REVIEW ARTICLE

# Cellular and functional renal injury and disease biomarkers: A literature review

Laura McPherson, Alexander A. Berlin, Shannon Wright

**McPherson L, Berlin AA, Wright S. Cellular and functional renal injury and disease biomarkers: A literature review. J Kidney Treat Diagn. 2022; 5(4):45-47.**

**ABSTRACT**

Biomarkers can be used to evaluate exposure to potentially harmful chemicals, their impact on organ function, or a person's susceptibility to a decline in organ function. They are defined as molecules in biological samples that are utilised as indicators of organ function. The kidneys are frequently exposed to a variety of medications and substances, and disorders like diabetes frequently result in renal function loss. This literature review includes results from clinical and experimental animal investigations on biomarkers that were published in 2021 and early 2022, concentrating on five subjects: 1) Diabetic kidney disease progression and severity; 2) severity and prognosis of Acute Kidney Injury (AKI) and chronic kidney disease (CKD); 3) conversion of AKI to CKD; 4) severity and prognosis of Renal Cell Carcinoma (RCC); and 5) identification of nephrotoxic drug and environmental chemical exposure.

**Key Words:** *Acute kidney injury (AKI); Chronic Kidney Disease (CKD); Diabetic Kidney Disease (DKD); Proteomics and metabolomics; Renal Cell Carcinoma (RCC); Chemically induced nephrotoxicity*

## INTRODUCTION

The present efforts to identify and apply biomarkers for assessing kidney function losses caused by illnesses, exposure to environmental toxins, or therapeutic medications whose efficacy is dose-limited by nephrotoxicity are the main subject of this study. It's crucial to start by giving some definitions to set the scene. Acute Kidney Injury (AKI), Chronic Renal Disease, and biomarker are examples of terms or processes that need definitions (CKD). It's also critical to recognise how the reactions of renal cells to pathological or disease states and exposures to nephrotoxic medicines or other substances are comparable. As a result, even though there will be a strong emphasis on clinical conditions like Diabetic Kidney Disease (DKD), the knowledge collected from such work will be pertinent and offer insights into biomarkers for nephrotoxicant exposure [1]. An indicator of a certain component of a biological reaction, a biomarker is a molecule that can be identified in biological samples like urine, plasma, serum, or tissue. Proteins that change in abundance or are covalently or chemically changed (for example, by oxidation), lipids that fluctuate in abundance or pattern, and different low-molecular-weight metabolites that may alter in abundance are examples of biomarkers. Here, the kidney is the main subject [2]. The three different kinds of biomarkers are impact biomarkers, exposure biomarkers, and susceptibility biomarkers. The biomarkers of effect are the most prevalent and accessible. These biomarkers are, by definition, chemicals that alter in quantity or form in response to alterations in organ function.Biomarkers of exposure are substances that show or prove that the targeted tissue has been exposed to a certain chemical. Contrary to the other two kinds of biomarkers, biomarkers of susceptibility are more diversified and frequently employed to denote increased sensitivity to the harmful consequences of a clinical condition or chemical exposure. In addition to proteins or metabolites, these biomarkers may also include social or dietary behaviours, comorbid diseases or chronic conditions, genetic polymorphisms, and others. The accepted or working definition of AKI is an increase of more than 0.3 mg/dL in less than 48 hours or more than 50% over the course of seven days. It is based on short-

*Editorial Office, Journal of Kidney Treatment and Diagnosis, Windsor, Berkshire, England*

*Correspondence: Shannon Wright, Editorial Office, Journal of Kidney Treatment and Diagnosis, Windsor, Berkshire, England, e-mail kidney@eclinicalsci.org*

*Received: 05-August-2022, Manuscript No. puljktd-22-5399; Editor assigned: 07-August-2022, PreQC No. puljktd-22-5399 (PQ); Reviewed: 14-August-2022, QC No. puljktd-22-5399 (Q); Revised: 17-August-2022, Manuscript No. puljktd-22-5399 (R); Published: 24-August-2022, DOI: 10.37532/ puljktd.22.5(4).45-47.*

term changes in Serum Creatinine (SCr). SCr is mostly linked to the glomerular filtration process and not directly to renal cellular injury or tissue damage when used to characterise AKI. SCr levels can therefore be thought of as a biomarker, but they are actually more of an operational or functional evaluation of kidney function. Although many types of AKI are reversible, there is some evidence that even moderate cases of reversible AKI can increase the risk of future episodes as well as the development of long-term kidney function reductions, or what is known as chronic kidney disease [3]. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines classify CKD as a disorder in kidney structure or function that lasts for at least three months and has consequences for one's health. The author lists diabetes mellitus (either type 1 or type 2), hypertension, and glomerulonephritis as the three most typical causes of CKD. Thus, the main types of CKD are membranous nephropathy, focal segmental glomerulosclerosis, lupus nephritis, immunoglobulin A nephropathy, and diabetic nephropathy (MN). With a global frequency of 11%–13%, CKD is a significant public health concern and a standalone risk factor for death, cardiovascular disease, and End-Stage Renal Disease (ESRD) [4]. Consequently, finding CKD biomarkers, they are especially helpful in determining prospective treatments and enhancing results because they can be used to categorise the disease's stage. This review and commentary's first objective is to examine recent advances in the identification and validation of numerous biomarkers for detecting the occurrence or severity of different types of kidney injury or illness as well as the progression of moderate to more serious or chronic conditions. Reviewing current progress in the identification and validation of biomarkers for the diagnosis and prognosis of diverse kinds of Renal Cell Carcinoma is the second objective (RCC). The third objective is to discuss recent work on discovering and validating biomarkers for exposure to various environmental contaminants and therapeutic medications whose efficacy is dose-limited by nephrotoxicity that the author and colleagues have done.

## REVIEW OF LITERATURE

A literature searches on kidney biomarkers turned up several articles, all of which were published in 2021 or early 2022 and included reviews, meta-analyses, and primary research investigations on both humans and animals. The extensive number of publications in a 14-month span (January 2021–February 2022) illustrates the interest in and translational significance of work on kidney biomarkers, even though the list of studies evaluated is by no means exhaustive [5]. Other than the ones mentioned above for SCr or Blood Urea Nitrogen (BUN), which are regularly assessed in clinical settings, there are no recognised standards unique to function as a biomarker in terms of quantitative criteria for validation of biomarkers. One would normally use a difference of 1.5 or 2.0-fold (if being more cautious) as a threshold for concluding a potential relationship between changing concentration and some impact or exposure for novel experimental biomarkers such as proteins or metabolites. Such a threshold is common in the domains of proteomics and metabolomics and is not just applicable to the assessment of possible biomarkers. Attempts to develop indicators to either detect severity of renal injury in diabetics or prognosis and likelihood of progression from moderate to more severe CKD in diabetic patients are two of the most popular areas of study in current kidney biomarker research. Because of the high prevalence of DKD, diabetes is the main cause of CKD and ESRD, making disease progression prevention in this population a crucial public health concern. Proteomics and metabolomics have been employed in several clinical investigations with plasma and/or urine samples from diabetic patients to discover biomarkers that may serve as indications of the severity of DKD or predictors of the progression from moderate to more severe CKD. For instance, researchers gathered 1513 individuals, including healthy adults, those with type 2 diabetes and DKD in the early stages and people with advanced DKD. The best indications of disease development, as with many other biomarker studies, were found to be a combination or battery of biomarkers in this investigation. Here, they state that the interaction between CD324 and 2-macroglobulin, cathepsin D, and predicted the course of DKD. During metabolomics research, they came to the conclusion that blood concentrations of glycerol-3-galactoside may serve as an independent diagnostic to predict DKD severity after discovering that abnormalities in galactose and glycerolipid metabolism were the most significantly altered metabolic pathways in DKD [6]. The author found that a combination of kidney injury molecule-1 (KIM-1), soluble tumor necrosis factor receptor-1 (sTNFR-1), and soluble tumor necrosis factor receptor-2 (sTNFR-2) were able to produce a sensitive and precise composite risk score to predict progression of kidney function decline in patients with type 2 diabetes and early-stage CKD. This composite risk score was based on plasma biomarkers and clinical parameters. A systematic analysis of 20 studies that found protein biomarkers in diabetic individuals was conducted by researchers. According to their findings, a panel of glomerular, inflammatory, and tubular biomarkers were identified. These included Angiopoietin-like 4 (*ANGPTL4*), 2-microglobulin, SMAD family member 1, and glypican-5 for glomerular disease, Monocyte Chemoattractant-1 (MCP-1) and adiponectin for inflammatory disease, and megalin, Vitamin D Binding Protein [VDBP], and mega However, they pointed out that the battery of proteins' predictive value was comparable to that of measures of albuminuria and Estimated Glomerular Filtration Rate (eGFR). The benefit of employing the panel of proteins instead of the more conventional techniques of assessment is how the kidneys work. Another study of patients found that higher plasma levels of KIM-1, TNFR-1, TNFR-2, MCP-1, Soluble Urokinase-type Plasminogen Activator Receptor (suPAR), and YKL-40 (a heparin- and chitin-binding glycoprotein) were associated with an increased risk for DKD progression. This study used a well-characterized subpopulation of diabetic patients with mild-to-moderate kidney disease from. Additionally, low-molecular-weight intermediary metabolite patterns in plasma or urine that can act as precise biomarkers have been discovered using metabolomics [7,8]. The author discovered that in type 1 and type 2 diabetes individuals, alterations in the patterns of arginine and tryptophan metabolites were connected to sharp drops in eGFR and rises in albuminuria. It is not surprising that this study found a variety of metabolites given the complexity and heterogeneity of the metabolome. Another metabolomic investigation, especially focusing on the citric acid cycle and related intermediates, tried to discover biochemical patterns linked with early-stage DKD. Lower levels of organic acids from the citric acid cycle, particularly methyl- and ethylmalonate, were found to be possible biomarkers for kidney damage in the early stages of DKD. Different RNA species have also attracted interest as possible biomarkers, in addition to proteins and low-molecular-weight metabolites. The scientists found urine mRNAs that could predict the severity and development of kidney disease in DKD patients with biopsy-proven disease using the public Gene

Expression Omnibus (GEO) library. In order to reflect varying levels of CKD and predict poor renal outcomes in DKD patients, the scientists identified 30 DKD-specific mRNAs and created an urine mRNA signature. Biomarker research have increasingly centered on microRNAs (miRNAs) rather than mRNAs in recent years. In a sample of 180 type 2 diabetic patients and 180 healthy controls, the authors primarily focused on the association between blood concentrations of miR-29a and DKD severity and risk for disease progression. They discovered that the development and progression of DKD was connected to serum miR-29a and cystatin C concentrations [9]. The evaluation of genetic predisposition was a final recent study on biomarkers for DKD onset or progression that used a completely different approach. The researchers searched for pertinent single nucleotide polymorphisms using a 70-gene bespoke target Next-Generation Sequencing Panel (SNPs). They discovered that RGMA (Repulsive Guidance Molecule BMP Co-Receptor A) rs1969589 CC genotype correlates with lower albumin-to-creatinine ratios in DKD patients and that MYH9 (Myosin p) rd710181 is inversely linked with DKD risk. No particular biochemical route was singled out by the authors as being particularly impacted by genetic diversity in DKD, highlighting the complexity of the genetic factors that affect the progression of diabetes illness. A rapid decline in kidney function is known as AKI. AKI can occur with a range of severity and can be brought on by a wide variety of substances and clinical conditions. There is an urgent need to find and validate more sensitive biomarkers that can detect losses in kidney function at an early stage and before these losses become significant and irreversible. Clinically used biomarkers, such as those used to measure eGFR, albuminuria, and urine output, are well-established in detecting large declines in kidney function. The results of several recent studies that used a variety of methodologies and concentrated on various classes of chemicals as possible biomarkers are summarized [10].

## CONCLUSION

The main finding from a review of these studies is that biomarkers, even those belonging to the same type of molecule, can be used for a variety of functions, including detecting exposure to an agent (such as a chemical or drug), detecting effects on kidney function, estimating renal disease prognosis, estimating risk for renal disease progression (for example, from AKI to CKD), and predicting susceptibility to renal injury from disease or exposures. Although diabetes is a prevalent underlying cause of renal illness, finding biomarkers that specifically predict AKI or CKD that is connected to diabetes rather than other underlying diseases or chemical exposures may be of interest. Numerous biomarkers that have been demonstrated to be helpful for DKD severity or DKD progression are also helpful for other types of AKI or CKD. Some biomarkers have only been found to be associated with diabetes-related AKI or CKD. Just by chance, investigations utilizing cohorts of diabetic people or experimental animals with DKD discovered the biomarkers.

## REFERENCES


1. Fuentes Calvo, C Cuesta, S M Sancho Martínez et al. Biomarkers of persistent renal vulnerability after acute kidney injury recovery. Science Rep, 11 (2021),. 21183
2. S Liu, Y Gui, M S Wang, et al. Serum integrative omics reveals the landscape of human diabetic kidney disease. Mol Metabol, 54 (2021), 101367
3. R Sauriasari, D D Safitri, N U Azmi. Current updates on protein as biomarkers for diabetic kidney disease: a systematic review. Ther. Adv. Endocrinol. Metab., 12 (2021),. 1-13
4. S W Waijer, T Sen, C Arnott, et al. Heerspink. Association between TNF receptors and KIM-1 with kidney outcomes in early-stage diabetic kidney disease. Clin J Am Soc Nephrol, 17 (2022), pp. 251-59
5. Q Jin, R C W Ma. Metabolomics in diabetes and diabetic complications: insights from epidemiological studies. Cells, 10 (2021), 2832 [CrossRef] [Google Scholar]
6. Y H Lee, J W Seo, M Kim, et al. Urinary mRNA signatures as predictors of renal function decline in patients with biopsy-proven diabetic kidney disease. Front Endocrinol, 12 (2021),774436
7. Q Liu, M Wang, T Xu, et al. Significance of serum miR-29a in the occurrence and progression of diabetic nephropathy: a cross-sectional study. J Clin Lab Anal, 28 (2021), Article e24210
8. M Zhang, Y Zhang, M Wu et al. Importance of urinary mitochondrial DNA in diagnosis and prognosis of kidney diseases. Mitochondrion, 61 (2021),. 174-78
9. S Sun, Z Liu, C Chen et al. Serum fibroblast growth factor 23 for early detection of acute kidney injury in critical illness. Am J Transl Res, 13 (2021), 12141- 51
10. I Sandokji, J H Greenberg. Plasma and urine biomarkers of CKD: a review of findings in the CKiD study. Semin Nephrol, 41 (2021),. 416- 26