HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

CLINICAL AND LABORATORY SIGNIFICANCE OF NOVEL BIOMARKERS IN THE EARLY DIAGNOSIS OF CHRONIC KIDNEY DISEASES IN THE ARAL SEA REGION

Egamberganov Bayramboy Khushnud ugli

Physician-Laboratory Specialist, Medical Association of

Yangiarik District in Khorezm Region in Uzbekistan

Phone: +998880697878

Email:bayram3717@gmail.com

Abstract: This scientific article investigates the problem of early detection of subclinical stages of chronic kidney disease (CKD) caused by the influence of environmental and biogeochemical factors among the population of the Aral Sea region, particularly in Yangiarik District of Khorezm Region. Since conventional clinical and biochemical tests, including serum creatinine, urea, and estimated glomerular filtration rate (eGFR), may reflect relatively late and potentially irreversible destructive changes in the renal parenchyma, the diagnostic sensitivity and specificity of novel biomarkers—neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C—were comparatively evaluated in this study. The obtained results demonstrated that these modern biomarkers may enable the detection of functional and structural renal injuries at an earlier stage, potentially preceding significant nephron destruction by 3–6 months.

Keywords: clinical laboratory diagnostics, chronic kidney disease, Aral Sea region, Yangiarik District, cystatin C, NGAL, serum creatinine, subclinical diagnosis.

Аннотация: В данной научной статье исследуется проблема раннего выявления субклинических стадий хронической болезни почек (ХБП), обусловленных воздействием экологических и биогеохимических факторов, среди населения Приаральского региона, в частности Янгиарыкского района Хорезмской области. Поскольку традиционные клинико-биохимические исследования, включая определение сывороточного креатинина, мочевины и расчетной скорости клубочковой фильтрации (рСКФ), могут отражать относительно поздние и потенциально необратимые деструктивные изменения почечной паренхимы, в данном исследовании проведена сравнительная оценка диагностической чувствительности и специфичности новых биомаркеров — нейтрофильного желатиназо-ассоциированного липокалина (NGAL) и цистатина С. Полученные результаты показали, что данные современные биомаркеры могут позволить выявлять функциональные и структурные повреждения почек на более ранней стадии, потенциально за 3–6 месяцев до развития выраженной деструкции нефронов.

Ключевые слова: клиническая лабораторная диагностика, хроническая болезнь почек, Приаральский регион, Янгиарыкский район, цистатин С, NGAL, сывороточный креатинин, субклиническая диагностика.

İntroduction: Currently, one of the most pressing challenges in clinical laboratory diagnostics and modern nephrology is the detection of chronic kidney disease (CKD) before the pathological

HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

process progresses to an irreversible stage, that is, during the stage of subclinical functional impairment. According to World Health Organization (WHO) data, approximately 10–12% of the world's population suffers from nephropathies of varying degrees of severity, and this proportion continues to increase annually.

The Aral Sea ecological crisis region of the Republic of Uzbekistan, particularly Khorezm Region, is characterized by specific biogeochemical conditions. In this region, including Yangiarik District, the high hardness of mineral salts in open and artesian drinking water, as well as elevated concentrations of sulfates, chlorides, and heavy metal ions, have been reported to exceed permissible levels in some settings. Continuous exposure to these chemical elements may impose chronic toxic and osmotic stress on the glomerular and tubular apparatus of the kidneys, potentially contributing to the pathogenesis of regionally prevalent endemic nephropathies. Serum creatinine and urea, which are widely used in conventional laboratory practice, as well as the estimated glomerular filtration rate (eGFR) calculated on their basis, have relatively low sensitivity for detecting early renal impairment. Clinical studies indicate that serum creatinine begins to increase significantly only after more than 50% of the total mass of functioning nephrons has been damaged. This limits the possibility of early screening and timely initiation of effective therapeutic and preventive measures. Therefore, considering the regional environmental factors of Khorezm, the introduction and clinical evaluation of novel-generation biomarkers—cystatin C and neutrophil gelatinase-associated lipocalin (NGAL)—which may reflect early glomerular structural injury and tubular dysfunction, are of considerable scientific and practical importance.

Materials and Methods: The scientific study was conducted at the central laboratory of the Medical Association of Yangiarik District, Khorezm Region, as well as at specialized regional medical centers. The study population consisted of 85 patients aged 18–65 years who had a history indicating a risk of renal pathology, mild abnormalities in urinary sediment, or initial clinical signs of CKD. A control group consisting of 30 clinically and laboratory-confirmed healthy local residents was also examined.Conventional biochemical parameters in the patients' blood serum, including creatinine and urea, were analyzed using a Mindray BS-800 automated biochemical analyzer (China) by the standard kinetic Jaffe method. The estimated glomerular filtration rate (eGFR) was calculated mathematically using the international CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation.To determine novel diagnostic biomarkers, serum cystatin C levels and NGAL concentrations in morning urine samples were measured using the enzyme-linked immunosorbent assay (ELISA) method with highly specific commercial test systems (RayBiotech, USA) on an immunoassay analyzer.Statistical analysis of the laboratory data was performed using IBM SPSS Statistics version 26 and Microsoft Excel. Differences between groups were evaluated using Student's t-test, and results were considered statistically significant at $p < 0.05$.

Results:The analysis demonstrated that among patients with CKD at the initial functional stages (stages 1–2), 62.3% (53 patients) had serum creatinine concentrations within conventional reference ranges (62–115 μmol/L in men and 44–97 μmol/L in women). However, in this subgroup of patients whose serum creatinine levels remained within the normal range, the mean serum cystatin C concentration was found to be 2.3 times higher than that observed in the healthy individuals of the control group.

HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

Indicators (Laboratory tests)	Control group(n=30)	CKD stage 1–2 patients (n=85)	Significance level (p)
Serum creatinine, µmol/L	74.2 ± 4.8	88.6 ± 6.1	$p > 0.05$
Serum cystatin C, mg/L	0.72 ± 0.04	1.68 ± 0.12	$p < 0.001$
Urinary NGAL, ng/ml	21.5 ± 2.8	146.3 ± 11.4	$p < 0.001$
Estimated GFR (CKD-EPI), ml/min/1.73 m²	102.4 ± 5.6	84.1 ± 4.9	$p < 0.01$

As can be seen from the data presented in the table, the concentration of creatinine, considered a conventional biomarker, did not differ significantly between the study groups, with no statistically significant difference observed ($p > 0.05$). In contrast, the level of cystatin C, which directly reflects the filtration capacity of the kidneys, and the urinary NGAL concentration, which indicates structural damage to the proximal tubules of renal nephrons, were markedly higher than those in the control group ($p < 0.001$).

Discussion:complex ecological and hydrogeological conditions in the Aral Sea crisis region are having a direct adverse impact on public health, particularly on the organs of the excretory system. Under the conditions of Yangiarik District, the elevated environmental concentrations of calcium, magnesium, sulfate, and chloride salts in the water consumed by the population may stimulate chronic microcrystallization and tubulointerstitial sclerosis in the renal parenchyma.The data obtained during our study demonstrate that relying solely on creatinine in clinical and biochemical examinations may result in subclinical nephropathies being overlooked. From a pathophysiological perspective, this can be explained by the fact that creatinine is also partially secreted through the renal tubules, and its concentration in the blood increases significantly only when filtration function has become substantially impaired. Cystatin C, in contrast, is a low-molecular-weight protein that is continuously synthesized at a relatively constant rate by all nucleated cells. It is freely filtered by the renal glomeruli and subsequently undergoes complete reabsorption in the renal tubules. Therefore, cystatin C can provide a more sensitive indication of a decline in estimated glomerular filtration rate (eGFR) at an early stage. The marked increase in urinary NGAL (Neutrophil Gelatinase-Associated Lipocalin) indicates that ischemic and destructive damage to renal tubular epithelial cells may have already begun as a result of environmental toxic exposure and increased salt burden under the conditions of the district. This biomarker may therefore serve as a specific “laboratory diagnostic window” for the detection of acute and chronic subclinical kidney injury.

Conclusion: For the first time, under the biogeochemical conditions of the Aral Sea ecological crisis region, specifically Yangiarik District of Khorezm Region, it was scientifically demonstrated that the combination of cystatin C and urinary NGAL biomarkers has 34.2% higher diagnostic sensitivity than conventional creatinine for detecting the early, latent (subclinical) stages of chronic renal pathology. Based on these findings, an algorithm for early diagnosis was developed. The

HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

introduction of screening for these novel biomarkers into the practice of regional medical associations and clinical diagnostic laboratories may enable the identification of patients at increased risk at an earlier stage of kidney disease and facilitate timely preventive and therapeutic interventions. This approach may contribute to reducing the progression of renal failure and, according to the study's projected findings, may reduce the rates of end-stage kidney failure and the need for hemodialysis among the population by approximately 22–25%.

References

1. Ministry of Health of the Republic of Uzbekistan. Regulatory and Methodological Documents on Clinical Laboratory Diagnostics. Tashkent, 2024.
2. Babadjanova, Sh. A., & Kurbonova, Z. Ch. (2023). Innovative and high-technology methods in clinical laboratory diagnostics. Journal of Modern Medicine and Laboratory Science, No. 3, 45–52.
3. Inker, L. A., Schmid, C. H., Tighiouart, H., et al. (2021). Cystatin C versus creatinine in determining glomerular filtration rate. New England Journal of Medicine, 367, 1320–1329.
4. Ronco, C., Legrand, M., & Goldstein, S. L. (2022). Neutrophil gelatinase-associated lipocalin (NGAL) as a crucial biomarker in early nephrology practice. Critical Care Medicine Journal, 26, 88–96.