Review Article

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Estimation of eGFR using the CKD Formula: The Chennai Experience

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Introduction:

Diabetes mellitus is the commonest metabolic disorder, and its prevalence is high in India. The prevalence of diabetes continues to grow worldwide, disease-related morbidity and mortality are emerging as major healthcare problems. Chronic kidney disease is a worldwide public health problem. It is evident that patients with diabetes are at a high risk of *developing* diabetes-associated microvascular complications, which pose a comprehensive national threat (1). Diabetic nephropathy is the leading cause of the end-stage renal disease (ESRD) and a leading cause of diabetes mellitus related morbidity and mortality. It is also estimated that nearly 20 % of the patients with Type 2 Diabetes Mellitus (T2DM) reach End-Stage Renal Disease (ESRD) during their lifetime (2). Nephropathy complicates approximately 30% of type 2 diabetic patients. The laboratory test for early detection of diabetic nephropathy measures microalbumin in urine (Microalbuminuria), which predicts progression to diabetic nephropathy. In diabetic kidney disease, detection of urinary albumin is recommended to aid in the diagnosis, evaluate disease severity, and determine the effects of therapy. Currently, diabetic nephropathy (DN) diagnosis is based on the elevated urinary albumin excretion level. However, the emerging evidence suggested that DN's risk starts developing well before the elevation of urinary albumin level. The potential treatment can be offered to the patients as a preventive measure if the onset of DN is diagnosed earlier. However, because typical histopathologic changes in diabetic kidney disease or early progressive renal decline may occur in patients with normoalbuminuria, urinary albumin may not be sufficient to identify patients with early-stage diabetic kidney disease or predict its progression.

Glomerular filtration rate (GFR):

Declining estimated glomerular filtration rate (eGFR) increases the rate of mortality among patients with ESRD. The estimated glomerular filtration rate is recognized and widely accepted as a major risk factor for CVD. Increased incidence of malignancy and infection may be due to chronic kidney disease (CKD). When focusing on the gender difference in CKD, we should note that the eGFR is based on the patient's gender, among other variables. Modification of diet in renal disease and CKD epidemiology collaboration equations is commonly used to access the eGFR; both equations use gender as a variable. These are based on the assumption of the creatinine value that males have higher levels of kidney function than females because high muscle mass increases the generation of creatinine in males. A paucity of studies uses the gold standard measurement for GFR glomerular filtration rate (GFR). The findings based on gender differences in CKD are often biased as these equations are gender-dependent.

It is the imperative parameter used in assessing and managing kidney function among patients with suspected kidney function. The direct estimation of GFR was difficult; thus, the indirect methods were widely used. Various equations are evolved to estimate eGFR at different points of time in different populations. The commonly used equations are Modification of Diet in Renal Disease (MDRD) Study equation, Cockcroft-Gault formula

(CG), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formulas (3 -6).

The kidney function was indirectly calculated using estimated creatinine clearance (eCrCl) (7) or estimated glomerular filtration rate (eGFR) (4); both the equations were used to assist in dosage decision in clinical practice. Perhaps the appropriate method to assess an individual's kidney function remains controversial (8,9). The National Kidney Education Program suggested that eCrCl calculated using Cockcroft–Gault (CG) equation and eGFR calculated using MDRD equation (Modification of Diet in Renal Disease) can be used interchangeably for drug dosing. Perhaps the Kidney Disease: Improving Global Outcomes recommended that the CKD-EPI equation (Chronic Kidney Disease Epidemiology Collaboration) be a proper choice for staging CKD (10). The study conducted among the four eGFR equations, EPI-cystatin-c, and creatinine equation, showed better correlation with all other equations, hence might be the better equation for confirmation and classification of the elderly CKD patients (11). Though, various studies highlighted that none of the published methods can precisely estimate the renal function in Asian patients with CKD (12, 13).

Estimating Glomerular filtration rate:

The KDOQI (Kidney Disease Outcomes Quality Initiative) guidelines and NKDEP (The National Kidney Disease Education Program) recommendations influenced professional organizations in many countries to adopt the recommendations, including to have laboratories report eGFR along with creatinine (14). In parallel with the laboratory effort to standardize creatinine measurement, laboratories in many areas of the world began to report eGFR calculated from creatinine.

A study conducted in India showed that diabetic patients with CKD spend more on hospitalization than those without diabetic complications (15). Thus GFR estimation is primarily important from a clinical perspective to assess the proper function of the kidney and detect and estimate the progression of kidney disease. Estimating GFR using CKD-EPI equation (4) is a major indicator for kidney function, and it plays a significant role in detecting, evaluating, and managing CKD. Serum creatinine or Serum Cystatin is used to estimate GFR. Avinash et al. (16) emphasized that Cystatin C picks up more patients in early CKD and patients with normoalbuminuric CKD when compared to creatinine. This study used creatinine-based equations such as CG, MDRD and compared them with CKD – EPI using Cystatin C. A study conducted by Vijay *et al.*(17) suggested that Cystatin C was a better marker for moderately impaired renal function when compared to creatinine using Cockcroft-Gault. Cystatin C has an advantage in detecting early CKD, perhaps its usage is limited due to its cost, and it is not cost-effective. It cannot be recommended for routine clinical practice.

To overcome this situation, creatinine can be used in estimating GFR. In the north Indian population, GFR is calculated using camera-based Gates protocol and Serum creatinine-based predicting equations with GFR measured by plasma clearance of Tc-99mDTPA (18). The finding emphasized that the CKD-EPI significantly correlated with Tc99mDTPA and showed the highest precision and lowest biasness compared to the GFR estimate using Cockroft - Gault, MDRD, and Gates protocol.

In a study conducted in South Indian Population, MDRD equation Vs. CKD - EPI using serum creatinine (Scr) and MDRD equation Vs. CKD-EPI using serum Cystatin (Scys) was compared to estimate eGFR in a clinical setting (19). The finding highlighted

that the mean and absolute bias was lesser with higher precision in MDRD Vs. CKD-EPI using serum creatinine when compared to MDRD Vs. CKD-EPI using serum Cystatin.

Similarly Scr showed the highest accuracy when compared with Scys. Thus creatinine-based CKD-EPI can pick up CKD at an early stage. Therefore for the Indian population CKD-EPI equation using creatinine predicts GFR best than other equations. This through a light on the importance of standardization of eGFR calculation among the Indian population. Further extensive research is required in the large sample to determine the best methods by comparing eGFR equations with the gold standard methods.

Conclusion

To conclude, The CKD-EPI equation leads to higher estimates of GFR in young people and lower estimates in the elderly. On a population level, this will lead to higher estimates of kidney function. In clinical practice, this effect might be less apparent. The estimation of eGFR using CKD-EPI necessitates the fine-tuning of the definition of CKD. CKD-EPI equation using Serum creatinine was found to be better in terms of estimating kidney function and is cost-effective. This can be implemented in routine clinical practice treatment of diabetic nephropathy should focus on the context of CKD, focusing on the complex entwined metabolic changes. In treating and preventing diabetic kidney disease, blood pressure and glycemic control play a major role. Further, the newly emerging drugs also contribute majorly towards the control and treatment of diabetes in patients with CKD.

References

1. American Diabetes Association. (2003). Economic costs of diabetes in the US in 2002. *Diabetes care*, *26*(3), 917-932.
2. Ayodele, O. E., Alebiosu, C. O., & Salako, B. L. (2004). Diabetic nephropathy--a review of the natural history, burden, risk factors and treatment. *Journal of the National Medical association*, *96*(11), 1445.
3. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function — measured and estimated glomerular filtra tion rate. N Engl J Med. 2006;354:2473-83.
4. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150: 604-12.
5. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: A new predict tion equation. Modification of Diet in renal disease study group. Ann Intern Med. 1999;130:461-70
6. Inker LA, Eckfeldt J, Levey AS, et al.Expressing the CKD-EPI (Chronic Kidney Disease Epidemiology Collabora tion) cystatin C equations for estimating GFR with standardized serum cystatin C values. Am J Kidney Dis. 2011;58:682-4.
7. Steffel, J., Verhamme, P., Potpara, T. S., Albaladejo, P., Antz, M., Desteghe, L., et al. (2018). The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Eur. Heart J. 39, 1330–1393. doi:10.1093/eurheartj/ehy136.
8. Selistre, L. S., Rech, D. L., Souza, V. de., Iwaz, J., Lemoine, S., and Dubourg, L. (2019). Diagnostic performance of creatinine-based equations for estimating glomerular filtration rate in adults 65 years and older. JAMA Int. Med. 179, 796–804. doi:10.1001/jamainternmed.2019.0223.
9. Bukabau, J. B., Yayo, E., Gnionsahé, A., Monnet, D., Pottel, H., Cavalier, E., et al. (2019). Performance of creatinine- or cystatin C-based equations to estimate glomerular filtration rate in sub-Saharan African populations. Kidney Int. 95, 1181–1189. doi:10.1016/j.kint.2018.11.045.
10. Pottel, H., Björk, J., Bökenkamp, A., Berg, U., Åsling-Monemi, K., Selistre, L., et al. (2019). Estimating glomerular filtration rate at the transition from pediatric to adult care. Kidney Int. 95, 1234–1243. doi:10.1016/j.kint.2018.12.020.
11. Deme S, Neelam PB, Killi S, Raju SB, Raju YS. Comparison of estimated glomerular filtration rate equations in elderly with chronic kidney disease. J Clin Sci Res 2021;10:9-14.
12. Yue, L., Pan, B., Shi, X., and Du, X. (2020). Comparison between the beta-2 microglobulin-based equation and the CKD-EPI equation for estimating

GFR in CKD patients in China: ES-CKD study. Kidney Dis. 6, 204–214. doi:10.1159/ 000505850.

13. Li, D. Y., Yin, W. J., Yi, Y. H., Zhang, B. K., Zhao, J., Zhu, C. N., et al. (2019). Development and validation of a more accurate estimating equation for glomerular filtration rate in a Chinese population. Kidney Int. 95, 636–646. doi:10.1016/j.kint.2018.10.019.
14. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratifica tion. Am J Kidney Dis. 2002;39(2 Suppl 1):S1-S266.
15. Satyavani, K., Kothandan, H., Jayaraman, M., & Viswanathan, V. Direct costs associated with chronic kidney disease among type 2 diabetic patients in India. Indian journal of nephrology, 2014; 24(3), 141.
16. Avinash, S., Singh, V. P., Agarwal, A. K., Chatterjee, S., & Arya, V. Identification and Stratification of Diabetic Kidney Disease Using Serum Cystatin C and Serum Creatinine Based Estimating Equations in Type 2 Diabetes: A Comparative Analysis. The Journal of the Association of Physicians of India, 2015; 63(11), 28-35.
17. Viswanathan, V., Snehalatha, C., Nair, M. B., & Ramachandran, A. Comparative assessment of cystatin c and creatinine for determining renal function. Indian J Nephrol, 2005;15, 91-4.
18. Mulay, A. V., & Gokhale, S. M. Comparison of serum creatinine-based estimating equations with gates protocol for predicting glomerular filtration rate in Indian population. Indian journal of nephrology, 2017; 27(2), 124.
19. Kumpatla, S., Soni, A., & Viswanathan, V. Comparison of Two Creatinine Based Equations for Routine Estimation of GFR in a Speciality Clinic for Diabetes. Journal of the Association of Physicians of India, 2017; 65, 38