

Objectives: Hispanics represent the largest racial/ethnic minority group in the USA and exhibit a high prevalence of obesity, diabetes, non-alcoholic fatty liver disease, and metabolic syndrome (MetS). Prior studies indicate that variation in fatty acid desaturase (FADS) gene cluster linked to an ancestral haplotype are associated with a reduced capacity to produce circulating omega-3 (n-3) highly unsaturated fatty acids (HUFAs). These FADS variants occur at high frequencies in Amerind Ancestry populations, such as Mexican Americans (MxAm). The aim of this study was to determine the influence of variation in FADS and other related genes (ELOVL5 and ELOVL2) in the HUFA biosynthetic pathway on the risk of cardiometabolic disease (CMD) a MxAm population.

Methods: To discern associations between genotypes, fatty acids, and cardiometabolic indicators, regression models were employed, with adjustments for covariates, using data from 493 self-identified Mexican American (MxAm) participants. We analyzed 20 single nucleotide polymorphisms (SNPs) located in the FADS cluster region as well as SNPs from ELOVL5 and ELOVL2. The levels of 37 fatty acids present in complex lipids were quantified using GC/FID. Cardiometabolic markers included lipoproteins, anthropometric measurements (weight, height, waist-hip ratio, adiponectin) and biomarkers including AST/ALT, insulin, glucose, HbA1c, HOMA-IR, Matsuda and disposition indices.

Results: Individuals with ancestral FADS genotypes exhibited lower levels of the n-6 HUFA arachidonic acid (ARA), and significantly diminished levels of n-3 HUFAs, including eicosapentaenoic acid (EPA). This resulted in an ARA/EPA of ~20:1. Furthermore, SNPs in both FADS and ELOVL2/5 were linked to MetS phenotypic expressions. For example, the FADS SNP rs174455 demonstrated a strong association with fasting insulin and HOMA-IR. The presence of two ancestral alleles corresponded to a 45% and 41% increase in these levels, respectively.

Conclusions: The marked associations between FADS variants, extremely low n-3 HUFA levels, and CMD biomarkers highlight the potential influence genetically-impacted HUFAs regulation on CMD risk within MxAm. This provides a strong rationale for future studies and clinical trials to explore a precision nutrition approach that utilizes n-3 HUFA supplementation for this population.