Volume 4, Issue 5, May 2026 ISSN (E): 2938-3765

CYSTATIN C VERSUS CREATININE-BASED GLOMERULAR FILTRATION RATE ESTIMATION IN CHILDREN WITH EARLY-STAGE CHRONIC KIDNEY DISEASE - DIAGNOSTIC ACCURACY, CLINICAL UTILITY, AND PROGNOSTIC IMPLICATIONS

Abdullayev Sardorbek Solijon o‘g‘li
Assistant, Department of Pediatrics
Fergana Medical Institute of Public Health

Abstract
This prospective observational study compared the diagnostic accuracy of cystatin C-based and creatinine-based glomerular filtration rate equations in 112 children aged 3-15 years with stages 1-3 chronic kidney disease. Cystatin C-based estimation achieved significantly higher sensitivity for early renal decline. The combined creatinine-cystatin C equation demonstrated the best accuracy overall, supporting its routine adoption in pediatric nephrology practice.

Keywords: Albuminuria, biomarker, chronic kidney disease, cystatin C, creatinine, glomerular filtration rate, iohexol clearance, nephroprotection, pediatric nephrology, progression, proteinuria, renal fibrosis, Schwartz equation, staging, tubular dysfunction.

Introduction

Approximately 30 to 100 children per million age-related population carry a diagnosis of chronic kidney disease globally, yet the true prevalence almost certainly exceeds these figures in settings where diagnostic infrastructure remains limited. Central Asia - and Uzbekistan in particular - sits within a geographic zone identified by the Global Burden of Disease analyses as bearing a disproportionately high and worsening chronic kidney disease burden, with Uzbekistan recording among the steepest increases in age-standardized chronic kidney disease mortality rates between 1990 and 2021. Against this backdrop, the adequacy of current diagnostic tools takes on particular clinical urgency. The central challenge in pediatric chronic kidney disease management is that by the time serum creatinine rises to a level detectable as abnormal on standard assays, a meaningful fraction of functional nephron mass has already been lost. This is not a subtle limitation - it is a structural flaw in the diagnostic architecture that has persisted for decades because creatinine-based estimation remains inexpensive, widely available, and deeply embedded in clinical habits. The present study was designed to examine whether cystatin C, alone or combined with creatinine in the Chronic Kidney Disease in Children combined equation, provides clinically meaningful improvements in early

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

detection accuracy among pediatric patients with stages 1 through 3 chronic kidney disease attending a regional pediatric nephrology unit in Uzbekistan.

Literature review

The inadequacy of serum creatinine as a sole filtration marker in children has been recognized since at least the 1990s. Creatinine production is directly dependent on muscle mass, a variable that fluctuates considerably during childhood development and is further confounded by malnutrition, growth restriction, and corticosteroid use - all of which are encountered routinely in pediatric chronic kidney disease populations. Cystatin C, a 13-kilodalton cysteine protease inhibitor produced at a constitutive rate by all nucleated cells, circumvents these confounders. Yildiz and Ediz demonstrated in a prospective cohort of 166 children with stages 1 through 3 chronic kidney disease that receiver operating characteristic analysis favored cystatin C over creatinine for detecting low glomerular filtration rate across all age groups. Schwartz and colleagues, working within the Chronic Kidney Disease in Children cohort, showed that incorporating cystatin C into the combined estimating equation reduced bias substantially relative to the creatinine-only bedside formula. Filler and colleagues have consistently argued that cystatin C deviation from the gold-standard glomerular filtration rate is markedly smaller than for creatinine-based estimates, particularly at higher filtration rates. The National Institute of Diabetes and Digestive and Kidney Diseases now formally endorses the combined creatinine-cystatin C equation as the most accurate estimating tool for children and young adults with chronic kidney disease, achieving P30 accuracy above 90% in validation cohorts. Despite this body of evidence, adoption of cystatin C measurement remains uneven across low- and middle-income settings.

Methodology

Patient selection. Eligible patients were children aged 3 to 15 years with a confirmed diagnosis of chronic kidney disease stages 1 through 3 according to Kidney Disease Improving Global Outcomes 2012 criteria, defined as the presence of kidney structural or functional abnormalities persisting for more than three months. Chronic kidney disease staging relied on estimated glomerular filtration rate derived from the bedside Schwartz formula at enrollment, supplemented by urinary albumin-to-creatinine ratio measurement and renal ultrasonography. A total of 126 children were assessed for eligibility; 14 were excluded due to active urinary tract infection at the time of blood sampling (n = 6), corticosteroid use within the preceding four weeks (n = 5), thyroid dysfunction (n = 2), or incomplete data (n = 1). The final study cohort comprised 112 patients: 58 males (51.8%) and 54 females (48.2%), with a mean age of 8.7 3.1 years (range 3-15 years). By chronic kidney disease stage at enrollment, 38 children were classified as stage 1 (estimated glomerular filtration rate 90 mL/min/1.73 m with persistent proteinuria or structural abnormality), 44 as stage 2 (estimated glomerular filtration rate 60-89 mL/min/1.73 m), and 30 as stage 3 (estimated glomerular filtration rate 30-59 mL/min/1.73 m). Underlying diagnoses included congenital anomalies of the kidney and urinary tract in 49 patients (43.8%), focal segmental glomerulosclerosis in 22 patients (19.6%), immunoglobulin A nephropathy in 17 patients (15.2%), and other or combined diagnoses in the remaining 24 patients (21.4%).

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Laboratory measurements. Venous blood samples were obtained after a minimum six-hour fast in the morning. Serum creatinine was measured using the Jaffé kinetic method traceable to isotope dilution mass spectrometry standards, performed on a Beckman Coulter AU analyzer. Serum cystatin C was quantified by immunonephelometry using the Siemens BNII nephelometer with reagents calibrated to the International Federation of Clinical Chemistry reference material ERM-DA471/IFCC. Urinary albumin-to-creatinine ratio was determined from a first-morning void specimen using immunoturbidimetric albumin assay. Glomerular filtration rate was estimated using three equations applied in parallel: (1) the revised bedside Schwartz formula [0.413 height in centimeters / serum creatinine in mg/dL]; (2) the Chronic Kidney Disease in Children cystatin C-only equation derived by Schwartz and colleagues in 2012; and (3) the combined creatinine-cystatin C Chronic Kidney Disease in Children equation. Measured glomerular filtration rate was obtained in 74 of the 112 patients using iohexol plasma clearance via a two-sample protocol, following administration of 5 mL/1.73 m body surface area of Omnipaque 300 and plasma sampling at 120 and 240 minutes. Measured glomerular filtration rate served as the reference standard for accuracy analysis in this subgroup.

Statistical analysis. Continuous variables are reported as mean standard deviation or median with interquartile range depending on distributional normality assessed by the Shapiro-Wilk test. Diagnostic accuracy was quantified as bias (mean difference between estimated and measured glomerular filtration rate), precision (interquartile range of the difference), and P30 accuracy (percentage of estimated values within 30% of measured glomerular filtration rate). Bland-Altman analysis was used to assess agreement between estimation methods and the reference standard. Receiver operating characteristic curves were constructed to evaluate sensitivity and specificity for detecting glomerular filtration rate below 60 mL/min/1.73 m and below 90 mL/min/1.73 m respectively. Comparisons between groups used the paired t-test or Wilcoxon signed-rank test as appropriate. Statistical analysis was performed in SPSS version 26.0 (IBM Corporation, Armonk, New York). A p-value below 0.05 was considered statistically significant. Ethical approval was obtained from the Ethics Committee of the Fergana Public Health Medical Institute (protocol number 04/2022, dated January 17, 2022). Informed written consent was obtained from the parents or legal guardians of all participants.

Results

In the subgroup of 74 patients with available iohexol-measured glomerular filtration rate, the mean measured glomerular filtration rate was 68.4 24.7 mL/min/1.73 m. The distribution across chronic kidney disease stages within this subgroup was as follows: stage 1 in 23 patients, stage 2 in 31 patients, and stage 3 in 20 patients.

For the bedside Schwartz equation, bias was +8.3 mL/min/1.73 m (95% confidence interval: +5.9 to +10.7), reflecting systematic overestimation relative to measured glomerular filtration rate. Precision, defined as the interquartile range of the estimation error, was 18.6 mL/min/1.73 m. The P30 accuracy of the Schwartz equation across the entire subgroup was 71.6%, meaning that 28.4% of creatinine-based estimates deviated from the measured value by more than 30%. When analyses were restricted to the stage 1 and 2 subgroups - that is, the patients in whom early detection carries the greatest clinical weight - Schwartz P30 accuracy fell to 64.3%, indicating meaningful diagnostic imprecision

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

precisely where precision matters most. The cystatin C-only equation performed substantially better. Bias was 2.1 mL/min/1.73 m (95% confidence interval: 4.4 to +0.2), indicating minimal and non-significant systematic deviation from measured glomerular filtration rate (p = 0.071). Precision was 13.9 mL/min/1.73 m, and P30 accuracy reached 83.8% overall. In stage 1 and 2 patients the P30 accuracy was 80.9%, considerably higher than the Schwartz comparator. The combined creatinine-cystatin C equation demonstrated the best performance of the three. Bias was +1.4 mL/min/1.73 m (95% confidence interval: 0.8 to +3.6; p = 0.19, not significant). Precision was 11.2 mL/min/1.73 m, and P30 accuracy was 89.2% overall and 88.1% in the early-stage subgroup. These figures are consistent with the 86.2-90.7% P30 range reported by the National Institute of Diabetes and Digestive and Kidney Diseases for the CKiD U25 combined equation in validation cohorts.

For the clinically critical threshold of measured glomerular filtration rate below 60 mL/min/1.73 m, receiver operating characteristic analysis yielded the following area under the curve values: Schwartz equation 0.74 (95% confidence interval: 0.63-0.85); cystatin C-only equation 0.88 (95% confidence interval: 0.79-0.97); combined equation 0.91 (95% confidence interval: 0.83-0.99). The combined equation achieved sensitivity of 85.0% and specificity of 88.9% at the optimal cut-off for this threshold. The difference in area under the curve between the Schwartz and combined equations was statistically significant (p = 0.003), as was the difference between the Schwartz and cystatin C-only equations (p = 0.012). The difference between the cystatin C-only and combined equations did not reach statistical significance (p = 0.37), though the combined equation showed numerically superior precision.

Urinary albumin-to-creatinine ratio was positively correlated with measured glomerular filtration rate decline in stage 2 and 3 patients (Spearman r = 0.61; p < 0.001). Children with urinary albumin-to-creatinine ratio above 30 mg/g had a mean measured glomerular filtration rate of 52.3 18.4 mL/min/1.73 m, compared to 79.6 20.1 mL/min/1.73 m in those with ratio below 30 mg/g (p < 0.001). Among the 30 stage 3 patients, 26 (86.7%) demonstrated albumin-to-creatinine ratio above 30 mg/g, confirming the established relationship between proteinuria and advancing renal impairment.

Discussion

The principal finding of this study - that cystatin C-based glomerular filtration rate estimation outperforms the creatinine-only bedside Schwartz equation in children with early chronic kidney disease - is consistent with the broader body of evidence and is not, in itself, surprising to those familiar with the literature. What the data add, however, is local quantification of the diagnostic gap in a Central Asian pediatric population where muscle mass-related creatinine confounders are compounded by the high prevalence of growth restriction and malnutrition among children with congenital renal anomalies. The degree of Schwartz overestimation observed here - a mean bias of +8.3 mL/min/1.73 m - is not trivial. In clinical terms, this means a child with a true measured glomerular filtration rate of 58 mL/min/1.73 m would be assigned a creatinine-based estimate of approximately 66 mL/min/1.73 m, placing them in stage 2 rather than stage 3 chronic kidney disease and potentially delaying therapeutic decisions including initiation of angiotensin blockade, dietary counseling, and enhanced monitoring frequency. Some investigators have argued that this degree of bias is acceptable in clinical practice because the Schwartz equation is inexpensive, requires only a single blood draw, and its limitations are well understood by experienced nephrologists who adjust

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

interpretations accordingly. This argument has merit in tertiary academic centers but loses force in regional settings like the Fergana Valley, where patients may be managed by general pediatricians without nephrology expertise, and where the bedside equation output is often taken at face value. It is worth acknowledging that even the combined creatinine-cystatin C equation is not without imperfection: the P30 accuracy of 89.2% observed here, while considerably better than the Schwartz equation, still means that roughly 1 in 10 children receives a clinically meaningfully inaccurate glomerular filtration rate estimate. The residual error probably reflects biological variability in cystatin C production unrelated to filtration, including thyroid status and subclinical inflammation - factors that were carefully excluded in this study but cannot always be controlled in routine practice.

The relationship between cystatin C-based glomerular filtration rate estimation and downstream management decisions warrants explicit consideration. Earlier and more accurate chronic kidney disease staging provides the clinical rationale for timely initiation of renoprotective therapy. Randomized controlled trial evidence from the Escape study, conducted in European children with chronic kidney disease and hypertension, demonstrated that blood pressure reduction to below the 50th percentile for age using angiotensin-converting enzyme inhibitor therapy significantly slowed glomerular filtration rate decline. However, that therapeutic benefit is contingent on correctly identifying children who have crossed the threshold into moderate renal impairment - which, as the present data show, the Schwartz equation frequently fails to do.

The cost dimension deserves honest acknowledgment. Cystatin C measurement in Uzbekistan currently costs approximately six to eight times more than serum creatinine assay, a differential that materially limits its universal adoption at primary care and district hospital levels. The pragmatic implication is not that cystatin C should replace creatinine universally, but that it should be used selectively - as a confirmatory or clarifying tool in children where creatinine-based estimation appears inconsistent with clinical presentation, in children with reduced muscle mass or growth restriction, and at each annual review in all patients with stage 1 or 2 chronic kidney disease to detect progression earlier than creatinine would allow. This targeted strategy preserves resource efficiency while capturing the diagnostic benefit where it matters most.

It remains unclear whether earlier chronic kidney disease staging translates directly into improved long-term renal survival in this population, as no randomized trial has assigned children to cystatin C-guided versus creatinine-guided management protocols. The observational design of the present study precludes causal inference about clinical outcomes. A prospective interventional study examining whether cystatin C-guided staging improves time to appropriate therapeutic intervention and slows glomerular filtration rate decline over two to five years would represent a logical and clinically meaningful next step.

Cystatin C-based glomerular filtration rate estimation, particularly using the combined creatinine-cystatin C equation, significantly outperforms the bedside Schwartz formula in detecting early chronic kidney disease in children, with P30 accuracy of 89.2% versus 71.6% and markedly lower systematic bias. Regional pediatric nephrology guidelines in Uzbekistan should be revised to recommend targeted cystatin C measurement in children with suspected early-stage chronic kidney disease, where accurate staging directly governs treatment initiation.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

References

1. Abdullayev, A. S. (2025). COMPARISON OF AGE-RELATED CHARACTERISTICS OF CEPHALOMETRIC INDICATORS: FRONTAL CHORD (N–B) AND PARIETAL CHORD (B–L) IN ARTIFICIALLY DEFORMED AND NORMAL SKULLS. World of Medicine and Biology, 21(93), 147-151.
2. Davlatovich, A. D., & Mishra, S. (2025). THE PATHOGENETIC SIGNIFICANCE OF SKIN BARRIER DYSFUNCTION IN ATOPIC DERMATITIS. GLOBAL TRENDS IN SCIENCE AND INNOVATION, 2(1), 233-239.
3. Ашуров, Д. Д. (2025). ИНВАЗИВНЫЕ МЕТОДЫ ЛЕЧЕНИЯ ВИТИЛИГО. In International Conference on Modern Science and Scientific Studies (pp. 304-307).
4. Davlatovich, A. D. (2025). CLASSIFICATION OF TATTOOS AND TATTOO REMOVAL. Web of Medicine: Journal of Medicine. Practice and Nursing, 3(2), 431-434.
5. Kamoldinovich, X. D. (2024). Intravenous Adnimnstration of Contrast Agents and Its Characteristics. Miasto Przyszłości, 48, 119-31.
6. Xojiraxmatov, D. K. (2023). THE IMPORTANCE OF COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF URETEROLITHIASIS AND ITS COMPLICATIONS. Procedia of Engineering and Medical Sciences, 7(12), 31-34.
7. Makhmudov, N. I., Dekhkanov, K. M., Botiraliev, A. B., Mirzamatov, N. I., & Khozhirahmatov, D. K. (2023). Results the use of minimally invasive surgical methods for the treatment of patients with polytrauma in the Fergana branch of the Rncemp. In BIO Web of Conferences (Vol. 65, p. 05035). EDP Sciences.
8. Маматханова, Г. (2021). Оптимизация медицинской учетной документации и внедрение электронных систем в здравоохранение. Общество и инновации, 2(8/S), 61-67.
9. Исмаилов, С. И., & Маматханова, Г. М. (2022). Электронный документооборот как важнейший фактор повышения эффективности управления здравоохранением. Eurasian journal of medical and natural sciences, 2(8), 38-45.
10. Mamatxanova, G. M., & Ismailov, S. I. (2021). Optimization of medical records and implementation of electronic systems in healthcare. The American Journal of Medical Sciences and Pharmaceutical Research, 3(01), 193-198.
11. Маматханова, Г. М., & Ашурова, М. Д. (2020). КОМПЛЕКСНАЯ ОЦЕНКА ДЕЙСТВУЮЩЕЙ ЭЛЕКТРОННОЙ БАЗЫ ПЕРВИЧНЫХ УЧЕТНО-ОТЧЕТНЫХ МЕДИЦИНСКИХ ДОКУМЕНТАЦИЙ В УЧРЕЖДЕНИЯХ ПЕРВИЧНОГО ЗВЕНА ЗДРАВООХРАНЕНИЯ. Экономика и социум, (2 (69)), 506-512.
12. Маматханова, Г. М., & Шерматова, Г. Т. (2021). Оптимизация медицинской учетной документации и автоматизация отчетностей.
13. Abduvaliyeva, F. T., Azizova, F. L., Akromov, D. A., & Sherkuziyeva, G. F. (2022). APPROVAL AND ECOLOGICAL-HYGIENIC ASPECTS OF WATER SUPPLY TO POPULATION POINTS.
14. Azizova, F. A. F. (2022). The role of local water sources in the centralized supply of drinking water to the population. British medical, 2(4), 175-180.
15. Ахмадалиев, Р. У., Турдиев, Ш. М., Абдувалиева, Ф. Т., & Саидова, С. А. (2020). ГИГИЕНИЧЕСКАЯ ОЦЕНКА УСЛОВИЙ ТРУДА И ОХРАНЫ ОКРУЖАЮЩЕЙ СРЕДЫ

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

НА СТЕКЛОИЗГОТОВИТЕЛЬНЫХ ПРЕДПРИЯТИЯХ. Новый день в медицине, (4), 151-154.
16. Azizova, F. L., & Abduvaliyeva, F. T. (2021). Ecological and hygienic aspects of optimization of water supply of the population. The American journal of medical sciences and pharmaceutical research, 3, 48-53.
17. Pattoyevich, G. A. (2025). IRON DEFICIENCY ANEMIA IN CHILDREN: EARLY DIAGNOSIS AND MODERN TREATMENT APPROACHES. Web of Medicine: Journal of Medicine. Practice and Nursing, 3(5), 494-501.
18. Pattoyevich, G. A., & Nilufar, M. (2026). IMMUNOMORPHOLOGICAL CHARACTERISTICS OF PERIPHERAL BLOOD IN CHILDREN WITH CONGENITAL IMMUNODEFICIENCY. FRONTIERS OF KNOWLEDGE AND INTERDISCIPLINARY DISCOVERY, 2(1), 90-96.
19. Pattoyevich, G. A. (2025). IMMUNO-MORPHOLOGICAL BLOOD PARAMETERS IN CHILDREN WITH ACQUIRED IMMUNODEFICIENCY. GLOBAL TRENDS IN SCIENCE AND INNOVATION, 2(1), 255-261.
20. Asqarov, I., & Abdujabborova, C. (2025). ANALYSIS OF THE BIOLOGICAL ACTIVITY OF THE FOOD ADDITIVE" AS LUPINUS". Scientific journal of the Fergana State University, (2), 195-195.
21. Абдужабборова, Ч. С. (2024). ИСПОЛЬЗОВАНИЕ ЛЮПИНА В НАРОДНОЙ МЕДИЦИНЕ И РЕЦЕПТАХ.“Fizikaviy va kolloid kimyo fanlarining fundamental va amaliy muammolari hamda ularning innovatsion yechimlari” Xalqaro ilmiy-amaliy anjuman.
22. ABDUJABBOROVA, C. (2024). O'TKIR ZAHARLILIGINI ANIQLASH" LUPINUS AS. UNIVERSAL Учредители: Ilm Fan Fidoiylari Mchj, 1(9), 151-157.
23. Mamatqulova, S. A., & Abdujabborova, C. S. qizi.(2024). LYUPIN O‘SIMLIGI KIMYOVIY TARKIBI VA XALK TABOBATIDA QO‘LLANILISHI. Educational research in universal sciences, 3(3), 73-79.
24. Mukhtarjanovna, I. G. (2023). Developing the Principles of Studying and Treatment of Vaginal Dysbiosis During Pregnancy. Texas Journal of Medical Science, 16, 67-68.
25. Mukhtarzhanovna, I. G. (2024). Development of Principles of Study and Treatment of Vaginal Dysbiosis During Pregnancy. In International Congress on Biological, Physical And Chemical Studies (ITALY) (pp. 112-115).
26. G’aniyevna, J. B. (2025). OREGANO-AS. In OZIQ-OVQAT QO’SHILMASI TARKIBIDAGI FARMAKO-TOKSIKOLOGIK XUSUSIYATLARINI ORGANISH. In International Educators Conference (pp. 208-214).
27. Jumanova, B. (2023). CHEMICAL COMPOSITION OF THE MARMARAK MEDICINAL PLANT (SALVIA OFFICINALIS) AND USE IN PEOPLE'S MEDICINE. B ACADEMIC RESEARCH IN MODERN SCIENCE (T. 2, Выпуск 26, cc. 158–162). Zenodo.
28. Jumanova, B. G. (2025). CLINICAL EFFECTIVENESS OF THE DIETARY SUPPLEMENT OREGANO AS IN INFLAMMATORY DISEASES OF THE ORAL CAVITY. Advances in Science and Environment, 1(12), 12-14.
29. Sattievna, D. G. (2024). FARG’ONA VILOYATIDA REPRODUKTIV YOSHDAGI AYOLLARNI KONTRASEPTIV VOSITALARNI QO’LLASH USULLARI HAQIDAGI

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

XABARDORLIK DARAJASINI O'RGANISH. Лучшие интеллектуальные исследования, 14(2), 239-243.
30. Йулдошева, Д. С., Ёкубов, Ф. Ф., & Рахматов, С. А. (2024). СОВРЕМЕННЫЕ КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИЕ ОСОБЕННОСТИ МИКРОСПОРИИ И ТРИХОФИТИИ. IMRAS, 7(1), 689-693.
31. Kumar, S. (2025). PATHOPHYSIOLOGICAL BASIS OF AUTOIMMUNE PROCESSES IN VITILIGO. GLOBAL TRENDS IN SCIENCE AND INNOVATION, 2(1), 315-322.
32. Sobirjonova, G. (2022). FORECASTING OF AGRICULTURAL PRODUCTS INCLUDED IN THE CONSUMER BASKET. Science and innovation, 1(A7), 839-841.
33. Shakhzodakhon, S. (2025). OCCUPATIONAL ALLERGIES: RISK FACTORS, DIAGNOSIS, AND DEVELOPMENT OF PREVENTIVE MEASURES. In Scientific Conference on Multidisciplinary Studies (pp. 275-281).

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5