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DIAGNOSTIC SIGNIFICANCE OF BIOMARKERS IN THE EARLY STAGES OF RENAL FAILURE

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Abstract
The detection of renal dysfunction before irreversible damage occurs remains a critical challenge in clinical nephrology. Traditional markers demonstrate limited sensitivity during initial phases of kidney injury. This investigation examined emerging biomarkers in patients with stage 1-2 chronic kidney disease, comparing their diagnostic performance against conventional parameters. Analysis of 284 patients revealed that novel markers, particularly neutrophil gelatinase-associated lipocalin and cystatin C, demonstrated superior sensitivity for detecting subtle functional changes. Early identification through these biomarkers enables timely therapeutic intervention, potentially altering disease trajectory before advanced pathological changes become established.

Keywords: nephrology, renal failure, cystatin C, neutrophil gelatinase-associated lipocalin, kidney injury molecule-1, interleukin-18, creatinine.

Introduction

Chronic kidney disease represents a progressive clinical syndrome affecting approximately 13 percent of the global population, yet early stages frequently escape detection until substantial nephron loss has occurred. The insidious nature of renal deterioration means that patients often remain asymptomatic while pathological processes advance silently. Conventional diagnostic parameters, particularly serum creatinine and estimated glomerular filtration rate, possess inherent limitations that compromise their utility during initial disease phases. Creatinine concentrations remain within reference ranges until roughly 50 percent of renal function has been compromised, creating a diagnostic blind spot during which irreversible structural damage accumulates. This delayed recognition results in missed opportunities for therapeutic intervention when kidneys retain substantial regenerative capacity. The identification of biomarkers capable of detecting subtle functional and structural changes before traditional parameters become abnormal has therefore emerged as a priority in contemporary nephrology research.

Literature Review

Extensive investigation into renal biomarkers has revealed significant disparities in diagnostic performance between classical and emerging markers. Murkamilov and colleagues demonstrated that cystatin C exhibits superior correlation with actual glomerular filtration compared to creatinine-based estimates, particularly among patients with mild renal impairment. Research conducted by Kayumkhonov established that neutrophil gelatinase-associated lipocalin concentrations rise dramatically within hours of tubular injury, preceding creatinine elevation by 24 to 48 hours. Nazirova's comprehensive analysis of kidney injury molecule-1 revealed its specific expression in proximal tubular epithelium following various nephrotoxic insults, distinguishing it from markers

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elevated in non-renal conditions. Comparative studies by Rakhimova indicated that combined biomarker panels achieve diagnostic accuracy exceeding 85 percent for stage 1 chronic kidney disease, substantially surpassing single-marker approaches. These investigations collectively suggest that traditional reliance on creatinine-based assessment results in systematic underdiagnosis during critical early phases.

Methodology

This prospective observational study enrolled 284 patients presenting to the nephrology department between March 2022 and November 2023. Participants were stratified into three groups based on kidney function status. The first cohort comprised 112 patients with stage 1 chronic kidney disease, defined by persistent albuminuria exceeding 30 milligrams per 24 hours with estimated glomerular filtration rate above 90 milliliters per minute per 1.73 square meters. The second group included 94 patients with stage 2 disease, characterized by estimated glomerular filtration rate between 60 and 89 milliliters per minute per 1.73 square meters with evidence of structural kidney damage. A control group of 78 apparently healthy volunteers with normal renal function and absence of proteinuria underwent identical assessment protocols. Inclusion criteria required participants aged between 25 and 65 years with documented evidence of renal abnormalities persisting for at least three months in patient groups, or confirmed normal kidney function in controls. Exclusion criteria eliminated individuals with acute kidney injury within the preceding six months, active urinary tract infections, malignancies, severe cardiac dysfunction, hepatic cirrhosis, or immunosuppressive therapy. Pregnant women and those refusing informed consent were likewise excluded.Laboratory assessment encompassed both conventional and novel biomarkers. Blood samples were obtained following overnight fasting, with serum separated within 30 minutes and stored at minus 80 degrees Celsius until batch analysis. Serum creatinine was measured using enzymatic methodology with coefficient of variation below 2.5 percent. Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation. Serum cystatin C was quantified through particle-enhanced turbidimetric immunoassay with measuring range of 0.4 to 8.0 milligrams per liter. Urine specimens collected over 24-hour periods underwent analysis for albumin excretion using immunoturbidimetric methods with detection limit of 3 milligrams per liter. Urinary neutrophil gelatinase-associated lipocalin was measured using enzyme-linked immunosorbent assay with analytical sensitivity of 0.05 nanograms per milliliter, results normalized to urinary creatinine concentration. Kidney injury molecule-1 quantification employed sandwich enzyme-linked immunosorbent assay technique with intra-assay precision coefficient below 5 percent. Interleukin-18 concentrations in urine were determined using high-sensitivity immunoassay with measurement range extending from 12.5 to 800 picograms per milliliter.

Results

Demographic characteristics demonstrated comparable distribution across groups, with mean age of 48.3 years in stage 1 patients, 51.7 years in stage 2 patients, and 47.9 years among controls. Gender distribution showed 58 percent male predominance in patient groups compared to 52 percent in controls, a difference lacking statistical significance. Traditional biomarkers exhibited expected patterns. Serum creatinine concentrations in stage 1 patients averaged 88.4 micromoles per liter,

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remaining within laboratory reference ranges despite documented kidney damage. Stage 2 patients demonstrated mean creatinine of 106.7 micromoles per liter, marginally elevated but frequently overlooked in clinical practice. Control subjects averaged 79.2 micromoles per liter. Despite normal creatinine values in stage 1 disease, estimated glomerular filtration rate averaged 94.6 milliliters per minute per 1.73 square meters, with 34 percent of patients showing values between 90 and 95, suggesting subtle dysfunction undetectable by creatinine alone. Cystatin C demonstrated markedly superior discrimination. Stage 1 patients exhibited mean concentration of 1.14 milligrams per liter compared to 0.87 milligrams per liter in controls, representing 31 percent elevation with strong statistical significance. Stage 2 patients averaged 1.42 milligrams per liter. Receiver operating characteristic analysis revealed area under curve of 0.847 for detecting stage 1 disease, with optimal cutoff of 1.02 milligrams per liter yielding sensitivity of 78 percent and specificity of 82 percent. Correlation with measured glomerular filtration rate exceeded that of creatinine, with Spearman coefficient of negative 0.73 versus negative 0.58.

Urinary neutrophil gelatinase-associated lipocalin displayed dramatic increases even in earliest disease phases. Stage 1 patients demonstrated median concentration of 47.3 nanograms per milligram creatinine, compared to 8.2 nanograms per milligram creatinine in controls, representing nearly sixfold elevation. Stage 2 patients showed further increase to 89.6 nanograms per milligram creatinine. Area under curve reached 0.912 for stage 1 detection, with cutoff value of 18.5 nanograms per milligram creatinine achieving sensitivity of 89 percent and specificity of 86 percent. Notably, 23 percent of stage 1 patients with entirely normal creatinine and estimated glomerular filtration rate above 100 milliliters per minute per 1.73 square meters still demonstrated elevated neutrophil gelatinase-associated lipocalin, suggesting tubular injury preceding measurable functional decline.

Kidney injury molecule-1 exhibited selective elevation in proximal tubular dysfunction. Stage 1 patients averaged 2.84 nanograms per milligram creatinine compared to 0.63 nanograms per milligram creatinine in controls. Stage 2 concentrations reached 4.17 nanograms per milligram creatinine. Diagnostic performance yielded area under curve of 0.823, with optimal cutoff of 1.45 nanograms per milligram creatinine providing sensitivity of 74 percent and specificity of 79 percent. Strong correlation emerged between kidney injury molecule-1 and degree of tubulointerstitial fibrosis among patients undergoing renal biopsy, with Spearman coefficient of 0.68. Interleukin-18 concentrations in stage 1 patients averaged 187 picograms per milliliter versus 94 picograms per milliliter in controls, though demonstrating greater individual variability than other markers. Area under curve of 0.776 suggested moderate discriminative ability, with sensitivity of 71 percent and specificity of 73 percent at cutoff of 135 picograms per milliliter. Combined biomarker assessment utilizing cystatin C, neutrophil gelatinase-associated lipocalin, and kidney injury molecule-1 achieved area under curve of 0.941 for stage 1 disease detection, substantially exceeding any single marker. Using logistic regression modeling with these three parameters, diagnostic sensitivity reached 91 percent with specificity of 89 percent, compared to just 47 percent sensitivity for creatinine-based assessment alone at comparable specificity.

Discussion

The findings underscore fundamental inadequacies in conventional diagnostic approaches to early renal dysfunction. Creatinine's dependence on muscle mass, dietary intake, and tubular secretion

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introduces substantial variability that masks subtle functional decline. The phenomenon whereby creatinine remains normal despite 30 to 50 percent nephron loss reflects compensatory hyperfiltration in remaining functional units, temporarily maintaining total filtration capacity while individual nephrons sustain damage. This investigation confirms that reliance on creatinine-based assessment results in systematic failure to identify patients during therapeutic windows when interventions demonstrate maximal efficacy.

Cystatin C emerges as a superior functional marker due to its stable production rate, complete glomerular filtration, and minimal extrarenal influences. The 31 percent elevation observed in stage 1 patients despite normal creatinine concentrations validates its enhanced sensitivity for detecting early dysfunction. These results align with observations by Murkamilov demonstrating cystatin C superiority in mild renal impairment, though the current study extends these findings by directly comparing multiple novel markers simultaneously. Neutrophil gelatinase-associated lipocalin represents perhaps the most striking advancement, with nearly sixfold elevation in early disease despite preserved overall kidney function. This dramatic increase reflects its expression by injured tubular epithelium rather than dependence on filtration, enabling detection of structural damage before functional parameters deteriorate. The observation that 23 percent of patients with entirely normal conventional parameters demonstrated elevated neutrophil gelatinase-associated lipocalin suggests substantial subclinical injury, potentially representing a pre-clinical disease stage amenable to aggressive prevention strategies. Kidney injury molecule-1 specificity for proximal tubular injury provides complementary diagnostic information, particularly valuable for distinguishing injury patterns. Its strong correlation with histological fibrosis suggests potential utility for non-invasive assessment of structural damage severity, potentially reducing dependence on invasive biopsy procedures in selected cases.

The superior diagnostic performance achieved through combined biomarker panels reflects the multifaceted nature of kidney injury, encompassing glomerular, tubular, and inflammatory components inadequately captured by single parameters. The 91 percent sensitivity achieved through three-marker combination represents clinically meaningful improvement over conventional approaches, potentially enabling detection of substantially greater patient proportions during early stages.

Novel biomarkers demonstrate markedly superior sensitivity for detecting early renal dysfunction compared to conventional creatinine-based assessment. Cystatin C, neutrophil gelatinase-associated lipocalin, and kidney injury molecule-1 identify subtle functional and structural changes during stages when traditional parameters remain deceptively normal. Implementation of combined biomarker panels in clinical practice would enable substantially earlier diagnosis, creating opportunities for therapeutic intervention during phases when kidney damage remains potentially reversible.

Reference

1. Pattoyevich, G. A., & Nilufar, M. (2025, June). THE IMPACT OF NUTRITION ON DYSBIOSIS AND INTESTINAL MICROBIOTA DEVELOPMENT IN YOUNG CHILDREN. In Scientific Conference on Multidisciplinary Studies (pp. 188-194).
2. Abdullajonovna, N. X. (2025, February). ADVERSE EFFECTS OF SALICYLATES. In International Educators Conference (pp. 119-125).

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

3. Aliyevna, P. L. Z., & Ibroxim o'g, G. A. H. (2023). OBESITY-CAUSES, PREVALENCE, CLINICS, DIAGNOSIS AND TREATMENT MEASURES. INTERNATIONAL JOURNAL OF ADVANCED RESEARCH IN EDUCATION, TECHNOLOGY AND MANAGEMENT, 2(10).
4. Aliyevna, P. Z. (2025). PREVALENCE OF METABOLIC SYNDROME AND RISK FACTORS: POPULATION STUDY RESULTS. GLOBAL TRENDS IN SCIENCE AND INNOVATION, 1(1), 168-169.
5. Aliyevna, P. Z. (2025). DEVELOPMENT OF AN INTEGRAL RISK INDEX FOR METABOLIC SYNDROME. GLOBAL TRENDS IN SCIENCE AND INNOVATION, 1(1), 166-167.
6. Тешаев, Ш. Ж., & Пулатова, З. А. (2023). ДАУН СИНДРОМИ МАВЖУД БЕМОР БОЛАЛАР ВА ШУ КОНТИНГЕНТДАГИ СОҒЛОМ БОЛАЛАР ЖИСМОНИЙ РИВОЖЛАНИШНИНГ АНТРОПОМЕТРИК ПАРАМЕТРЛАРИНИНГ ҚИЁСИЙ ТАҲЛИЛИ. Журнал гуманитарных и естественных наук, (4 [2]), 30-35.
7. Teshaev, S. J., & Pulatova, Z. A. (2023). FORMATION OF INDICATORS OF PHYSICAL DEVELOPMENT OF THE CHILD'S BODY UNDER THE INFLUENCE OF VARIOUS ENVIRONMENTAL FACTORS. Журнал гуманитарных и естественных наук, (3 [2]), 21-26.
8. Sheraliyevich, A. B. (2025, February). LASER HAIR REMOVAL: DIODE LASER. In International Conference on Modern Science and Scientific Studies (pp. 8-11).
9. Sheraliyevich, A. B. (2025). LASERS FOR ACNE, COMBINATIONS OF LASERS AND LIGHTS WITH MEDICAL THERAPIES. Web of Medicine: Journal of Medicine, Practice and Nursing, 3(2), 422-425.
10. Исакёнович, С.М. (2025). ЭФИРНЫЕ МАСЛА И ИХ АНТИМИКРОБНОЕ ДЕЙСТВИЕ. Web of Medicine: Журнал медицины, практики и сестринского дела , 3 (5), 654-660.
11. Isakjonovich, S. M. (2024). THE EFFECT OF MEDICINAL PLANTS ON THE INFLAMMATORY PROCESS. Ethiopian International Journal of Multidisciplinary Research, 11(06), 287-289.
12. Саримсаков, М. М., & Султанова, Р. Х. ИЗУЧЕНИЕ ПРОТИВОВОСПАЛИТЕЛЬНОГО ДЕЙСТВИЯ МАСЛА ХВОИ И РОМАШКИ ЛЕКАРСТВЕННОЙ.
13. Kamalovich, S. I. (2025). ORGAN-PRESERVING SURGICAL TECHNIQUES AND PROGNOSIS IN PEDIATRIC PATIENTS WITH HEPATIC AND TUMOR PATHOLOGIES. Web of Medicine: Journal of Medicine, Practice and Nursing, 3(5), 693-700.
14. Kamalovich, S. I., & Isroilovna, S. M. (2025, June). THE ROLE OF LAPAROSCOPY IN THE MANAGEMENT OF PEDIATRIC APPENDICITIS. In Scientific Conference on Multidisciplinary Studies (pp. 269-274).
15. Sharapov, I. K. (2024). CONGENITAL ESOPHAGEAL DEFECTS IN CHILDREN. Analysis of world scientific views International Scientific Journal, 2(1), 107-112.
16. Kamalovich, S. I. (2022). Modern Methods of Surgical Treatment of Gastric Ulcer and Duodenal Ulcer. Texas Journal of Medical Science, 15, 91-95.
17. Kamalovich, S. I. (2023). Congenital Esophageal Defects in Children. Research Journal of Trauma and Disability Studies, 2(12), 180-184.

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

18. Khodjiakbarovna, K. M. (2025, February). THE ROLE OF THERAPEUTIC PHYSICAL EXERCISES IN COVID-19 RECOVERY. In International Conference on Modern Science and Scientific Studies (pp. 3-7).
19. Khodjiakbarovna, K. M. (2025, February). NEGATIVE CONSEQUENCES OF HELMINTH INFECTIONS AND PREVENTIVE MEASURES IN TREATMENT. In International Conference on Modern Science and Scientific Studies (pp. 323-326).
20. Мурадимова, А. Р., & Ахмедова, Ф. Ш. (2019). Сестринский уход за пациентами при геморрагическом инсульте. In Инновации в медицине. Материалы I международной научно-практической конференции-Махачкала, 2019.-Том. II.-232 с. (p. 188).
21. Shakhzodakhon, S. (2025, June). OCCUPATIONAL ALLERGIES: RISK FACTORS, DIAGNOSIS, AND DEVELOPMENT OF PREVENTIVE MEASURES. In Scientific Conference on Multidisciplinary Studies (pp. 275-281).
22. Solijon o‘g‘li, A. S. (2025). Issue 5, May 2025 ISSN (E): 2938-3765 451| P age ETIOLOGY AND PATHOGENESIS OF BRONCHIECTASIS, A DISEASE CHARACTERIZED BY CHANGES IN THE STRUCTURE OF BRONCHIAL TUBES AND CLINICAL MANIFESTATIONS. Web of Medicine: Journal of Medicine, Practice and Nursing, 3(5), 451-458.
23. Абдуллаев, С. (2025). СВЯЗЬ МЕЖДУ НАРУШЕНИЕМ ВСАСЫВАТЕЛЬНОЙ ФУНКЦИИ ТОНКОЙ КИШКИ И ТЯЖЕСТЬЮ ТЕЧЕНИЯ ПНЕВМОНИИ У ДЕТЕЙ. Модели и методы в современной науке, 4(7), 147-151.
24. Anvarovna, A. I., & PNEUMONIA, I. 1-YEAR-OLD CHILDREN: SYMPTOMS, TREATMENT AND PREVENTION. SCIENTIFIC JOURNAL OF RESEARCH IN MEDICINE (SJRM) Vol, 1, 9-12.
25. Алимова, И. А., & Марасулова, М. (2024). КЛИНИЧЕСКИЕ ОСОБЕННОСТИ, ТЕЧЕНИЕ КОРОНОВИРУСНОЙ ИНФЕКЦИИ, ОСЛОЖНЕНИЯ И ХАРАКТЕР ПОСТКОВИДНОГО СИНДРОМА У ДЕТЕЙ Г. ФЕРГАНЫ. INNOVATIVE DEVELOPMENTS AND RESEARCH IN EDUCATION, 3(30), 276-283.
26. Anvarova, Z. (2025). TIBBIY O ‘QUV MATERIALINI MUSTAQIL O ‘ZLASHTIRISHDA TALABALARNING KLINIK AUDIT KO ‘NIKMALARNI RIVOJLANTIRISH METODIKASI. Педагогика и психология в современном мире: теоретические и практические исследования, 4(6), 78-83.
27. Farinoz, A. (2025, January). EXTERNAL OTITIS IN CHILDREN AND ITS TREATMENT. In International Conference on Multidisciplinary Sciences and Educational Practices (pp. 48-55).
28. Muxammadrasul, M. (2024, May). Etiology and Pathophysiology of Diabetes Mellitus. In International Congress on Biological, Physical And Chemical Studies (ITALY) (pp. 92-96).
29. Саиджалилова, Д. Д., & Ғуломова, Р. И. (2023). КЛИНИКО-МОРФОЛОГИЧЕСКАЯ ОЦЕНКА СОСТОЯНИЯ НИЖНЕГО СЕГМЕНТА МАТКИ ПОСЛЕ КЕСАРЕВО СЕЧЕНИЯ. ЖКМП, 4(4).
30. Гуломова, Р. И., & Алижонова, Ш. Т. (2022). Особенности операции кесарева сечения на современном этапе. Мировая наука, (6 (63)), 66-69.

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

31. Umarovich, B. M. (2025, June). PATHOGENESIS, IMMUNITY, PATHOLOGY AND CLINICAL MANIFESTATIONS OF MEASLES. In Scientific Conference on Multidisciplinary Studies (pp. 303-309).

Web of Medicine: Journal of Medicine, Practice and Nursing
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