Abstract

Biomarkers are molecules that can be measured in the body and can reflect disease activity or progression. They can be used to diagnose and monitor disease, predict treatment response, and identify potential therapeutic targets. Several types of biomarkers have been studied in the context of IgA nephropathy, including protein, gene expression, epigenetic, and microRNA biomarkers. Biomarkers have the potential to improve the accuracy and specificity of the diagnosis of IgA nephropathy and predict the disease progression and response to treatment. However, further studies are needed to validate their diagnostic value in larger cohorts of patients and to integrate them into clinical practice. The development of multi-omics approaches that combine different types of biomarkers may provide a more comprehensive understanding of the disease pathogenesis and potential treatments.

Keywords: IgA nephropathy, End-stage renal disease, Chronic kidney disease, Hematuria, Biomarkers, Diabetic nephropathies


Copyright © 2023 The Author(s); Published by Nickan Research Institute. This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Immunoglobulin A (IgA) nephropathy is a common type of glomerulonephritis, which also known as Berger's disease, is a chronic kidney disease contributing to 20-40% of primary glomerular diseases, especially in Asian populations (1). IgA nephropathy is characterized by the deposition of IgA immune complexes in the mesangial region of glomeruli, leading to inflammation and progressive fibrosis. The primary clinical manifestation of IgA nephropathy is gross hematuria with or without proteinuria, but it can also produce asymptomatic microscopic hematuria and slowly progressive renal dysfunction (1,2).

The diagnosis of IgA nephropathy relies on a combination of clinical presentation, laboratory tests, histopathological examination, and exclusion of other kidney diseases (3,4). However, the accuracy and specificity of current diagnostic approaches have been limited, leading to a delay in the diagnosis and suboptimal treatment outcomes. Early diagnosis and intervention are crucial in preventing disease progression and preserving renal function. Biomarkers have emerged as a promising tool in the diagnosis and management of IgA nephropathy (5).

Several biomarkers have been investigated in the diagnosis and monitoring of IgA nephropathy. One of the most studied biomarkers is urinary protein excretion. Increased urinary protein excretion is a hallmark feature of IgA nephropathy and is used to monitor disease progression. However, proteinuria is not specific to IgA nephropathy and can also be present in other renal diseases (6).

Another promising biomarker is serum levels of galactose-deficient IgA1 (Gd-IgA1). Gd-IgA1 is a modified form of IgA1 that has been implicated in the pathogenesis of IgA nephropathy. Several studies have shown that serum Gd-IgA1 levels are elevated in patients with IgA nephropathy compared to healthy controls and other renal diseases. Furthermore, serum Gd-IgA1 levels have been shown to correlate with disease activity and histological findings on renal biopsy (7,8).

Serum levels of soluble urokinase-type plasminogen activator receptor (suPAR) have also been investigated as a potential biomarker in IgA nephropathy. suPAR is a marker of immune activation and inflammation and has been shown to predict the risk of disease progression in several renal diseases, including IgA nephropathy (9,10).

Other biomarkers that have been studied in IgA nephropathy include serum levels of complement components, such as C3 and C4, and markers of...
IgA nephropathy is a common form of glomerulonephritis that can lead to chronic kidney disease and end-stage renal disease. Several biomarkers have been investigated in the diagnosis and monitoring of IgA nephropathy. While urinary protein excretion remains, the most commonly used biomarker, serum levels of Cal-IgA1, suPAR, and other markers of immune activation, inflammation, and oxidative stress show promise in improving the diagnosis and management of IgA nephropathy. Further studies are needed to validate these biomarkers and determine their clinical utility in routine practice.

For this review, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ) and Embase, using different keywords including; IgA nephropathy, biomarkers, hematuria, mesangial area, prognosis, end-stage renal disease and chronic kidney disease.

Diagnosis of IgA nephropathy
IgA nephropathy is a relatively common chronic kidney disease, with an estimated prevalence of one in 1000 individuals. It typically affects young adults and can progress slowly over many years, leading to end-stage kidney disease in up to 30% of patients (13). Current treatment options for IgA nephropathy are limited and aimed at slowing disease progression and managing symptoms. IgA nephropathy occurs when an antibody called IgA forms immune complexes in the glomerular mesangial area. This can lead to inflammation and damage to the glomeruli, finally leading to reduced kidney function (3,14). The current diagnostic approach for IgA nephropathy involves a combination of clinical presentation, laboratory tests, and histopathological examination. However, the accuracy and specificity of these methods can be limited, leading to delays in diagnosis and suboptimal treatment outcomes (15,16).

Biomarkers in the IgA nephropathy
Protein biomarkers and several candidate biomarkers in IgA nephropathy have been extensively studied and identified, including serum creatinine, albuminuria, serum IgA, complement C3, C4, and activation products, and urinary levels of cytokines, chemokines, and growth factors (6,17). However, the specificity and sensitivity of these biomarkers have been variable, and their diagnostic value needs to be further validated in large-scale multicenter studies.

Gene expression biomarkers
Gene expression profiling has emerged as a promising tool for the diagnosis and monitoring of Immunoglobulin A nephropathy. Several studies have identified gene signatures that are associated with the disease progression and treatment response (18). For example, the upregulation of genes involved in the innate and adaptive immune response, such as IL-8, LCN2, and TLRs, has been associated with more severe disease. In contrast, the downregulation of genes involved in kidney function, such as nephrin and podocin, has been associated with kidney damage and poor prognosis (18,19).

Epigenetic biomarkers
Epigenetic modifications, such as DNA methylation and histone modifications, have been implicated in the pathogenesis of IgA nephropathy. Several studies have identified differential DNA methylation patterns in genes involved in immune regulation, mesangial cell proliferation, and fibrosis, suggesting their potential utility as diagnostic and prognostic biomarkers (20, 21).

MicroRNA biomarkers
MicroRNAs are small non-coding RNAs that regulate gene expression by targeting mRNA transcripts. Several studies have identified dysregulated microRNAs in IgA nephropathy, which are involved in the regulation of key pathways related to inflammation, fibrosis, and immune regulation. The identification of specific microRNAs as diagnostic and prognostic biomarkers may provide insights into the underlying pathogenesis and potential therapeutic targets (22).

Conclusion
In summary, biomarkers have the potential to improve the accuracy and specificity of the diagnosis of IgA nephropathy and predict the disease progression and response to treatment. However, their diagnostic value needs to be further validated in large-scale studies and integrated into clinical practice. The development of multi-omics approaches that combine different types of biomarkers, such as protein, gene expression, epigenetic, and microRNA biomarkers, may provide a more comprehensive and accurate picture of the disease pathogenesis and treatment response.

Authors' contribution
Conceptualization: RZ and AS.
Validation: RS.
Investigation: YKh and MB.
Resources: MA.
Data curation: EZ and RZ.
Writing-original draft: MA, RS, RZ, and MB.
Writing-review and editing: YKh, EZ, NSh, and AS.
Visualization: RS.
Supervision: AS.
Funding acquisition: All Authors.
## Conflicts of interest
The authors declare that they have no competing interests.

## Ethical issues
Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

## Funding/Support
None.

## References