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LETTER

Comment on: "Association of Fasting C-Peptide to High Density Lipoprotein Cholesterol Ratio with Non-Alcoholic Fatty Liver Disease in Chinese Type 2 Diabetes Mellitus Patients: A Cross-Sectional Study" [Letter]

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Dear editor

We read the recent article by Qian et al titled "Association of Fasting C-Peptide to High Density Lipoprotein Cholesterol Ratio (FHR) with Non-Alcoholic Fatty Liver Disease (NAFLD) in Chinese Type 2 Diabetes Mellitus Patients: A Cross-Sectional Study" published in *Diabetes, Metabolic Syndrome and Obesity*.[1] This research innovatively proposes FHR as a composite indicator and employs multiple statistical methods to explore non-linear relationships. However, critical flaws in study design, statistical analysis, data interpretation and result presentation compromise the findings' reliability and generalizability.

Study Design

Sample

The single-center design limits external validity, and no sample size calculation is reported, nor are the key parameters, particularly concerning for underpowered subgroup analyses, which may lead to insufficient statistical power and unstable effect estimates.

Outcome

NAFLD diagnosis relies on ultrasound without reported quality control[2] (such as inter-observer agreement among radiologists), risking misclassification. FHR failing to capture long-term stability and introducing measurement error.

Statistical

Methodological Inconsistency

The Abstract incorrectly cites "multiple linear regression" for the binary NAFLD outcome (actual logistic regression).

Missing

The findings should be interpreted with caution due to potential selection bias from participant attrition and missing data exceeding 10%. Furthermore, extreme outliers are unaddressed.

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Nonlinear and Subgroup Analyses

The FHR threshold lacks stability validation and biological rationale. Subgroup analyses omit multiple comparison correction, inflating Type I error.[3]

ROC Curve

The performance of FHR has not been validated against established insulin resistance indices (eg, TyG-BMI[4]) identified in previous studies using statistical tests. This prevents conclusions about whether FHR offers incremental value over existing biomarkers.

Collinearity

The manuscript does not report collinearity diagnostics for covariates in the multivariable model.[5]

Overinterpretation

Causal Inference

Cross-sectional design cannot support claims like "mitigating NAFLD through FHR reduction", which inappropriately implies causality.

Conclusion-Data Mismatch

The conclusion misrepresents the threshold effect—FHR ≤ 1.23 shows a stronger association (OR = 3.07) than FHR > 1.23 (OR = 1.20). Additionally, the Discussion mentions "Longitudinal increases in FHR during follow-up", creating confusion about the study design.

Qian et al's research provides a novel perspective for exploring NAFLD biomarkers; however, the reliability of its conclusions is weakened by methodological flaws and overinterpretation of cross-sectional data. Future research should validate the predictive value and clinical utility of FHR through multicenter, prospective, comparative, standardized, and gold-standard measurement approaches to confirm its role as a reliable NAFLD risk assessment tool.

Generative AI Statement

The authors declare that no Generative AI was used in the creation of this communication.

Data Sharing Statement

Data availability is not applicable as no data was generated in this communication.

Author Contributions

All authors participated in the writing of the article and approved the submitted version. The specific contributions of each author are as follows:

Hanwen Xu: Conceptualization, Data Curation, Visualization, Formal Analysis, Writing-Original Draft.

Kexin Hu: Supervision, Writing-Review & Editing, Project Administration.

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no known conflicts of interest or personal relationships that could influence the work reported in this communication.

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