Int. J. Morphol.,
44(2):373-379, 2026.

Morphological Alterations of the Glomerular Filtration Barrier Relevant to the Development and Progression of Diabetic Nephropathy

Alteraciones Morfológicas de la Barrera de Filtración Glomerular Relevantes en el Desarrollo y Progresión de la Nefropatía Diabética

Pamela Morales[1,2]; Daniel R. González[1] & Jessica Zúñiga-Hernández[1]

MORALES, P.; GONZÁLEZ, D. R. & ZÚÑIGA-HERNÁNDEZ, J. Morphological alterations of the glomerular filtration barrier relevant to the development and progression of diabetic nephropathy. *Int. J. Morphol., 44(2)*:373-379, 2026.

SUMMARY: Diabetes mellitus (DM) is a disease of high global concern due to its sustained increase in prevalence and mortality. One of its most significant complications is diabetic nephropathy (DN), which affects approximately 40 % of patients with DM and is the leading cause of end-stage renal disease (ESRD), requiring dialysis and kidney transplant. The etiopathogenesis of DN is complex and multifactorial, however, the hyperglycemic environment produces a persistent inflammatory state, hypertension and generalized oxidative stress, with overproduction of reactive oxygen species (ROS), key processes in the development of this pathology. In DN, alterations in the morphology of the glomerular filtration barrier (GFB) are observed. The GFB is made up of the endothelium of the fenestrated capillaries, the glomerular basement membrane (GBM), and podocytes. Each of these relevant structures undergoes substantial changes in DN, ultimately leading to kidney failure producing proteinuria, which is a reference biomarker for detecting kidney damage. The objective of this review is to analyze these morphological changes in detail and how they are related to the development and progression of DN, including the signaling pathways and cellular events involved.

KEY WORDS: Morphology; Glomerular basement membrane; Endothelium; Podocytes; Diabetic nephropathy.

INTRODUCTION

DM is a chronic metabolic disease characterized by persistent hyperglycemia. Its worldwide prevalence in adults has increased considerably in recent decades and is expected to continue rising, and its mortality increased 70 % between 2000 and 2019 and it is estimated that over 3.4 million people aged 20–79 died from diabetes-related causes in 2024. Furthermore, gestational diabetes is known to occur in one out of every five pregnancies, causing complications for both the mother and the baby. As of 2024, there were approximately 588 million adults (ages 20–79) worldwide affected by diabetes, and projected to rise alarmingly to 852 million by 2050, with a global increase of 45 %, if control and prevention measures are not taken, whereby DM is one of the fastest-growing global health challenges of the 21st century (International Diabetes Federation, 2025).

Approximately 10 % of diabetic patients suffer from type 1 DM (T1DM), that corresponds to an autoimmune disorder, characterized by the destruction of β-cells in the pancreatic islets and is the major type of diabetes in children and young adults, but can occur at any age. These patients require insulin treatment to survive. The remaining 90 % of diabetic patients suffer from T2DM, due to altered insulin secretion or action due to insulin resistance. The most significant increase in DM prevalence corresponds to T2DM, associated with obesity, excessive caloric intake, sedentary lifestyle, smoking, and genetic predisposition. In addition to being a highly prevalent disease, the high rate of undiagnosed cases is worrying (43 %), since this prevents adequate and timely treatment. 'Prediabetes' is a terminology used to describe impaired glucose tolerance and/or impaired fasting glucose. People with prediabetes are at higher risk of developing T2DM, cardiovascular disease and stroke (International Diabetes Federation, 2025).

DM presents macrovascular complications, including myocardial infarction, stroke, and atherosclerosis. Microvascular complications, such as nephropathy,

[1] Departamento de Ciencias Básicas Biomédicas, Facultad de Ciencias de la Salud, Universidad de Talca, Talca, Chile.
[2] Escuela de Medicina Veterinaria, Facultad de Recursos Naturales y Medicina Veterinaria, Universidad Santo Tomás, Talca, Chile.

Received: 2025-12-01 Accepted: 2026-01-31

retinopathy, and neuropathy, are also described. DN is the most relevant microvascular complication of DM, affecting 40-45 % of patients with DM. DN is the leading cause of ESRD, which represents a significant social and economic burden. Patients with ESRD require renal replacement therapy, such as dialysis or kidney transplant. Traditionally, DN is described in five stages of progression, which are classified according to the glomerular filtration rate, renal function, and urinary albumin excretion, and this progression is related to morphological changes in renal tissue. Its etiopathogenesis is not entirely clear, however, it is known that multiple mechanisms and pathways are involved, where inflammation and oxidative stress play a key role in the development and progression of DN. Chronic hyperglycemia induces structural and functional changes in the kidney, with notable damage to the GFB, resulting in albuminuria, an initial clinical marker for DN (Wang & Zhang, 2024).

The kidney is particularly susceptible to hyperglycemia, since glomerular, mesangial, and tubular cells operate independently of insulin levels, and their intracellular glucose uptake is directly influenced by systemic glucose levels. Hyperglycemia generates morphological alterations in the GFB, producing damage to the endothelium of the fenestrated capillaries and its glycocalyx, thickening of the GBM, apoptosis of podocytes and damage to their foot processes (FPs) and their slit diaphragms (SDs), leading to hyperfiltration. These changes are followed by tubular hypertrophy, tubular apoptosis, and increased extracellular matrix (ECM) deposition. These accumulations of EMC can be observed in the glomeruli forming the Kimmelstiel–Wilson nodules, and it has also been described an epithelial-mesenchimal transition (EMT) that produced more ECM in later stages, which ultimately leads to fibrosis and progressive loss of kidney function (Liu *et al*., 2022).

To better understand this pathology, it is necessary to contemplate kidney morphology in detail, especially at the level of the GFB, where structural changes begin to occur, as well as to recognize how each of its components is affected, resulting in proteinuria, the main marker of early kidney injury.

1. Etiopathogenesis of diabetic nephropathy

The etiopathogenesis of DN is complex and currently not fully understood; however, its development and progression are multifactorial, involving several pathways and mediators. At early stages, there is an overproduction of ROS, and generalized oxidative stress, which are considered key components of the development of this disease, with an imbalance between oxidant and antioxidant compounds, where ROS increase, causing damage to kidney tissue (Jin *et al*., 2023). The renin-angiotensin-aldosterone system is also described to play an important role in the progression of DN, since hyperglycemia stimulates the synthesis of renin and angiotensin II in glomerular mesangial cells, generating an increase in glomerular capillary pressure and hypertension, and also stimulates the production of ECM, renal cell proliferation and hypertrophy, and cytokine synthesis, all of which contribute to damage and the generation of proteinuria. In addition, oxidative stress stimulates the inflammatory process and macrophage infiltration in the kidney (Donate-Correa *et al*., 2021). DN is characterized by the overexpression of pro-inflammatory mediators, growth factors, cytokines, chemokines, and vasoactive molecules that produce structural and functional changes at the glomerular and tubular level. Persistent inflammation leads to tissue damage, and at later stages, this damage progresses to fibrosis, which is irreversible (glomerulosclerosis and interstitial fibrosis), driving to ESRD. Meanwhile, in the kidney, blood-derived cells as well as a variety of intrinsic renal cells (glomerular, endothelial, tubular, and mesangial cells) release inflammatory cytokines, leading to local immune and inflammatory responses (Liu *et al*., 2022).

There is evidence that sustained hyperglycemia leads to the formation of advanced glycation end products (AGEs), which play a central role in the pathogenesis of DN. The accumulation of the AGE receptor (RAGE) and the formation of AGEs trigger oxidative stress and inflammation, which structurally affect the kidney activating signaling pathways including protein kinase C (PKC), transforming growth factor-β (TGF-β), and nuclear factor-κB (NF-κB), leading tissue damage, apoptosis, and finally fibrosis (Wu *et al*., 2021).

The morphological alteration of the GFB due to the processes described above is a key factor that contributes to the development and progression of DN, and due to these changes, proteinuria is generated. Therefore, morphological modifications in GFB play a significant role in the pathogenesis of DN and is attracting attention as it is considered a target for promising future therapeutic research for this important disease, since each of its components is altered by the renal microenvironment (Daehn & Duffield, 2021).

1. 1. The glomerular filtration barrier

The GFB is a highly specialized structure for selective plasma ultrafiltration, based on charge and

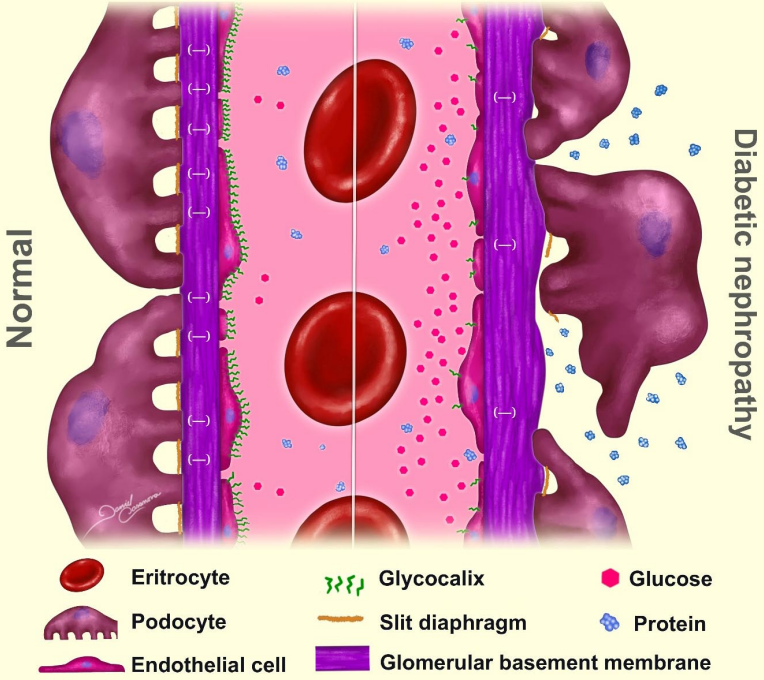

Fig. 1. Morphology of the glomerular filtration barrier in a normal state and the changes that occur in diabetic nephropathy. In a normal state (left), the glomerular filtration barrier is observed, which is formed by the endothelium of the fenestrated capillary. On its luminal side, the glycocalyx is visible. Also present is the glomerular basement membrane, which has a negative charge (-) that confers semipermeability, preventing the leakage of blood proteins. Podocytes, which make contact with the capillary via their processes, are also observed; between these processes, the slit diaphragms are visible. In the case of diabetic nephropathy (right), hyperglycemia activates processes that alter the conformation of the glomerular filtration barrier. Alteration of the capillary endothelium and disorganization and loss of the glycocalyx are observed; the glomerular basement membrane becomes disorganized and thickened, losing its negative charges (-), which allows plasma proteins to pass through this structure; on the other hand, the podocytes detach from the glomerular basement membrane, and there is alteration of their processes, where they shorten and fuse with each other, producing alteration and decrease of the diaphragmatic slits.

molecular size, conferring it high selectivity. Its functional integrity is preserved through the dynamic and coordinated interaction between glomerular endothelial cells (GECs), the glomerular basement membrane (GBM), and podocytes (Fig. 1), serving as a functional unit through which the kidney filters water, electrolytes, and low molecular weight solutes from the bloodstream into the urinary space (Machin *et al.*, 2023). GECs are highly specialized cells characterized by the presence of numerous fenestrae, circular transcellular pores of 60–80 nm in diameter. The GECs play critical roles in many physiological functions: vascular tone adjustment, blood cell trafficking, hemostatic balance, permeability, cell proliferation and survival, as well as being involved in mediation of innate and adaptive immunity. At the luminal surface of GECs is found the glycocalyx (Fig. 1), a 200–400 nm thick structure with negative charges due to its complex network of proteoglycans, glycoproteins, and glycolipids, playing a critical role in preserving the charge-selective properties of GFB. Heparan sulfate, chondroitin sulfate, dermatan sulfate, and hyaluronan are among the most important components of glycocalyx. Heparan sulfate is the most abundant, corresponding to 50–90 % of the glycocalyx. Glycosaminoglycans have negative charges, which is relevant to prevent protein loss from plasma (Amirpour-Najafabadi *et al.*, 2021).

Within the GFB is the GBM (Fig. 1), composed of inner, middle, and outer sublayers. The GBM shares several structural features with the typical basement membranes, including the presence of an electron-dense lamina, observable by electron microscopy. However, the GBM also exhibits some atypical features, notably thicker than most other basement membranes, a feature attributed to its developmental origin during glomerulogenesis, as it is formed by the fusion of two distinct basement membranes: that of the glomerular endothelium and the visceral epithelium (podocytes) (Smith *et al.*, 2023). This structure is composed primarily of laminin (mainly a5β2γ1), collagen IV, heparan sulfate (agrin, perlecan), and sulfated proteoglycans, all of which contribute to its structural and properties. Type IV collagen (α3.α4.α5 heterotrimers) is a major component of GBM and plays an important role in maintaining its integrity (Bülow & Boor, 2019).

The GFB also has a layer of podocytes (Fig. 1), also known as glomerular visceral epithelial cells. These are anatomically unique epithelial cells located within Bowman's space, where they are directly exposed to the primary filtrate. Podocytes have FPs enveloping the glomerular capillaries, with interdigitations. In between are SDs (Fig. 1), regarded as specialized adherens and tight junctions that play a central role in filtration, by providing charge and size selective barrier to macromolecules, having a pore size of ~3.8 nm, the same diameter of albumin. SD is composed of sialoglycoproteins, including podocalyxin and podoendin, imparting negative charges to the surface of podocytes, thus preventing filtration of plasma proteins. Additionally, the SDs consist of several proteins arranged

in a zipper-like structure. Studies have identified several proteins as integral components of the SDs, such as ZO-1 (zonula occludens-1), nephrin, CD2AP (CD2-associated protein), FAT, P-cadherin, NEPH1 (nephrin-like protein-1), and podocin (Kawachi & Fukusumi, 2020). Nephrin forms the transmembrane/extracellular portion of the SD, connecting adjacent FPs, while the cytoplasmic tails of these proteins interact with scaffold proteins, adapters, and signaling molecules to regulate the podocyte cytoskeleton. FPs contain a dense cytoskeletal network of actin filaments connected with an array of linker proteins, not only to the SD, but also to the GBM anchor proteins, such as a3b1 integrin and dystroglycan. These interactions are essential to maintain the highly ordered structure of the FPs. Podocytes regulate the growth, survival, differentiation, and permeability of GECs and maintain endothelial function and GFB integrity (Kocylowski *et al*., 2022).

Furthermore, there is evidence of crosstalk between the cells that constitute the GFB, via paracrine signaling, as well as by mechanisms known as "migracytosis" (Ardalan *et al*., 2022). The intercellular crosstalk is relevant for the GFB to fulfill its functions. Therefore, knowing in detail the components of the GFB as well as the interactions that exist between its components is fundamental, since these morphological characteristics are affected in DN (Hu *et al*., 2024).

1.2. Damage to the glomerular filtration barrier in diabetic nephropathy.

DN can be classified into four stages based on the type and degree of lesion in the glomerulus:I) GBM thickening and alterations in GFB; II) mesangial expansion; III) nodular sclerosis (Kimmelstiel–Wilson lesions); IV) advanced diabetic glomerulosclerosis (Lui *et al*, 2022). The GFB is altered early in the development of the disease, affecting the renal glomerulus, producing albuminuria, which is an early manifestation of diabetic nephropathy that can be associated with progression to ESRD. DN is characterized by specific pathophysiological changes in the renal glomerulus, proximal and distal convoluted tubules. Crucially, the adaptation of renal endothelial, mesangial, and proximal tubular cells to hyperglycemia is inefficient due to prolonged exposure to high glucose concentrations. Increased glucose internalization is cytotoxic, promoting damage to all cells comprising both the cortex and the renal medulla. Hyperglycemia is followed by an acute inflammatory process and increased oxidative stress, which directly affect the GECs. Prolonged exposure to high glucose concentrations can increase the susceptibility to injury of the vessel wall, by increasing endothelial permeability and altering the signaling pathways that govern endothelial nitric oxide synthase (eNOS) activation, leading to diminished nitric oxide (NO) production and subsequent GECs injury. This endothelial dysfunction is one of the early lesions in the development of DN (Hu *et al*, 2024).

The endothelial glycocalyx is essential to maintain the integrity of the endothelial barrier. In DN, the intracellular accumulation of glucose and its metabolites lead to endothelial dysfunction and significant disorganization and decrease of the glycocalyx, located on the luminal surface of GECs (Fig. 1). Furthermore, the glycocalyx can be degraded, playing a relevant role in the progression and severity of the disease (Machin *et al*., 2023). In DN, the decrease in the expression of some glycocalyx molecules, such as versican, decorin, and fibromodulin contributes to a decrease in the negative charge that the GBF (Fig. 1), resulting in an increase in the fractional renal clearance of albumin. Endomucin (EMCN) is a relevant component of the glycocalyx, and it has been described that in EMCN-knockout mice present a variety of defects, including increased infiltration of inflammatory cells, albuminuria, thickening of the glomerular basement membrane (GBM), as well as dysregulated capillary fenestrations and podocyte effacement (Hu *et al*., 2025).

In DN, multiple signaling pathways are activated, and numerous mediators are involved, among which oxidative stress is fundamental. The increase in ROS causes thickening of the glomerular and tubular basement membranes, altering the conformation of heparan sulfate, decreasing its binding to proteoglycans. Furthermore, collagen IV and laminin fibers become disorganized, resulting in thickening of the GBM (Fig. 1), one the earliest pathological signs of the disease. This disorganization and thickening are progressive over time, causing the GBM to lose its barrier properties and negative charges, and in more advanced stages of the disease, the increased damage and thickening will produce higher proteinuria (Fig. 1), which ranges from microalbuminuria to overt proteinuria (Ndisang, 2018).

Podocytes are highly affected by the hyperglycemic environment, inflammation, and oxidative stress, as evidenced by podocyte loss through detachment from the GBM or apoptosis. Furthermore, it is described that in DN anchoring proteins such as integrin $\alpha 3\beta 1$ decrease, generating podocyte detachment (Fig. 1). Additionally, alterations in their processes are observed, including widening and shortening of the FPs and a marked decrease in SDs (Fig. 1). On the other hand, nephrin and podocin are decreased in DN, altering and decreasing SDs

(Sunilkumar *et al*., 2025) (Fig. 1). These modifications generate changes in the electric charge and increase permeability to plasma proteins (Fig. 1), producing proteinuria (Kitsiou *et al*., 2003).

In DN, the persistent inflammation in the glomerulus promotes the expression of pro-inflammatory and pro-fibrotic molecules, such as TGF-β1, interleukin-1 (IL-1), IL-6, IL-8, IL-18 and tumor necrosis factor-alpha (TNF-α), that induce damage to the GFB. Furthermore, in DN, increased levels of chemokines induce inflammatory cells recruitment and migration. Several inflammatory chemokines participate in the pathogenesis of renal damage in DN, particularly monocyte chemotactic protein-1 (MCP-1), intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) which act as chemoattractant molecules for inflammatory cells. Among them, neutrophils and macrophages play a relevant role in promoting the inflammatory process and generating structural damage (Pérez-Morales *et al*., 2019). The connective tissue growth factor (CTGF), and NF-κB produce podocyte apoptosis, depletion, decreased survival, and GECs apoptosis (Wang & Zhang, 2024), TGF-β and NF-κB, play pivotal roles in the advancement of DN by fostering the accumulation of extracellular matrix and renal fibrosis (Dwivedi & Sikarwar, 2025). Renal fibrosis is a pathological process of excessive deposition of ECM in the kidney under the long-term high glucose, inflammation and oxidative stress. This fibrotic process increases over time, is progressive, and is associated to a poor prognosis. Epithelial-mesenchymal transition (EMT) is a process present in DN where epithelial cells lose intercellular connections, detach from the basement membrane, and thereby lose their epithelial phenotype and acquire a mesenchymal cell phenotype. This transition is characterized by the loss of epithelial proteins such as cytokeratin and E-cadherin, and the acquisition of mesenchymal markers such as a-smooth muscle actin (α-SMA) and vimentin. EMT may be a chemokine and inflammatory cell-dependent reaction. Glomerular podocytes and endothelial cells also undergo a transition following damage and the phenotypic modification of podocytes leads to proteinuria and glomerulosclerosis. EMT is induced through three main converging signaling pathways: TGFβ/Smad, integrin/ILK, and Wnt/β-catenin (Chen *et al*., 2022).

Advanced glycation end products (AGEs) are a heterogeneous class of molecules, produced by the non-enzymatic glycation reaction between the carbonyl moiety of reducing sugars and the amino groups of biomacromolecules (proteins, lipids or nucleic acids) via nucleophilic addition. AGEs and their receptors (RAGEs) are elevated in DN, producing rearrangements of the renal architecture and dysfunction. AGEs commonly accumulate in renal compartments (vessels, glomeruli, tubules and interstitial space). The interaction of AGEs with RAGEs contributes to apoptosis and podocyte sloughing, as well as to the EMT, mainly through the activation of the NF-κB signaling pathway, increasing ECM production (Tan *et al*., 2010). Podocytes produce matrix metalloproteinases (MMPs), which are important in the remodeling of the ECM. Therefore, podocyte injury can alter the balance between the synthesis and degradation of GBM, causing changes in its thickening (Naylor *et al*., 2021).

Furthermore, expansion of the mesangial matrix with an increase in mesangial cells is described, producing glomerulus hypertrophy and increased intraglomerular capillary pressure. During the development of DN, high glucose concentrations and chronic hypoxia cause oxidative stress, inflammation, and accumulation of extracellular matrix resulting in mesangial damage, including mesangial proliferation, mesangial matrix expansion and mesangiolysis. In later stages of DN, the Kimmelstiel-Wilson nodules can be observed in the glomeruli, observed as masses of different sizes that compress the capillaries and correlate with an impaired filtration rate, associated with poor renal prognosis (Zhou *et al*., 2022).

Dysregulation of intercellular communication at cell-cell junctions is another causal factor in DN, and elucidating the interactions between GECs, podocytes, and GBM is at the foundation for a better understanding of the pathophysiology of renal dysfunction in DN. The dynamic interplay between podocytes, GECs and the GBM may be fundamental for effective filtration. The clarification of the simultaneous interactions between the components of the GFB is relevant for understanding the pathophysiology of kidney dysfunction in DN (Ndisang, 2018). During the progression of DN, the mechanisms of intracellular cell interactions in the glomerulus at different stages have different emphases. In the early stage of DN, there is a tendency towards loss of podocytes and angiogenesis disorders, and the GFB begins to be damaged. The increased ROS production contributes to the further progression of DN. In the transitional period, mesangial expansion and sclerosis accompanied by overproduction of ECM, gradually lead to renal fibrosis and ultimately develop into the late stage of DN. The overactivation of a series of renal fibrotic pathways, with TGF-β as the core and the release of exosomes eventually aggravate the renal fibrotic process, resulting in a sharp decline in renal function and developing into the ESRD (Hu *et al*., 2024). The main alterations in each of the components of the GFB are summarized in Table I.

Table I. Main alterations in the components of the glomerular filtration barrier and the mechanisms involved in DN.

Structure	Alteration	Mechanisms	References
Glomerular endothelial cells	Endothelial dysfunction; endothelial cell apoptosis; capillary rarefaction; loss endothelial fenestrations; glomerular endothelial mitochondrial dysfunction; endothelial-mesenchymal transition (EMT).	Inflammatory response; changes in structural enzymes; reduction in nitric oxide bioavailability; advanced glycation end products; Increased oxidative stress and ROS; increased growth factors; hypertension; macrophages infiltration; increased of proinflammatory cytokines	Hu *et al*., 2024; Chen *et al*. ,2022; Donate-Correa *et al*., 2021; Dwivedi & Sikarwar, 2025; Jin *et al*., 2023; Pérez-Morales *et al*., 2019; Lui *et al*., 2022; Kitsiou *et al*., 2003; Wu *et al*., 2021; Ndisang, 2018; Wang & Zhang, 2024.
Glycocalyx	Changes in the thickness of glycocalyx, glycocalyx degradation and its disappearance	Inflammatory response; increased oxidative stress and ROS; reduction in nitric oxide bioavailability; TGF-β signaling pathway	Amirpour-Najafabadi *et al*., 2021; Hu *et al*., 2025; Machin *et al*., 2023.
Glomerular basement membrane	Alteration in the distribution of Type IV collagen; decrease in the labelling for heparan sulfate proteoglycan; disorganization of the extracellular matrix; thickening of the glomerular basement membrane	Inflammatory response; increased oxidative stress and ROS; hypertension; increased of AGEs-RAGE	Bülow & Boor, 2019; Donate-Correa *et al*., 2021; Dwivedi & Sikarwar, 2025; Wu *et al*., 2021; Lui *et al*., 2022; Naylor *et al*., 2021; Tan *et al*., 2010; Wang & Zhang, 2024; Pérez-Morales *et al*., 2019.
Podocytes	Disruptions in podocyte function; hypertrophy; shedding foot processes; reduced density for detachment and apoptosis; loss of foot processes; reduced slit diaphragms; reduced levels of nephrin and podocin; endothelial-mesenchymal transition (EMT); rearrangement of podocyte cytoskeleton	Lipotoxicity; hemodynamic abnormalities, mitochondrial dysfunction; impaired autophagy; increased oxidative stress and ROS; inflammatory response; hypertension; increased of AGEs-RAGE	Donate-Correa *et al*., 2021; Hu *et al*., 2024; Pérez-Morales *et al*., 2019; Jin *et al*, 2023; Dwivedi & Sikarwar, 2025; Lui *et al*, 2022; Kawachi & Fukusumi, 2020); Wu *et al*., 2021; Kocylowski *et al*., 2022; Suynikumar *et al*., 2025; Tan *et al*., 2010); Wang & Zhang, 2024.

CONCLUSIONS

DM, and consequently DN, is highly relevant to global public health due to the sustained increase in their prevalence and mortality worldwide, considered as pandemics. Approximately 40 % of patients with T1DM and T2DM will develop DN, and this is the leading cause of ESRD, requiring dialysis and kidney transplant. Therefore, it is essential to thoroughly understand the morphological alterations in the GBF that occur in the hyperglycemic environment of the kidney and the triggering mechanisms. Although the etiopathogenesis of DN is not fully understood, it has been described as complex and multifactorial, with hyperglycemia leading to a persistent inflammatory state and increased oxidative stress, hypertension and increase in AGEs, processes that result in significant damage to the morphology of the GFB. The damage begins in the GECs and its glycocalyx, then affecting the GBM and podocytes, all these alterations that begin early in the development of DN and can worsen if appropriate measures are not taken. A morphologically altered GFB results in hyperfiltration, where microalbuminuria can initially be identified. However, if these alterations and the disease progress over time, a more marked proteinuria can be produced. Therefore, proteinuria is considered a relevant clinical marker in DN. A better understanding of the morphological changes that occur in the GFB in DN, as well as the associated molecular pathways, are essential, as this information will contribute to the development of new targeted therapies for this prevalent pathology.

MORALES, P.; GONZÁLEZ, D. R. & ZÚÑIGA-HERNÁNDEZ, J. Alteraciones morfológicas de la barrera de filtración glomerular relevantes en el desarrollo y progresión de la nefropatía diabética. *Int. J. Morphol., 44(2)*:373-379, 2026.

RESUMEN: La diabetes mellitus (DM) es una enfermedad de gran preocupación mundial debido a su aumento sostenido en prevalencia y mortalidad. Una de sus complicaciones más significativas es la nefropatía diabética (ND), ya que afecta aproximadamente al 40 % de los pacientes con DM y es la principal causa de enfermedad renal terminal (ERT), que requiere diálisis y trasplante. La etiopatogenia de la ND es compleja y multifactorial, sin embargo, el entorno hiperglicémico produce un estado inflamatorio persistente, hipertensión y estrés oxidativo generalizado con sobreproducción de especies reactivas de oxígeno (ROS), procesos claves en el desarrollo de la enfermedad. En la ND existen alteraciones en la morfología de la barrera de filtración

glomerular (BFG). La BFG está constituida por el endotelio de los capilares fenestrados, la membrana basal glomerular (MBG) y los podocitos. Cada una de estas estructuras son relevantes y sufren cambios sustanciales en la ND, lo que finalmente conduce a insuficiencia renal y produce proteinuria, un biomarcador de referencia para detectar daño renal. El objetivo de esta revisión es analizar en detalle estas condiciones morfológicas que afectan a la BFG y cómo éstas se relacionan con el desarrollo y progresión de la DN, involucrando las vías y procesos que intervienen en estos cambios.

PALABRAS CLAVE: Morfología; Membrana basal glomerular; Endotelio; Podocitos; Nefropatía diabética.

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Corresponding author:
Jessica Zuñiga-Hernandez
Departamento de Ciencias Básicas Biomédicas
Facultad de Ciencias de la Salud
Universidad de Talca
Avenida Lircay S/N
Talca
CHILE

Email: jezuniga@utalca.cl