

Abstract

Introduction: In South Africa (SA) and Sub-Saharan Africa (SSA), the burden of chronic kidney disease (CKD) is unknown, associated risk is poorly characterised, and equations to estimate glomerular filtration rate (eGFR) have limited validation. This study aimed to determine the population prevalence of CKD, identify associated risk factors, and measure kidney function using iohexol (mGFR) as the reference for comparing eGFR equations. If inaccurate, a model would be developed to better predict eGFR, therefore more accurately determining CKD burden.

Methods: The research was conducted in the MRC/Wits-Agincourt Unit, Bushbuckridge, Mpumalanga Province. To determine population prevalence of CKD and associated risk, 2 021/2 759 adults, aged 20 to 80 years were recruited (prevalence of CKD negligible in those younger than 20). CKD prevalence was determined by measuring albuminuria (albumin: creatinine ratio (ACR) $\geq 3\text{mg}/\text{mmol}$) and estimating GFR (eGFR $< 60\text{ml}/\text{min}/1.73\text{m}^2$), using the CKD-EPI (creatinine) equation without ethnicity coefficient. CKD was confirmed with repeat screening after three months. Genotyping determined *APOL1* renal risk variants. To measure GFR, a subsample of $\sim 1\,000$ adults were recruited, stratified by eGFR and sex. Serum creatinine, cystatin C and GFR were measured using the slope-intercept method for iohexol plasma clearance (mGFR). eGFR equations were compared to mGFR, a new eGFR equation was modelled and validated, and multiple imputation modelling trained on mGFR was used to predict CKD. Data was pooled with Malawi and Uganda for analysis.

Results: In SA, the WHO age standardised population prevalence of CKD was 4.0% (95% CI 3.1-4.9). Risk factors comprised high risk *APOL1* genotypes (OR 1.95; 95% CI 1.20-3.17); hypertension (OR 3.34; 95% CI 1.92-5.79); diabetes (OR 3.28 95% CI 1.61-6.70), HIV infection (OR 1.89; 95% CI 1.18-3.03) and hyperuricaemia (OR 1.85; 95% CI 1.13-3.05). Pooled data for mGFR included 2 578 of 3 025 participants. Overall and by country, creatinine-based equations overestimated kidney function compared to mGFR. The greatest bias occurred at low kidney function, where the proportion with mGFR $< 60\text{ml}/\text{min}/1.73\text{m}^2$ was more than double that estimated from creatinine. A new model for estimating GFR did not outperform existing equations, and no eGFR equation achieved the benchmark of estimated GFR within $\pm 30\%$ of mGFR for $\geq 75\%$ of participants. Imputation modelling

estimated prevalence of kidney disease as two- to three-fold higher than creatinine-based estimates across six SSA countries.

Conclusion: In South Africa, CKD is prevalent and associated with high risk *APOL1* genotypes, HIV infection and cardiometabolic diseases. In Sub-Saharan Africa, estimating GFR using serum creatinine substantially underestimated individual and population-level burdens of CKD, and cystatin C may be a preferable biomarker. Our findings have implications for individual care and public health policy, supporting implementation of screening for early detection and prevention of progression of CKD in those who are at risk.