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CORRESPONDENCE

Response: The role of carbonic anhydrase I and II enzymes in the pathogenesis of gestational diabetes mellitus and their relationship with oxidative stress

We would like to express our sincere appreciation for the interest and thoughtful comments that Drs Amini and Mehri have shown in our recent publication,[1] which evaluated the relationship between carbonic anhydrase (CA) isoenzymes and oxidative stress in pregnancies affected by gestational diabetes mellitus (GDM). Their letter highlights the scientific value of further exploration of biochemical pathways that may contribute to the pathophysiology of GDM, a field in which research remains relatively limited despite its considerable clinical relevance.

The authors correctly noted that CA-I and CA-II are primarily found in the cytosol of erythrocytes and various tissues rather than being actively secreted into the circulation. This important physiological detail supports the mechanistic interpretation that elevated circulating CA levels may indicate oxidative injury, increased cellular turnover, or compromised membrane stability, which are all commonly observed in GDM.[2,3] Indeed, hyperglycemia-associated redox imbalance is known to promote erythrocyte fragility, protein leakage, and abnormal enzymatic release.[4,5] Our findings support this biological plausibility and enhance our conceptual understanding of how metabolic stress during pregnancy can extend beyond traditional glucose-centric pathways. Furthermore, we acknowledge the authors' observation that enzyme-linked immunosorbent assay–based immunoassays quantify total protein, regardless of catalytic activity. This is a particularly relevant point, as oxidative modification of zinc-binding histidine residues can impair enzyme activity despite elevated immunoreactive levels.[6] As the authors suggest, we intend to incorporate direct enzymatic activity measurements and serum zinc profiling in future work to determine whether the observed elevation indicates the activation, inactivation, or oxidative denaturation of CA isoenzymes. Integrating these molecular assessments may improve diagnostic interpretation and translational potential.

Drs Amini and Mehri also emphasize the limitations of a single time-point assessment given the dynamic nature of maternal metabolism and oxidative pathways throughout gestation. We agree that temporal profiling is essential to determine whether changes in CA precede the development of hyperglycemia or are instead a consequence of glucose dysregulation. Our ongoing prospective study includes longitudinal sampling during the early, middle, and late stages of pregnancy, as well as postpartum follow-up. We anticipate that these findings will validate the use of CA measurements as prognostic or early screening biomarkers for GDM and its complications. Despite these limitations, our study—the first to our knowledge to quantify circulating CA-I and CA-II in pregnancies complicated by GDM—supports the hypothesis that altered acid–base balance, oxidative stress, and endothelial-microvascular dysfunction are interconnected processes in the disease. Establishing this link adds a novel dimension to biomarker research in maternal-fetal medicine. As the authors kindly noted, our findings open promising scientific avenues and encourage further mechanistic and clinical exploration.

We are grateful to Drs Amini and Mehri for engaging in an academic dialogue that advances the refinement of biochemical markers in the care of high-risk pregnancies. Continued collaborative discourse will undoubtedly support the development of more precise, biologically informed strategies for the early detection and prevention of adverse metabolic outcomes during pregnancy.

AUTHOR CONTRIBUTIONS

R.M. drafted the initial response. A.Ş.E., T.R.K, F.İ., and A.A.U all contributed to the final revision.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data available on request.

DECLARATION OF GENERATIVE AI

This study did not make substantial use of generative AI technologies or large language models.

Rauf Melekoğlu[1]
Ayşe Şebnem Erenler[2]
Tuğba Raika Kiran[3]
Feyza İnceoğlu[4]
Aysel Alkan Uçkun[5]

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[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Inonu University, Malatya, Turkey
[2]Department of Medical Biology, Faculty of Medicine, Malatya Turgut Ozal University, Malatya, Turkey
[3]Department of Medical Biochemistry, Faculty of Medicine, Malatya Turgut Ozal University, Malatya, Turkey
[4]Department of Biostatistics, Faculty of Medicine, Malatya Turgut Ozal University, Malatya, Turkey
[5]Department of Environmental Engineering, Faculty of Engineering, Adiyaman University, Adiyaman, Turkey

Correspondence
Aysel Alkan Uçkun, Department of Environmental Engineering, Faculty of Engineering, Adiyaman University, 02040 Adiyaman, Turkey.
Email: ayseluckun@gmail.com

ORCID

Aysel Alkan Uçkun https://orcid.org/0000-0002-8957-7476

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