cystatin C-based equation was significantly better than creatinine-based equation in terms of bias, precision and accuracy in children with early CKD. Authors also found that adding creatinine to the cystatin C-based formula did not improve the accuracy of predicted GFR. The major strength of this study is its methodologic rigor. The authors have rightly used Bland-Altman plots in the data analysis which strengthened the study conclusions and provided a more precise evaluation of agreement. Further research is required – on a large, well-defined pediatric population with carefully matched controls – to confirm the usefulness of cystatin based estimation of GFR in patients with early CKD.

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Estimating Accurate Glomerular Filtration Rate in Children

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A reliable and accurate assessment of glomerular filtration rate (GFR) is critical for diagnosing acute and chronic kidney impairment, intervening early to prevent end-stage renal failure, prescribing nephrotoxic drugs and drugs cleared by a failing kidney, and monitoring for side effects of medications. Estimation of GFR using exogenously administered substances is well established and precise, but these methods are cumbersome and time consuming [1].

Plasma creatinine is the most commonly used index for estimating renal function in the clinical practice. Due to its small size and lack of protein binding, it is freely filtered through the glomerulus. However, it is also actively secreted by the proximal tubules at unpredictable rates. Moreover, with decreasing GFR, the fraction of tubular secretion increases, leading to an over-estimation of 10-40% when compared to that of inulin clearance [2]. Especially in children, estimation of creatinine is difficult, as there is a muscle mass related increase in plasma creatinine in children after 2 years of life. Moreover, plasma creatinine may change in cases of excessive dietary intake of meat, malnourished children and anorectic adolescents [3]. On the other hand, cystatin C is produced endogeneously at a constant rate, is freely filtered by the glomerulus, and is completely reabsorbed and catabolised by the renal tubule cells. Blood levels of

cystatin C have been found to be a reliable indicator of renal function. The levels of cystatin C are independent of age, height, obesity and malnutrition [3,4]. Recent studies also suggest that serum cystatin-C is better than serum creatinine in detecting acute kidney injury in critically ill children [2]. Due to high cost, difficult assay methodologies and standardization, and non-availability of definite cut-off values, cystatin C has still not replaced creatinine in the clinical practice.

To compensate for the increasing muscle mass during childhood, creatinine based formulae which include height and muscle mass have been developed. The most commonly used formula is the Schwartz formula. The low muscle mass in malnourished children, may influence the value of k, and may affect the GFR estimation, and thus may lead to over-estimation of GFR in this subset [3]. Moreover, the value of k should be different based on the method of estimation of serum creatinine. Schwartz, *et al.* [5], using the enzymatic method of creatinine estimation, recently proposed a new k value of 0.413. To improve the bias and accuracy of the GFR estimation, it is important for all the pediatricians to understand that the value of k should be locally derived based on the method of creatinine estimation, reference GFR estimation and the local population characteristics. Hari, *et al.* [6], based on the regression analysis, found the value of k to be 0.42 in Indian children where the creatinine was estimated by kinetic Jaffe method and ^{99m}Tc-DTPA GFR was the reference GFR.

Cystatin-C based equations have been found to have better accuracy of predicting GFR, as compared to the creatinine based equations. The combined equations have generally been found to have better accuracy in the estimation, than individual equations [2]. In the current issue of Indian Pediatrics, Hari, *et al.* [7] prove that cystatin-C equations have better accuracy [7]. They also found that the combined cystatin-C and creatinine-based equation was not better than only cystatin-C or creatinine based equation. The strengths of the study are testing the equation in the GFR 60-90 mL/min/1.73m^2. Early detection of chronic kidney disease and monitoring of renal function deterioration requires an equation which works well in early stages of chronic kidney disease. Another strength of this study is its relevance for the pediatricians in India which can help in the current clinical practice. There is a need to have more studies in children and adolescents with an early chronic kidney disease, to enhance the use of these equations.

It is important for pediatricians to understand that children and adolescents with early chronic kidney disease and a well-maintained fluid and electrolyte balance, the urinalysis may be entirely normal. Therefore, a reduced GFR may serve as the only clinical sign of kidney damage. Early intervention in the course of renal impairment offers the best chance of preventing end stage renal disease in children. There currently exists no equation for monitoring acute changes in GFR [8]. However, the equations developed till now, may be able to determine longitudinal changes in GFR over time. The parameters used in the equation may be used on the locally available marker, which has been standardized according to the local laboratory.

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