Comment on "Significant association between insulin-like growth factor 2 mRNA-binding protein 2, interleukin–6 polymorphisms, and type 2 diabetes mellitus"

Dear Editor,

The original article, "Significant association between insulin-like growth factor 2 mRNA-binding protein 2, interleukin–6 polymorphisms, and type 2 diabetes mellitus" published in the *Journal of Research in Medical Sciences*, is a valuable contribution.[1] The study aimed to determine the assessment of the polymorphism of the insulin-like growth factor 2 mRNA-binding protein 2 and interleukin-6 among type 2 diabetes mellitus in Saudi patients.[1] I agree with the study's rationale that considering the rising prevalence of diabetes, there is an immense need to ensure its early detection to avoid the development of complications.

I thoroughly read the article and have some critical observations and suggestions to improve the overall quality. The use of the term "significant association" in the title gives an impression that even before the start of the study, the authors have established a statistically significant relationship, which could lead to potential bias or misinterpretation. Under ideal circumstances, the title should be neutral and not presuppose the study's findings. The general rule of writing the methodology section is that it has to be self-explanatory and reproducible, but this has not been followed uniformly. As it was a case–control study, there were multiple concerns, namely, it has not been defined how cases and controls were selected (selection bias) and were they randomly chosen or specific recruitment strategies used?[2] The authors have not mentioned how exclusions regarding participants with diabetes, endocrine, hepatic, or renal diseases were ascertained (viz. medical records, laboratory reports, self-reporting, etc.).[1]

Matching is a crucial aspect of a case–control study and is done to reduce confounding, but surprisingly there is no mention of whether cases and controls were matched based (viz. cases and controls are generally matched for age, gender, etc.).[2] As the study was performed across three different institutions, there is a lack of uncertainty about the standardization of procedures across these study settings. It was reported that the study lasted for 4 years, but the reason (viz. problems with recruitment, data collection, or follow-ups) for this long duration is unclear. Although the American Diabetes Association criteria were followed, it is not mentioned which version (year) of the criteria was employed, as these are periodically updated. My biggest concern was that the formula used for sample size calculation was appropriate for cross-sectional studies, not case–control studies.[1] In case–control studies, sample size depends on the expected odds ratio, power, and exposure prevalence in controls, not on disease prevalence.[2] Further, there is no justification for increasing the calculated sample size from 206 to 250, as precision or power improvement must be justified mathematically.

To summarize, the current study adds useful information about the utility of genetic markers in the early detection of diabetes. However, the study findings would be more valid if the authors had provided more information about the study participants, matching, and sample size, which could undermine the study's validity and reproducibility.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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Submitted: 16-Dec-2024; **Revised:** 05-Apr-2025;
Accepted: 16-Apr-2025; **Published:** 26-May-2025

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Quick Response Code:

Website: https://journals.lww.com/jrms

DOI: 10.4103/jrms.jrms_727_24

How to cite this article: Shrivastava SR. Comment on "Significant association between insulin-like growth factor 2 mRNA-binding protein 2, interleukin–6 polymorphisms, and type 2 diabetes mellitus". J Res Med Sci 2025;30:28.