

# Podocyte infolding glomerulopathy; current concepts



Azadeh Khayyat<sup>1</sup>, Mohammad Ali Esmail Pour<sup>2</sup>, Hamid Nasri<sup>3\*</sup>

<sup>1</sup>Pathology Department of Medical College of Wisconsin, Milwaukee, WI, USA

<sup>2</sup>Internal Medicine Department of UNC Health Blue Ridge, Morganton, NC, USA

<sup>3</sup>Nickan Research Institute, Isfahan, Iran

## Correspondence to:

Prof. Hamid Nasri, Email:  
hamidnasri@med.mui.ac.ir,  
hamidnasri@yahoo.com

**Received:** 15 Apr. 2023

**Accepted:** 15 July 2023

**ePublished:** 4 Aug. 2023

**Keywords:** Podocyte infolding glomerulopathy, Podocyte cytoskeleton, Renal insufficiency, Proteinuria, Renal failure, Nephrotic syndrome, Hypoalbuminemia, Edema, Hyperlipidemia

## Abstract

Podocyte infolding glomerulopathy is a rare form of glomerular disease that can lead to proteinuria, chronic kidney disease, and end-stage renal disease. While the cause of podocyte infolding glomerulopathy is currently unknown, it is thought to be related to abnormalities in the glomerular basement membrane (GBM) structure and function. In this condition, the podocytes fold inward and form pockets or invaginations. This can lead to damage and scarring of the glomeruli, impairing kidney function. Diagnosis is typically made through clinical and laboratory tests, and treatment focuses on managing symptoms and slowing the progression of chronic kidney disease. Further research is needed to understand the pathophysiology of podocyte infolding glomerulopathy better and develop more effective treatments for this condition. Symptoms of podocyte infolding glomerulopathy may include proteinuria, hematuria, and decreased kidney function. Treatment options may include medications to control blood pressure and reduce proteinuria and immunosuppressive therapy to reduce inflammation and slow the progression of kidney damage.

**Citation:** Khayyat A, Esmail Pour MA, Nasri H. Podocyte infolding glomerulopathy; current concepts. J Prev Epidemiol. 2023;x(x):e35221. doi: 10.34172/jpe.2023.35221.



## Introduction

Podocyte infolding glomerulopathy is a newly described condition form of glomerular disease that is characterized by the infolding of podocytes (specialized cells that form the outer layer of the kidney's filtering units) into the underlying glomerular basement membrane (GBM) (1,2). This condition can cause proteinuria, leading to chronic kidney disease and end-stage renal disease (2). This article will review the current understanding of podocyte infolding glomerulopathy, including its epidemiology, clinical presentation, pathophysiology, diagnosis, and treatment. The exact cause of podocyte infolding glomerulopathy is unknown, but it is believed to be related to genetic mutations that affect the structure and function of the podocytes. Most cases with podocyte infolding glomerulopathy have an underlying autoimmune disorder like rheumatoid arthritis, lupus nephritis, mixed connective tissue disease, Sjögren syndrome, and autoimmune thyroiditis (2).

## Search strategy

For this review, we conducted a comprehensive search using various databases: PubMed,

## Key point

Podocyte infolding glomerulopathy is a rare renal disease that presents with nephrotic syndrome and is characterized by the accumulation of folded podocytes within the GBM. Podocyte infolding glomerulopathy is considered on kidney biopsy by infolding or protrusion of podocyte cytoplasm into the GBM, across with intramembranous cytoplasmic microspherules or microtubules.

Google Scholar, Directory of Open Access Journals (DOAJ), Web of Science, EBSCO, Scopus, and Embase. We utilized different keywords such as podocyte infolding glomerulopathy, podocyte cytoskeleton, renal insufficiency, proteinuria, renal failure, nephrotic syndrome, hypoalbuminemia, edema, hyperlipidemia, end-stage renal disease, renal biopsy, glomerular basement membrane, chronic kidney disease, hematuria, and hypertension.

## Epidemiology of podocyte infolding glomerulopathy

Podocyte infolding glomerulopathy is rare, with only a few cases reported in the literature. It has been described in individuals of all ages but appears more common in

males than females (3).

### Clinical presentation of podocyte infolding glomerulopathy

The clinical presentation of podocyte infolding glomerulopathy includes proteinuria, hematuria, and hypertension. In some cases, patients may also present with edema and renal insufficiency. Symptoms may be mild or severe, depending on the extent of podocyte infolding and GBM damage (2).

### Pathophysiology of podocyte infolding glomerulopathy

The exact cause of podocyte infolding glomerulopathy is currently unknown. However, it is thought to be related to abnormalities in the GBM structure and function, leading to gaps or spaces that allow podocytes to fold over and infold into the GBM. This process can damage podocytes and disrupt normal blood filtration in the kidneys, leading to proteinuria and other symptoms (2,4).

### Diagnosis of podocyte infolding glomerulopathy

The diagnosis of podocyte infolding glomerulopathy is typically made through clinical and laboratory tests. This may include a physical examination, blood tests, urine tests, and imaging studies such as ultrasound or magnetic resonance imaging (MRI). Sometimes, a kidney biopsy may be necessary to confirm the diagnosis and determine the extent of GBM damage (5,6).

### Treatment of podocyte infolding glomerulopathy

There is no specific treatment for podocyte infolding glomerulopathy. Instead, treatment is focused on managing the symptoms and slowing the progression of chronic kidney disease. This may include medications to control blood pressure, reduce proteinuria, and protect the kidneys from further damage. Dialysis or kidney transplantation may sometimes be necessary to treat end-stage renal disease (2,4,7,8).

### Conclusion

Podocyte infolding glomerulopathy is a rare renal disease that presents with nephrotic syndrome and is characterized by the accumulation of folded podocytes within the GBM. The pathogenesis of this condition remains unclear, but it is believed to be related to abnormalities in the podocyte cytoskeleton. Diagnosis requires a renal biopsy, while

treatment options are limited due to its rarity. Further research is needed to understand this condition better and develop effective treatment strategies.

### Authors' contribution

Conceptualization: HN.

Data curation: HN.

Investigation: HN.

Resources: HN.

Project management: HN.

Supervision: HN.

Validation: HN, AK.

Visualization: HN, AK.

Writing-original draft preparation: HN.

Writing-reviewing and editing: MAEP, AK.

### Ethical issues

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

### Conflicts of interest

The authors declare that they have no competing interests.

### Funding/Support

None.

### References

1. Matthai SM, Mohapatra A, Mathew AJ, Roy S, Varughese S, Danda D, et al. Podocyte Infolding Glomerulopathy (PIG) in a Patient With Undifferentiated Connective Tissue Disease: A Case Report. *Am J Kidney Dis.* 2018;72:149-153. doi: 10.1053/j.ajkd.2017.11.023.
2. Ting JA, Hung W, McRae SA, Barbour SJ, Copland M, Riaz M. Podocyte Infolding Glomerulopathy, First Case Report From North America. *Can J Kidney Health Dis.* 2021;8:20543581211048357. doi: 10.1177/20543581211048357.
3. Feng Y, Wang W, Zou Y, Chen T, Wang W, Li G, et al. Podocyte Infolding Glomerulopathy: A Case Series Report and Literature Review. *J Clin Med.* 2023;12:1088. doi: 10.3390/jcm12031088.
4. Kwon KW, Jeong HJ, Lee JH. Podocytic infolding glomerulopathy: A case report. *Ultrastruct Pathol.* 2016;40:374-377. doi: 10.1080/01913123.2016.1229703.
5. Bhowmick SS, Lang AE. Movement Disorders and Renal Diseases. *Mov Disord Clin Pract.* 2020;7:763-779. doi: 10.1002/mdc3.13005.
6. Wöstmann F, Müller RU, Göbel H, Benzing T, Becker JU, Bartram MP. Case report: a peculiar glomerulopathy in a patient suffering from nephrotic syndrome. *BMC Nephrol.* 2019;20:326. doi: 10.1186/s12882-019-1478-8.
7. Haruhara K, Kanzaki G, Tsuboi N. Nephrons, podocytes and chronic kidney disease: Strategic antihypertensive therapy for renoprotection. *Hypertens Res.* 2023;46:299-310. doi: 10.1038/s41440-022-01061-5.
8. Pugh D, Gallacher PJ, Dhaun N. Management of Hypertension in Chronic Kidney Disease. *Drugs.* 2019;79:365-379. doi: 10.1007/s40265-019-1064-1.