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Equilibrio de Hardy-Weinberg y estratificación poblacional en el análisis del polimorfismo rs61330082 y el síndrome metabólico

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Dear Editor,

In their recent article published in Nutrición Hospitalaria, González-Sánchez et al. (1) present a case-control study exploring the association between the rs61330082 polymorphism in the visfatin (NAMPT) gene and metabolic syndrome in a sample of Mexican individuals. The authors report no significant differences in genotype or allele frequencies

between cases and controls under different inheritance models. While the study is a valuable contribution to understanding the genetic basis of metabolic syndrome, we believe an additional methodological consideration is necessary: the evaluation of the Hardy-Weinberg equilibrium (HWE).

We conducted a post hoc HWE analysis using the genotypic data provided by the authors. Both the case group ($n = 30$; $\chi^2 = 3.44$; $p > 0.05$) and the control group ($n = 168$; $\chi^2 = 3.01$; $p > 0.05$) conformed to HWE. However, when combining both groups ($n = 198$), the overall genotype distribution deviated significantly from equilibrium ($\chi^2 = 5.33$; $p < 0.05$), due to an excess of heterozygotes. Such deviations—despite non-significant allele frequency differences—have been recognized as potential indicators of genotyping error, population stratification, or sampling artifacts (2,3).

To explore whether this disequilibrium reflects population structure, we incorporated data from the MXL population (Mexican ancestry in Los Angeles) from the 1000 Genomes Project (4), which was in HWE ($\chi^2 = 0.20$; $p > 0.05$). When adding MXL to the original sample (total $n = 262$), the combined data no longer showed significant deviation ($\chi^2 = 3.11$; $p > 0.05$). This supports the hypothesis that subtle stratification between cases and controls—potentially unaccounted for in the original design—may explain the observed deviation, as has been discussed in joint modeling approaches for HWE in case-control studies (5).

While this observation does not invalidate the authors' main conclusions, it underscores the importance of assessing HWE not only in control groups, but also in combined samples, especially when investigating common variants in admixed populations. Doing so can help identify hidden population structure and increase the interpretability of genetic association findings.

Conflicto de intereses: los autores declaran no tener conflicto de interés.

Inteligencia artificial: los autores declaran no haber usado inteligencia artificial (IA) ni ninguna herramienta que use IA para la redacción del artículo.

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