Khan *et al.*
The Egyptian Journal of Internal Medicine (2023) 35:27
https://doi.org/10.1186/s43162-023-00216-1

The Egyptian Journal of Internal Medicine

LETTER TO THE EDITOR

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Limitations in FABP4 as a biomarker for diabetic nephropathy: a critique of Shaker et al.

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Dear Dr. Radwan,

We have read the scholarly article titled "Serum fatty acid-binding protein 4 (FABP4) as a biomarker for early detection of diabetic nephropathy in type 2 diabetes" written by Shaker et al. [1] and appreciate the hard work put into researching a potential biomarker for early detection of diabetic nephropathy. However, we would like to highlight certain aspects of the study.

Firstly, the standard control group is not age-matched with the diabetic group, and the two groups have a statistically significant age difference. A previous study in Spain matched both groups within the same age interval, as age is an independent predictor of serum FABP4 and urinary FABP4 levels, which could skew the findings [2]. The ELISA kit for detecting serum FABP4 levels did not show any cross-reactivity to human FABP1, FABP2, FABP3, or FABP5, which should have been mentioned [3]. Additionally, it is still being determined whether the control group was allowed to exercise before serum sample collection, as circulating FABP4 levels significantly correlate with norepinephrine levels during exercise testing, which could lead to false negative results and confound the study's findings. Furthermore, several drugs have been shown to interfere with serum FABP4 levels, and therefore, it is essential to seek a relevant drug history and rule out any medications with known effects on serum FABP4 levels to avoid potential bias. It is also proposed that urinary FABP1 and FABP4 be measured instead of FABP4 alone to better characterize renal injury [4]. The exclusion criterion is not very elaborate, and it needs to be clarified whether individuals with thyroid disorders or a history of lipid-lowering therapy were included in the study. This is important because both overt hyper- and hypothyroidism and lipid-lowering treatment have been shown to affect circulating FABP4 levels [5]. Lastly, FABP4 levels must be adjusted for menopausal status, age, and sex, as menopausal status is an independent risk factor for elevated serum FABP levels [6].

In conclusion, while the study by Shaker et al. is commendable for its focus on finding a potential biomarker for the early detection of diabetic nephropathy, certain study aspects should be considered for a more accurate and reliable assessment of FABP4 levels as a biomarker. These include matching the control group for age, ruling out medications that may affect FABP4 levels, measuring both urinary FABP1 and FABP4, and adjusting for menopausal status and age and sex.

Acknowledgements
None.

Authors' contributions
Aimen Waqar Khan: conceptualization, writing the original draft, final approval, and agreeing to the accuracy of the work. Mishal Abid: reviewing and editing. Sameer Abdul Rauf: reviewing and editing. The author(s) read and approved the final manuscript.

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Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declarations

Ethics approval and consent to participate
None.

Competing interests
The authors declare that they have no competing interests.

Received: 30 March 2023 Accepted: 9 April 2023
Published online: 14 April 2023

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