LETTER TO THE EDITOR
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Biomarkers Associated with Progression of Diabetic Kidney Disease: Do They Hold the Same Meaning for Blacks and Women?

We read with interest the study by Coca et al., which examined the association of plasma TNF receptor-1 (TNFR-1), TNFR-2, and kidney injury molecule-1 (KIM-1) on renal outcomes in patients with type 2 diabetes mellitus. These investigations were performed on plasma samples from two previously conducted clinical trials involving patients with incident and progressive diabetic kidney disease (DKD) \((n=1636)\). The findings support prior studies. In 2012, Niewczas et al. connected circulating markers of the proinflammatory cytokine (TNF-\(\alpha\)) and the TNF pathway to the inflammatory state in DKD as a potential biomarker of DKD progression. These novel investigations \((n=410)\) revealed the predictive capacity of plasma TNFR-1 and TNFR-2 in determining future DKD ESRD events. Since then, these studies have been replicated in predominantly white cohorts, with a few in other racial groups including American Indians and Chinese. One study by Chode et al., involved blacks \((n=359)\), but it did not determine renal outcomes.

In the study by Coca et al., sampling was performed in only 293 (18%) blacks and 195 (12%; predominantly Veterans Affairs population) women. Race and sex were adjusted for in the statistical models. This, however, would not necessarily detect differences between populations either at baseline or over time. In many situations, race/ethnicity and sex have significant biologic effects on the measurement and interpretation of biomarkers. For example, recently, Bajaj et al. found significantly lower plasma levels of N-terminal pro-BNP \((n=1998)\) in healthy blacks compared with whites in both sexes. On the basis of that and other studies, it now appears that clinical utilization of natriuretic peptides may benefit from race-specific thresholds. Are race or sex also important considerations in the interpretations needed of TNFR-1, TNFR-2, and KIM-1?

In this study by Coca et al., a stratified assessment by race and by sex may help inform whether TNFR levels necessitate race-sex specific thresholds for their interpretation. In particular, statistical models that assess for effect modification (statistical interaction) by race (or sex) on TNFRs and KIM-1 levels in predicting DKD ESRD events may be helpful. Ultimately, further studies in large cohorts more representative of different populations are needed. In their absence, persistence of studies with small samples sizes in these populations may not permit systematic reviews and meta-analyses to further elucidate race/sex differences.

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REFERENCES


See related Letters to the Editor, “Authors’ Reply,” on pages 1782–1783.