucasians and African Americans.⁴

Examination of the prevalence of obesity in Latin America allows estimation that cases of NAFLD will continuously increase over coming years. In the 2016 World Health Organization (WHO) report, prevalence of overweight/obesity among adults in Latin America reached 62.8% in men and 59.8% in women, and regions in Latin America and the Caribbean had the highest mean body mass index in persons younger than 19 years (see <https://www.who.int>). Also, as in other parts of the world, the increase in T2DM prevalence

may also be a contributing factor to increased prevalence of NAFLD in some Latin America countries. For example, Mexico and Brazil are currently among the top 10 countries with the most adults with T2DM.¹⁴

Physical inactivity is also highly prevalent in the region. According to the WHO, Latin America and the Caribbean regions ranks first among regions in inactivity in the world with a prevalence rate of insufficient physical activity of 32%.¹⁵ Also, a recent report of physical behaviors of 64,034 adolescents from the region showed that only 15% of adolescents were physically active.¹⁶

Finally, because the gut microbiome plays an important role in NAFLD/NASH pathophysiology, it would be of interest to study region-specific patterns that may contribute to a higher NAFLD prevalence or different disease severity. However, data from Latin America are currently scarce^{17,18} and insufficient to reach any conclusion.

CONCLUSIONS AND PERSPECTIVES

Latin America is a region composed of countries with heterogeneous genetic background and marked differences in socioeconomic conditions, lifestyles, diets and cultural traditions. Although available data are scarce, it is likely that some populations, particularly those with a high proportion of Native American ancestry, have a genetic predisposition to development of NAFLD and eventually have a more severe disease. In addition, risk factors for NAFLD, such as obesity, T2DM, and physical inactivity, are alarmingly prevalent in the region and, as in other parts of the world, will increasingly contribute to liver-related health burden in the near future. Latin America faces challenges to institute public policies (i.e., educational programs, regulations, taxes, and subsidies) that appropriately address NAFLD risk factors and promote healthy lifestyles and reducing consumption of unhealthful food.

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