ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF ARTIFICIAL INTELLIGENCE

ISSN: 2692-5206, Impact Factor: 12,23
American Academic publishers, volume 05, issue 05,2025

Journal: https://www.academicpublishers.org/journals/index.php/ijai

KIDNEY STRUCTURAL AND FUNCTIONAL CHANGES IN EXPERIMENTAL ULCERATIVE COLITIS: MORPHOLOGICAL AND MORPHOMETRIC PERSPECTIVES

Kaymanova Kamila Imamovna

Bukhara state medical institute

https://orcid.org/0009-0004-7738-6578

kamila_kaymanova@bsmi.uz

Abstract: Ulcerative colitis (UC), a chronic inflammatory bowel disease, is primarily known for affecting the colonic mucosa; however, accumulating evidence points to significant extra-intestinal manifestations, including renal involvement. Experimental models of UC, particularly those induced by dextran sulfate sodium (DSS) and trinitrobenzene sulfonic acid (TNBS), have revealed notable morphological and morphometric alterations in kidney structure and function. These include glomerular hypertrophy or atrophy, interstitial fibrosis, tubular degeneration, and changes in renal volume and architecture. The underlying mechanisms are multifactorial and involve systemic inflammation, oxidative stress, immune-mediated injury, and renal ischemia. Morphometric analyses in these models serve as valuable tools to quantify kidney damage and correlate it with disease severity. Understanding the renal implications of UC is crucial for early diagnosis, prevention of long-term kidney complications, and development of targeted therapeutic strategies. This review consolidates current findings on morphological and morphometric kidney changes in experimental UC, highlighting both histopathological insights and potential clinical relevance.

Keywords: Ulcerative colitis; kidney; renal morphology; morphometry; experimental colitis; DSS model; TNBS model; glomerular damage; interstitial fibrosis; oxidative stress; systemic inflammation; renal dysfunction; animal models; extra-intestinal manifestations.

Introduction. Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) that primarily affects the colon and rectum. However, UC has been associated with various extra-intestinal manifestations, including renal dysfunction. While the gastrointestinal tract is the primary target, studies have increasingly noted changes in renal morphology and function in patients with UC. Animal models of UC, particularly those induced in laboratory settings, have provided valuable insights into these renal alterations. The pathophysiological mechanisms that link UC to kidney involvement remain an area of active research, and various studies have demonstrated both morphological and morphometric changes in the kidneys in experimental models of UC.

This review focuses on the available literature concerning the changes in kidney structure and function in experimental ulcerative colitis models, highlighting key findings and providing insight into potential mechanisms behind these alterations.

The systemic inflammation observed in UC patients is believed to be a major contributor to renal pathology. Pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6), which are elevated during UC

ISSN: 2692-5206, Impact Factor: 12,23
American Academic publishers, volume 05, issue 05,2025
Journal: https://www.academicpublishers.org/journals/index.php/ijai

flare-ups, can reach distant organs, including the kidneys, through the bloodstream (Torres et al., 2017). The kidneys, being highly vascular organs, are particularly susceptible to these systemic inflammatory signals.

Moreover, UC-related renal abnormalities extend beyond inflammation alone. In experimental models, renal changes can range from glomerular damage, interstitial fibrosis, and tubular alterations to altered kidney size and function (Iglesias et al., 2020). Renal fibrosis, a key feature of chronic kidney disease (CKD), has been observed in UC-induced models, often as a result of the inflammatory cascade and oxidative stress (Sleiman et al., 2017). These structural changes can lead to kidney dysfunction, manifesting as proteinuria, impaired glomerular filtration rate (GFR), and electrolyte imbalances (Singh et al., 2021).

ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF ARTIFICIAL INTELLIGENCE

ISSN: 2692-5206, Impact Factor: 12,23
American Academic publishers, volume 05, issue 05,2025

Journal: https://www.academicpublishers.org/journals/index.php/ijai

Morphological and Morphometric Kidney Changes in UC. The kidneys in experimental UC models show a wide range of morphological changes, which are indicative of the kidney's response to chronic systemic inflammation. Studies have noted alterations in kidney size, glomerular architecture, and tubular structure, often characterized by glomerulosclerosis, tubular dilation, and interstitial fibrosis (Liu et al., 2018; Alimohammadi et al., 2019). Morphometric analysis, which quantifies these structural changes, is a valuable tool in assessing the severity of kidney damage in UC models (Gao et al., 2020). These alterations can be used as biomarkers of kidney injury and provide insight into the extent of renal involvement in UC.

Mechanisms of Renal Damage in UC. Multiple mechanisms contribute to renal damage in UC. The most prominent of these include systemic inflammation, oxidative stress, renal ischemia, and endothelial dysfunction (Kant et al., 2018). The release of pro-inflammatory cytokines from the inflamed gut can stimulate the systemic immune response, which ultimately reaches the kidneys, exacerbating inflammation and fibrosis (Zhao et al., 2019). Oxidative stress, a key feature of UC, further compounds kidney injury by generating reactive oxygen species (ROS) that damage kidney cells and tissues (Sleiman et al., 2017). Additionally, renal ischemia, due to changes in renal vascular dynamics, is frequently observed in UC models and further contributes to renal damage (Zhu et al., 2021).

Experimental UC Models and Renal Pathophysiology. Experimental UC models, particularly those involving DSS and TNBS, offer valuable insights into how UC-related inflammation translates into renal pathology. DSS-induced colitis, for example, leads to systemic inflammation that impacts various organs, including the kidneys. Studies have shown that DSS treatment results in significant kidney changes such as glomerular hypertrophy, glomerulosclerosis, and tubulointerstitial fibrosis, all of which are observed in human UC (Gul et al., 2016). These experimental models also allow for the assessment of renal function using parameters such as urine protein levels, serum creatinine, and glomerular filtration rate, providing a comprehensive picture of kidney involvement in UC (Kant et al., 2018).

Clinical Relevance. Renal dysfunction is a clinically significant concern in UC patients, especially those with long-standing or severe disease. While the kidneys are not typically the focus of UC management, studies suggest that the renal consequences of UC may contribute to the overall burden of disease. Therefore, recognizing and understanding the renal implications of UC is crucial for early diagnosis, management, and prevention of kidney-related complications in UC patients. The exploration of potential therapeutic strategies to mitigate renal damage, such as antioxidants or anti-inflammatory agents, is an area of ongoing research (Sharma et al., 2019; Iglesias et al., 2020).

1. Morphological Changes in Kidneys in Experimental UC Models

Several experimental models of UC, including the use of chemicals like dextran sulfate sodium (DSS) or trinitrobenzene sulfonic acid (TNBS), have been used to simulate the condition and study its effects on the kidneys.

a. Renal Inflammation and Edema

- Studies have observed that experimental UC leads to increased renal inflammation. This is evidenced by a higher number of inflammatory cells (like neutrophils and macrophages) infiltrating the renal tissue. This inflammation results in renal edema, characterized by swelling of kidney tissue due to fluid accumulation.

ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF ARTIFICIAL INTELLIGENCE

ISSN: 2692-5206, Impact Factor: 12,23
American Academic publishers, volume 05, issue 05,2025

Journal: https://www.academicpublishers.org/journals/index.php/ijai

- Histopathological examinations of kidney sections from UC animal models show areas of congestion, glomerular atrophy, and interstitial nephritis. These changes suggest that the kidneys may be affected by systemic inflammation arising from UC.

b. Renal Fibrosis

- Fibrosis, or the excessive deposition of extracellular matrix components like collagen, has been reported in the kidneys of UC models. This is indicative of a chronic inflammatory state that may lead to scarring and impaired kidney function. Renal fibrosis is associated with alterations in glomerular and tubulointerstitial structures.
- In some models, there is evidence of tubular dilation and epithelial cell damage, further contributing to kidney dysfunction.

c. Glomerular Damage

- Experimental UC models often show glomerular hypertrophy or atrophy. Glomeruli, which are responsible for filtration, may experience structural changes due to inflammatory and fibrotic processes. The glomerular basement membrane may become thickened, which disrupts normal filtration and can lead to proteinuria.

d. Renal Blood Flow and Vascular Changes

- UC may lead to changes in renal vascularity, with some studies reporting altered renal blood flow. Vascular changes, including thickening of blood vessel walls and increased vascular resistance, can lead to impaired kidney perfusion.
- Renal ischemia due to vascular changes may exacerbate kidney injury, particularly in the context of inflammation and systemic stress.

2. Morphometric Changes in Kidneys in Experimental UC Models

Morphometry involves the quantitative analysis of organ structure, and in the context of UC, it provides detailed information on the extent of kidney damage.

a. Changes in Kidney Size

- Several studies have demonstrated reduced kidney size in UC models, possibly due to atrophic changes in renal parenchyma. This reduction in size correlates with the degree of inflammation and fibrosis observed in the kidneys.
- Renal weight has been measured in some studies as a marker of kidney damage, with a significant decrease noted in UC-induced models.

b. Glomerular and Tubular Measurements

- Morphometric analyses of glomeruli in UC models typically show alterations in glomerular volume and shape. There may be an increase in glomerular area, reflecting hypertrophy or compensatory enlargement due to damage.
- Similarly, tubular changes, such as dilatation or loss of brush border integrity, have been noted. These changes suggest impairment in renal tubular function, contributing to electrolyte and fluid imbalances.

c. Histomorphometric Indexes

- Some studies use histomorphometric indexes to assess kidney damage, such as the extent of glomerulosclerosis, tubulointerstitial fibrosis, and inflammation. These indexes help quantify the degree of kidney injury in response to UC.
- Increased collagen deposition in the interstitial space is a key morphometric indicator of fibrosis in UC models. Additionally, the proportion of glomeruli affected by sclerosis can be measured to assess the severity of glomerular damage.

ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF ARTIFICIAL INTELLIGENCE

ISSN: 2692-5206, Impact Factor: 12,23
American Academic publishers, volume 05, issue 05,2025

Journal: https://www.academicpublishers.org/journals/index.php/ijai

3. Mechanisms Underlying Renal Changes in UC Models

The mechanisms linking UC to renal changes are complex and involve both direct and indirect pathways:

a. Systemic Inflammation

- UC is characterized by chronic intestinal inflammation, which leads to the release of pro-inflammatory cytokines (such as TNF-α, IL-1, and IL-6) into the bloodstream. These cytokines can exacerbate inflammation in distant organs, including the kidneys.
- The kidney, being highly vascularized, is susceptible to these circulating pro-inflammatory mediators, leading to renal damage.

b. Oxidative Stress

- Oxidative stress plays a key role in the pathogenesis of UC and its associated renal damage. Free radicals generated in the inflamed gut may enter systemic circulation and reach the kidneys, contributing to oxidative damage in renal tissues. Increased levels of reactive oxygen species (ROS) can impair kidney cell function, leading to tubular necrosis, glomerular damage, and fibrosis.

c. Renal Ischemia

- The inflammation associated with UC may also cause systemic vasoconstriction, which reduces renal blood flow and can lead to ischemic damage. Ischemia and hypoxia further promote renal injury and fibrosis.

d. Altered Gut-Kidney Axis

- There is increasing recognition of the "gut-kidney axis," which highlights how changes in gut microbiota and intestinal permeability can influence kidney function. In UC, increased intestinal permeability (leaky gut) and dysbiosis (microbial imbalance) could contribute to kidney inflammation and damage through the immune system.

e. Endothelial Dysfunction

- The systemic inflammation and oxidative stress seen in UC may impair endothelial function. Endothelial cells play a crucial role in maintaining vascular integrity, and dysfunction can lead to increased vascular permeability, altered blood flow, and renal damage.

4. Renal Dysfunction in UC Models

Experimental studies have shown that the renal dysfunction observed in UC models can manifest as:

- **Proteinuria**: Increased protein excretion is a common sign of glomerular injury.
- **Renal Insufficiency**: Reduced glomerular filtration rate (GFR) and other signs of kidney insufficiency may be observed in UC models, reflecting impaired renal function.
- **Electrolyte Imbalances**: Due to tubular damage, alterations in sodium, potassium, and chloride balance can occur.

5. Potential Therapeutic Interventions

Given the kidney involvement in UC, several therapeutic approaches have been investigated in experimental models:

- **Antioxidant Therapies**: Antioxidants like N-acetylcysteine (NAC) have shown promise in reducing oxidative stress and ameliorating renal damage.

ISSN: 2692-5206, Impact Factor: 12,23
American Academic publishers, volume 05, issue 05,2025
Journal: https://www.academicpublishers.org/journals/index.php/ijai

- **Anti-inflammatory Agents**: Drugs targeting pro-inflammatory cytokines or inflammatory pathways have been used to reduce kidney injury in UC models.
- **Renal Protective Agents**: Agents that protect against fibrosis, such as angiotensin II receptor blockers (ARBs), may help reduce the progression of renal damage.

6. Conclusion. Experimental models of ulcerative colitis provide valuable insights into the renal changes associated with this disease. Morphological and morphometric alterations in the kidneys, such as inflammation, fibrosis, glomerular damage, and impaired tubular function, are consistently observed. These changes are thought to be mediated through systemic inflammation, oxidative stress, and renal ischemia, among other mechanisms. Understanding these renal alterations in UC may lead to better strategies for preventing or mitigating kidney damage in patients with this chronic condition. Further studies are needed to explore the precise mechanisms and develop targeted therapeutic interventions to protect kidney function in individuals with UC.

References:

1. Gul, H., Alimohammadi, M., & Arumugam, R. (2016). Morphological and functional alterations of the kidney in experimental ulcerative colitis. Journal of Renal Pathology, 22(4), 197-205.
2. Iglesias, M., Ziegler, K., & Aouad, R. (2020). Kidney fibrosis and damage in experimental colitis models: A morphometric and histopathological analysis. Nephrology Research, 58(5), 315-325.
3. Kant, S., Sharma, P., & Soni, A. (2018). Systemic inflammation and kidney involvement in experimental models of ulcerative colitis: Insights from animal studies. Inflammatory Bowel Diseases, 24(9), 2105-2112.
4. Liu, J., Zhang, X., & Chen, L. (2018). Effects of UC on kidney morphology and function: A detailed analysis of renal changes in a DSS-induced model of ulcerative colitis. Journal of Clinical Nephrology, 46(3), 282-291.
5. Sleiman, G., Daugherty, P., & Zou, Y. (2017). The role of oxidative stress in kidney injury in ulcerative colitis: A study in experimental models. Free Radical Biology and Medicine, 108, 244-251.
6. Sharma, P., Singh, D., & Yadav, A. (2019). Role of antioxidant therapies in alleviating kidney damage in ulcerative colitis. Renal Medicine, 32(1), 52-63.
7. Torres, J., Bonovas, S., & Albanese, A. (2017). Extra-intestinal manifestations of ulcerative colitis: Systemic involvement and its impact on management. World Journal of Gastroenterology, 23(7), 123-130.
8. Zhu, L., Deng, Q., & Xu, H. (2021). Renal ischemia and kidney dysfunction in experimental colitis: A pathway for systemic inflammation. Journal of Inflammation, 19(5), 189-198.