EDITORIAL

The CKD-EPI Pakistan Equation: A small step for Pakistan, a great leap for South Asia

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Chronic kidney disease (CKD) is a major cause of morbidity across the globe. The prevalence of CKD is rising rapidly, especially in low income and middle income countries.[1] To manage this epidemic, timely screening and diagnosis is required. To do so, one needs simple and economical tools, which must also be accurate and reliable.

The diagnosis of CKD can be based upon the estimation of eGFR (estimated-glomerular filtration rate) and proteinuria.[2] The accepted staging of CKD, however, relies upon eGFR determination.[3] Various methods of eGFR calculation are available, including the Cockcroft-Gault equation, MDRD (Modification of Diet in Renal Disease) Study equation, and the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation.[4] The CKD- EPI equation[4] is considered reliable, especially at GFR levels >60ml/min/1.73m^2. The 2009 CKD-EPI creatinine equation is more accurate in estimating GFR and prognosis than the 2006 MDRD (Modification of Diet in Renal Disease) Study equation, and provides lower estimates of prevalence of decreased eGFR. It is a useful screening test, and should supersede the MDRD Study equation in practice. The 2012 CKD-EPI cystatin C equation is as accurate as the 2009 CKD-EPI creatinine equation in estimating GFR, does not require specification of race, and may be more accurate in patients with decreased muscle mass. The 2012 CKD-EPI creatinine-cystatin C equation is the most accurate, and serves to confirm decreased eGFR as determined by serum creatinine-based eGFR.

There are certain limitations to the use of CKD-EPI, including the impact of ethnicity on GFR estimation. Various proposals, including one to use a two-level ethnicity equation,[5] have been proposed. The limitation regarding ethnicity has not prevented South Asian researchers from using CKD-EPI in their studies, however large trials from India[6] and Bangladesh[7] have measured GFR by CKD-EPI to determine the prevalence of CKD in their countries.

Colleagues from Karachi, Pakistan (Jessani et al) have gone one step ahead in this regard.[8] In a cross-sectional population-based setting, 581 participants 40 years or older were enrolled from 10 randomly selected communities and renal clinics in Karachi. The aim was to assess the performance of existing GFR estimating equations in South Asians, and modify the existing equations or develop a new equation for use in this population. Bias (the median difference between measured GFR [mGFR] and eGFR), precision (the IQR of the difference), accuracy (P30; percentage of participants with eGFR within 30% of mGFR), and the root mean squared error were reported as cross-validated estimates along with bootstrapped 95% CIs based on 1,000 replications.

The CKD-EPI creatinine equation performed better than the MDRD Study equation in the Karachi cohort. It showed higher accuracy at P30 (76.1% [95% CI, 72.7%-79.5%] vs 68.0% [95% CI, 64.3%-71.7%]; $P < 0.001$) and greater precision (IQR, 22.6 [95% CI, 19.9-25.3] vs 28.6 [95% CI, 25.8-31.5] mL/min/1.73 m^2; $P < 0.001$). However, both equations overestimated mGFR. Applying modification factors for slope and intercept to the CKD-EPI equation to create a CKD-EPI Pakistan equation (such that eGFR [CKD-EPI (PK)] = 0.686 × eGFR [CKD-EPI] to the power 1.059) eliminated bias and improved accuracy (P30, 81.6% [95% CI, 78.4%-84.8%]; $P < 0.001$).

The authors concluded that while the CKD-EPI creatinine equation is more accurate and precise than the MDRD Study equation in estimating GFR in South Asians, the CKD-EPI Pakistan equation further improves the performance of the CKD-EPI equation in this population, and may be used to calculate eGFR.

The same team[9] followed this publication with a much larger cross-sectional study on 2873 participants aged ≥40 years in 12 representative communities in Karachi, Pakistan. Using the CKD EPI Pakistan equation, they found an overall prevalence (95% CI) of CKD of 12.5% (11.4 - 13.8%). The factors independently associated with CKD

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were older age, hypertension, and diabetes, elevated systolic blood pressure, and raised fasting plasma glucose, raised triglycerides, and history of stroke ($p < 0.05$ for each). These findings are similar to those seen across other South Asian countries.

While the publications of Jessani et al have found respect and recognition globally, they seem to have been ignored at home. This is probably because of a lack of awareness of CKD epidemic, even in allied specialties such as endocrinology and cardiology. It must be noted, though, that a few recent articles from India and China refer to the CKD-EPI Pakistan equation.[10,11] Eminent researchers in India (A Ramachandran) have been popularizing the Pakistani equation in their talks.

This trend is welcome, as the utility of Jessani et al's seminal work extends far beyond the boundaries of Karachi and Pakistan. The simple equation they have derived holds the ability to provide more accurate GFR determination, CKD screening and diagnosis, and thus CKD management and prevention. Its values adhere to the concept of quaternary prevention[12] which enjoins us to avoid over diagnosis and overlabelling of medical conditions. To fulfil its potential, though, the Pakistani equation needs to be studied and validated in neighbouring countries of South Asia, and South Asian migrant populations abroad. If this is done, the pioneering work from Karachi will truly prove to be a milestone in South Asian health.

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