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Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

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GWAS of extreme creatinine and cystatin C levels provides genetic insights into kidney function

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Objectives : Genome-wide association studies (GWAS) have been performed kidney function, as measured by estimated glomerular filtration rate (eGFR), and have identified hundreds of genome-wide significant loci. However, differences in the effects of genetic variation between populations on kidney function are currently unknown, rendering polygenic risk scores (PRS) poorly transferrable across populations. We aimed at understanding the complex relationships between genetic variation, kidney function biomarkers (creatinine and cystatin C), eGFR, and chronic kidney disease (CKD).
Methods : We performed a GWAS on CKD and eGFR on 479,806 UK Biobank (UKBB) individuals divided into four populations: Africans, European, East Asians and South Asians. We investigated the associations between creatinine, cystatin C, eGFR levels and CKD between different populations in the UKBB.
Results : Overall, we identified 417 loci, including 112 (26.9%) novel loci not previously in CKD and eGFR GWAS. We observed 14 loci in non-European populations, including 11 unique to non-European populations. Individuals of African descent had the highest serum creatinine levels, 1.23 times higher than East Asians (80.1 μmol/L and 65.3 μmol/L, respectively). Similarly, South Asians had the highest cystatin C levels, on average 1.17 higher than East Asians (0.96 mg/L and 0.82 mg/L, respectively), whereas East Asians had higher eGFR levels than other populations.
Conclusions : Our study shows the complex relationships between kidney function genetics and the serum levels of the two biomarkers that are used to assess kidney function and diagnose CKD. These differences suggest that genetic differences between populations likely affect the levels of the biomarkers used to measure kidney function and, therefore, influence the measurement of eGFR and, consequently, the diagnosis of CKD. Therefore, the accuracy of the evaluation in kidney function will likely improve by dividing individuals according to their biomarker levels and investigating the different GWAS associations.