ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603632

The Relationship between Diabetes Mellitus and Diabetic Nephropathy: A Review of Historical Findings and Current Perspectives

Edwin Vaca Hernández
Orcid ID: 0009-0003-8343-4380
Universidad Nacional Del Oriente

Abstract:- The study aims to analyze the historical evolution and recent advances in the diagnosis, treatment, and management of diabetic nephropathy, from its identification in the 1930s to current innovations in personalized medicine and multidisciplinary strategies. Among the most relevant findings, microalbuminuria stands out as an early marker, along with the importance of intensive glycemic control and the development of therapies such as SGLT2 inhibitors, which have demonstrated significant renal and cardiovascular benefits. Additionally, the role of biomarkers and genomics in early disease detection and advances in kidney transplants that have improved patient survival and quality of life are emphasized. The study concludes that personalized strategies and comprehensive approaches represent fundamental progress in effectively preventing and treating this renal complication.

Keywords:- *"Diabetic Nephropathy," "Nodular Glomerulosclerosis," "Diabetes Mellitus," "Albuminuria," and "Reno-Protective Treatment.*

I. INTRODUCTION

Diabetic nephropathy is one of the severe chronic complications of diabetes mellitus, affecting approximately 20%-40% of diabetic patients (1) (2). It is the leading cause of chronic kidney failure globally and represents a significant challenge for healthcare systems due to its clinical and economic impact (3). The growing prevalence of diabetes mellitus, driven by factors such as population aging, urbanization, and sedentary lifestyles (4), has also increased the incidence of diabetic nephropathy, critically affecting patients' quality of life and long-term prognosis (5).

Clinically, diabetic nephropathy is a progressive disorder that primarily affects the glomeruli, tubules, and renal interstitium (6). Its initial manifestation is characterized by persistent microalbuminuria, which progresses to proteinuria and a reduction in the glomerular filtration rate, eventually leading to end-stage renal disease if not adequately addressed. These changes are mediated by a set of complex pathophysiological mechanisms, including chronic hyperglycemia, oxidative stress, hemodynamic alterations, and inflammatory processes (1). Despite advances in pharmacological therapies, early diagnosis remains a challenge, particularly in subclinical stages (1).

From a pathophysiological perspective, the progression of diabetic nephropathy is driven by the interaction of multiple metabolic, inflammatory, and hemodynamic processes that progressively alter renal structure and function. Chronic hyperglycemia and advanced glycation end products (AGEs) play a key role in this process (7) (8). Prolonged hyperglycemia promotes the formation of AGEs, molecules that accumulate in the glomerular basement membrane and activate specific receptors known as RAGE (9). This interaction induces inflammation and renal fibrosis through the production of pro-inflammatory cytokines and pro-fibrotic factors, such as transforming growth factor-beta (TGF-β).

Oxidative stress is another critical mechanism in the progression of diabetic nephropathy (3) (10). Hyperglycemia generates reactive oxygen species (ROS), which damage renal cells and amplify chronic inflammation. This mechanism contributes to glomerular basement membrane thickening and endothelial dysfunction, key elements in the deterioration of renal function (1). Similarly, hemodynamic alterations also play a significant role in disease progression. Glomerular hyperfiltration, mediated by the activation of the renin-angiotensin-aldosterone system (RAAS), increases intraglomerular pressure, causing mechanical damage to podocytes and promoting glomerulosclerosis (1) (8).

Chronic inflammation is characterized by the persistent activation of inflammatory cytokines such as TNF-α and IL-6, which promote cellular apoptosis and macrophage infiltration, exacerbating renal damage (6) (1) (11). This process perpetuates the deterioration of renal function and contributes to the development of chronic kidney failure. In parallel, podocyte damage, involving podocyte loss, weakens the glomerular filtration barrier, leading to persistent proteinuria and progression toward nodular glomerulosclerosis. Renal fibrosis is another key phenomenon in the advanced stages of diabetic nephropathy. TGF-β stimulates the accumulation of extracellular matrix in the renal interstitium and glomerulus, promoting fibrosis and tubular atrophy. These structural changes account for the progressive loss of renal function in patients with advanced diabetic nephropathy.

Advances in understanding the pathophysiology of diabetic nephropathy have led to the development of targeted therapies aimed at modulating these pathological

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603632

mechanisms. For instance, SGLT2 inhibitors have demonstrated not only a reduction in glomerular hyperfiltration but also mitigation of oxidative stress and inflammation, thereby slowing disease progression (3) (10) (12). Moreover, the identification of emerging biomarkers, such as cystatin C and VEGF, has improved early diagnosis, enabling more personalized and effective management (9) (11).

This article aims to comprehensively explore the pathophysiological mechanisms, advances in diagnosis, and therapeutic strategies for diabetic nephropathy, highlighting the importance of a multidisciplinary approach to improve clinical outcomes and reduce disease burden. Through a review of historical and contemporary findings on the relationship between diabetes mellitus and diabetic nephropathy, the article underscores therapeutic innovations and the limitations of reviewed studies. By identifying areas where knowledge remains limited, it seeks to propose future directions for research in this field. This comprehensive approach will provide an overview of progress in understanding diabetic nephropathy, treatment options, and a solid foundation for future experimental studies to optimize prevention and management of this renal complication in diabetic patients.

II. METHODOLOGY

The information search was conducted through consultations of national and international sources in the health field, including PubMed, Scielo, and Google Scholar. Boolean operators (AND, OR, and NOT) were employed to obtain precise and relevant results.

The initial search was performed in the academic databases mentioned above using key descriptors such as "diabetic nephropathy," "nodular glomerulosclerosis," "diabetes mellitus," "albuminuria," and "reno-protective treatment." A preliminary filtering identified 335 articles, after which titles and abstracts were reviewed, excluding those not directly addressing the relationship between diabetes mellitus and diabetic nephropathy. This process reduced the selection to 220 articles meeting the relevance criteria and objectives of the review.

Subsequently, specific criteria (see Table 1) were applied to narrow the selection to 77 articles, ensuring the quality and relevance of the studies. A final evaluation of each article was conducted based on its complete content, thematic relevance, and methodological rigor, resulting in the selection of 20 key and precise articles for the preparation of this review.

Table 1 Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Publications between 2019 and 2023 highlighting historical and current milestones in diabetic nephropathy.	Articles without peer review or from non-academic sources.
Studies focused on diagnosis, pathophysiology, prevalence, and reno-protective treatments.	Studies superficially addressing diabetic nephropathy without providing concrete or relevant data.
Peer-reviewed articles with experimental, observational, or review approaches.	Articles without abstracts or full texts in English or Spanish.
Quantitative or qualitative data on innovations in managing diabetic nephropathy (SGLT2 inhibitors, ACE inhibitors).	Duplicate studies or those lacking conclusive results on the diabetes mellitus-diabetic nephropathy relationship.

Source: Own Elaboration.

The analysis was supported by the historical-logical method, complemented by theoretical approaches such as inductive-deductive and analysis-synthesis methods.

III. RESULTS AND DISCUSSION

The relationship between diabetic nephropathy and the underlying inflammatory and metabolic processes is central to understanding the progression of this renal complication in patients with diabetes mellitus (13) (14). This link is manifested in a complex interaction between chronic hyperglycemia, oxidative stress, and the activation of inflammatory pathways, leading to progressive damage to renal structures. This section presents key findings that integrate historical and contemporary perspectives to highlight the most relevant factors, such as inflammatory biomarkers, molecular mechanisms, and emerging therapeutic strategies.

The analysis contextualizes this evidence within the current framework of renal medicine, evaluating its impact on early diagnosis and timely intervention to prevent progression to advanced stages of chronic kidney failure (15). Additionally, significant advancements in the use of biomarkers such as cystatin C and C-reactive protein (CRP) are explored, along with the efficacy of innovative therapies, including SGLT2 inhibitors and RAAS modulators (9) (16) (17).

A stage-by-stage analysis follows, examining the historical evolution and recent advances in understanding and managing diabetic nephropathy. This emphasizes the importance of comprehensive strategies to address this complication effectively.

- *Stage I: "1930–1950: Foundations of Knowledge on Diabetic Nephropathy"*

In the 1930s, the relationship between kidney failure and diabetes mellitus was analyzed for the first time (18) (13). Kimmelstiel and Wilson made a fundamental contribution by describing diabetic nephropathy as a specific complication of diabetes mellitus for the first time (15). Their discovery identified nodular glomerulosclerosis as a characteristic

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603632

lesion in the renal glomeruli of diabetic patients and defined diabetic nephropathy as a distinct clinical entity.

They also revealed how glucose deposits and metabolic products alter the structure of renal vasculature, leading to basement membrane thickening and mesangial expansion, key processes in the progression to kidney failure. This finding laid the groundwork for exploring the relationship between chronic hyperglycemia, oxidative stress, and advanced glycation end products (AGEs) with progressive kidney damage (8). It also marked the beginning of diagnostic strategies, such as the evaluation of microalbuminuria, and therapies aimed at preventing the progression of diabetic nephropathy. The legacy of this discovery continues to guide advances in biomarkers and reno-protective treatments.

In the 1940s, recognizing the relationship between diabetes and chronic kidney failure allowed for a more systematic understanding of the connection between diabetes mellitus and chronic kidney failure. Although the term "diabetic nephropathy" was not yet fully defined, studies began to show that chronic kidney failure was a common complication in patients with long-standing diabetes, especially in those with poor glycemic control.

This period also marked the beginning of understanding markers such as proteinuria and reduced glomerular filtration rate (GFR) as key indicators of kidney damage. From a histopathological perspective, early findings identified characteristic changes in renal glomeruli, basement membrane thickening, and mesangial expansion. These structural features, observed in patients with chronic diabetes mellitus, were essential in distinguishing chronic kidney failure associated with diabetes from other kidney diseases.

These advances highlighted the importance of the relationship between hyperglycemia and the progressive deterioration of kidney function, even though the underlying mechanisms were not yet fully understood. This period laid the groundwork for future investigations that delved into the pathophysiological mechanisms of diabetic nephropathy, including RAAS activation, oxidative stress, and chronic inflammatory processes, which are today considered critical factors in the progression of this renal complication.

The 1950s began with the consolidation of diabetic nephropathy as a chronic complication. These advances were significant for understanding and managing diabetic nephropathy. The introduction of renal biopsy as a diagnostic tool was key in identifying specific histological features associated with diabetic nephropathy, such as glomerular basement membrane thickening, mesangial expansion, and glomerular sclerosis. These findings marked a milestone in recognizing renal alterations related to diabetes mellitus.

During this period, advanced histology techniques allowed for more detailed observation of structural lesions in renal glomeruli. These observations underscored the importance of processes such as glomerular hyperfiltration and oxidative stress, laying the groundwork for understanding the progression to chronic kidney failure. The formal recognition of diabetic nephropathy as a chronic complication of diabetes mellitus was consolidated in 1955. This milestone was supported by studies linking persistent microalbuminuria with progressive structural damage in the kidneys of patients with type 1 diabetes, emphasizing its impact on clinical progression and the need for early management.

These advances not only defined diabetic nephropathy as a clinical complication but also guided the implementation of diagnostic and therapeutic strategies. The classification of the disease into progressive stages allowed for more precise clinical management, highlighting the role of pathophysiological factors such as chronic hyperglycemia, RAAS activation, and chronic inflammation. These historical findings have been fundamental in the development of modern treatments and preventive strategies, emphasizing the importance of early diagnosis and personalized management to reduce progression to end-stage kidney disease.

The author concludes that advances in understanding diabetic nephropathy since the 1930s have been critical for its diagnosis and treatment. The initial discoveries by Kimmelstiel and Wilson established diabetic nephropathy as a complication of diabetes mellitus, and subsequent research identified key pathophysiological mechanisms, such as oxidative stress and renal dysfunction. The introduction of diagnostic tools such as renal biopsy and microalbuminuria has enabled early diagnosis and the development of targeted therapies, highlighting the importance of a personalized approach to preventing chronic kidney failure.

- *Stage II: "1951–1989: Advances in Understanding, Diagnosis, and Treatment of Diabetic Nephropathy"*

The 1960s were key to better understanding diabetic nephropathy, with three fundamental developments contributing to a deeper comprehension of this microvascular complication.

First, the use of renal biopsy and electron microscopy allowed for the identification of early structural alterations in the renal glomerulus, such as glomerular basement membrane thickening, mesangial matrix expansion, and podocyte loss. These findings explained the progression of the disease, from glomerular hyperfiltration to chronic kidney failure.

Second, in 1962, genetic factors that increased susceptibility to diabetic nephropathy were identified. Genetic polymorphisms related to the immune system and glucose metabolism were associated with a higher risk of kidney damage in patients with type 1 and type 2 diabetes, opening new areas of research for personalized therapies and prevention. Finally, in 1968, studies pointed out that arterial hypertension was not only a secondary complication of diabetes but also an independent factor that accelerated kidney damage, activating glomerular hyperfiltration, oxidative stress, and RAAS activation, consolidating it as a key mechanism in the pathophysiology of diabetic nephropathy (8).

The 1970s marked a turning point in managing diabetic nephropathy. First, the increasing prevalence of the disease,

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603632

along with the introduction of insulin and improved survival rates of diabetic patients, led to an increase in chronic complications such as diabetic nephropathy. This phenomenon drove greater medical interest in the early diagnosis and comprehensive management of these complications.

In 1974, dialysis therapies emerged as a therapeutic option for patients with chronic kidney failure secondary to diabetes, prolonging patient life and altering disease prognosis, though it represented an economic challenge for healthcare systems due to growing demand. In 1979, microalbuminuria was identified as an early marker of kidney damage, enabling interventions before the disease progressed to advanced stages, also linking microalbuminuria with a higher risk of cardiovascular complications and establishing it as a key prognostic marker.

The 1980s were crucial in the evolution of diabetic nephropathy management, with two fundamental advances: strict glycemic control and the use of angiotensin-converting enzyme inhibitors (ACEIs) (12) (13). In this decade, various studies, including the Diabetes Control and Complications Trial (DCCT), demonstrated that maintaining glucose levels within normal ranges significantly reduced the risk of diabetic nephropathy progression. This approach reaffirmed the importance of monitoring parameters such as glycated hemoglobin (HbA1c) to improve long-term clinical outcomes while confirming that chronic hyperglycemia triggers pathological mechanisms such as AGE accumulation and oxidative stress.

In 1981, ACEIs began to be investigated as a therapeutic option to slow the progression of renal damage in diabetic patients. These medications proved effective in reducing intraglomerular pressure, decreasing proteinuria, and protecting renal function by preventing structural changes in glomeruli. In 1987, their use was formalized as a standard intervention, confirming that they not only improved proteinuria control but also offered significant cardiovascular benefits, such as reducing adverse events associated with chronic kidney disease, slowing progression to chronic kidney failure.

In the author's view, understanding, diagnosing, and treating diabetic nephropathy experienced significant advancements. The introduction of techniques such as renal biopsy and electron microscopy allowed for the identification of key structural alterations in renal glomeruli, essential for understanding disease progression. Furthermore, the discovery of genetic factors and the relationship between hypertension and kidney damage opened new avenues for treatment and prevention. In subsequent decades, strict glycemic control and ACEI use consolidated disease management, improving long-term outcomes and reducing progression to end-stage kidney disease.

- *Stage III: "1990-2019: Diagnostic, Therapeutic, and Genomic Revolution in Diabetic Nephropathy"*

The 1990s were pivotal in intensifying research on the molecular mechanisms of diabetic nephropathy, the recognition of early markers, and the association between type 2 diabetes and chronic kidney failure. This period laid the foundation for more effective diagnostic and therapeutic strategies. During this decade, there was a deeper understanding of how chronic hyperglycemia induces kidney damage through multiple pathways. Oxidative stress was identified as a crucial mechanism, as hyperglycemia increases the production of ROS, which damage cell membranes, proteins, and DNA, contributing to progressive kidney damage. This mechanism is also related to the accumulation of AGEs, which interfere with the functions of endothelial and glomerular cells. Furthermore, the fundamental role of inflammatory cytokines such as TNF-α and interleukin-6 (IL-6) in exacerbating glomerular damage was discovered.

In 1993, microalbuminuria was consolidated as an early marker and a crucial predictive factor for the progression of diabetic nephropathy. Its detection allowed for identifying patients at higher risk of chronic kidney failure, facilitating early therapeutic interventions, such as intensive glycemic and blood pressure control. These strategies proved effective in delaying kidney damage progression and improving long-term outcomes. The standardization of tests for detecting microalbuminuria, such as the albumin-creatinine ratio in urine, significantly improved the sensitivity and specificity of early diagnosis, consolidating this marker as a key tool in clinical practice.

Subsequently, in 1998, type 2 diabetes was recognized as one of the main causes of chronic kidney failure, especially in patients with hypertension and obesity. Studies conducted in the late 1990s demonstrated that patients with type 2 diabetes have a higher risk of developing nephropathy due to the coexistence of factors such as arterial hypertension and systemic inflammation. These factors amplify kidney damage related to hyperglycemia. This discovery led to a shift in the therapeutic approach, which included both metabolic control and managing comorbidities such as obesity and dyslipidemia to prevent or slow the progression of diabetic nephropathy.

During the 2000s, angiotensin receptor blockers (ARBs) became established as an effective treatment for diabetic nephropathy, complementing ACE inhibitors. These medications demonstrated additional benefits in some cases. ARBs act by blocking the interaction of angiotensin II with AT1 receptors, reducing vasoconstriction and intraglomerular pressure, which decreases stress on renal glomeruli and slows progression toward chronic kidney failure. Studies demonstrated that ARBs reduce proteinuria and protect kidney function, improving the long-term prognosis of patients with diabetic nephropathy. Moreover, ARBs emerged as a more tolerable option for patients who could not use ACE inhibitors due to side effects such as cough or angioedema.

In 2002, the DCCT marked a milestone in managing type 1 diabetes by demonstrating that intensive glucose control can prevent microvascular complications, including diabetic nephropathy. The study's main findings revealed a significant reduction in the incidence of microalbuminuria and macroalbuminuria in patients maintaining strict glycemic

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603632

control. Continuous monitoring of HbA1c was consolidated as an essential tool for preventing kidney damage progression. These results drove the implementation of educational programs and technological tools to improve diabetes management, highlighting the importance of rigorous glucose level control in preventing kidney complications.

The introduction of SGLT2 inhibitors in 2008 marked a significant change in managing type 2 diabetes and its renal complications. These medications block glucose reabsorption in the proximal tubules, lowering blood glucose levels and alleviating metabolic stress on the kidneys. Additionally, they have hemodynamic effects, such as reducing glomerular hyperfiltration, which protects kidney function and reduces the risk of end-stage renal disease. Studies such as EMPA-REG OUTCOME and CREDENCE demonstrated that SGLT2 inhibitors not only delay the progression of diabetic nephropathy but also reduce cardiovascular events, offering a comprehensive approach to treating patients with type 2 diabetes.

Subsequently, during the 2010s, diabetic nephropathy became consolidated as the leading cause of chronic kidney failure in several developed countries. This fact underscored the urgent need to better understand genetic and environmental risk factors associated with disease progression. Advances in genomic medicine allowed for identifying specific genetic variations that predispose diabetic patients to developing diabetic nephropathy. These discoveries have been fundamental in designing personalized prevention strategies and targeted therapeutic approaches that could offer more effective treatments tailored to individual patient characteristics.

In 2014, studies reinforced the idea that proper blood pressure and glucose level control is crucial for delaying the progression of diabetic nephropathy. Maintaining blood pressure levels below 130/80 mmHg and an HbA1c level below 7% has been shown to reduce rates of end-stage renal disease in patients with diabetic nephropathy. These data align with international guidelines for managing the disease. Furthermore, it was highlighted that intensive management of these parameters not only slows the progression of diabetic nephropathy but also reduces associated cardiovascular events.

In 2019, the FDA approved the use of empagliflozin, an SGLT2 inhibitor, as a specific treatment for diabetes with diabetic nephropathy (16). Empagliflozin has proven effective in reducing intraglomerular pressure, improving kidney function, and lowering proteinuria levels. Studies such as EMPA-REG OUTCOME demonstrated additional benefits, such as reducing cardiovascular mortality and disease progression. This medication not only improves glycemic control but also offers hemodynamic benefits that help mitigate chronic kidney damage in diabetic patients.

In conclusion, research on diabetic nephropathy advanced significantly between 1990 and 2019, with major discoveries improving its diagnosis and treatment. According to studies from 1993, microalbuminuria was consolidated as an essential predictive marker, enabling earlier interventions. Over the years, as highlighted by the DCCT of 2002, intensive glucose control has proven crucial for preventing kidney complications. Additionally, the development of treatments such as SGLT2 inhibitors, approved in 2019, has transformed disease management. These advances reinforce the importance of an integral and personalized approach, as noted by the author, to slowing the progression of diabetic nephropathy.

- *Stage IV: "2020 to the Present: Personalized Medicine and New Therapeutic Paradigms in Diabetic Nephropathy"*

In the 2020s, personalized medicine has emerged as an essential approach in managing diabetic nephropathy. This paradigm is based on the combination of genetic information, biomarkers, and clinical data to offer specific treatments tailored to the unique characteristics of each patient. One of the most important advances has been the development of emerging biomarkers that enable earlier and more precise detection of the progression of diabetic nephropathy. Examples of these biomarkers include cystatin C and proteins related to inflammatory processes and renal fibrosis (9) (19). These advances provide a more dynamic view of ongoing kidney damage, significantly improving therapeutic decision-making.

Additionally, the introduction of gene therapies, especially with technologies like CRISPR-Cas9, has opened new possibilities for modifying genes related to susceptibility to diabetic nephropathy. Although these therapies are still in experimental stages, they offer hope for direct intervention in the underlying mechanisms of the disease. Another fundamental aspect of advances in this decade is the multidisciplinary approach to treating diabetic nephropathy. Collaboration among nephrology, endocrinology, cardiology, and nutrition has improved the comprehensive care of patients, enabling more effective identification and management of risk factors such as hypertension, dyslipidemia, and obesity.

In 2022, SGLT2 inhibitors continued to solidify their role as a key pharmacological option in the treatment of diabetic nephropathy. In addition to their benefits in glucose control, these medications have been shown to reduce progression to end-stage renal disease and decrease adverse cardiovascular events, particularly heart failure, in patients with diabetic nephropathy. Other emerging drugs, such as finerenone, a selective mineralocorticoid receptor antagonist, have also shown efficacy in reducing inflammation and renal fibrosis in patients with diabetic nephropathy and type 2 diabetes. DPP-4 inhibitors and new ultra-long-acting insulin formulations have been incorporated as complementary tools in the comprehensive management of diabetes and its renal complications, providing more options for disease treatment.

Regarding advancements in kidney transplantation, significant improvements have been achieved in surgical techniques, reducing operative time and postoperative complications (17). These improvements have been

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603632

especially beneficial for diabetic patients with advanced chronic kidney failure. Additionally, new immunosuppression protocols, such as more specific immunosuppressive drugs, have decreased acute graft rejection rates and improved long-term survival. This advancement has been crucial for patients with diabetic nephropathy, who are more susceptible to infections and metabolic complications. Overall, these innovations have expanded transplant eligibility for older patients and those with advanced comorbidities, evidencing significant improvements in quality of life and life expectancy.

In conclusion, the author highlights that advances in personalized medicine and new therapeutic treatments have revolutionized the management of diabetic nephropathy since 2020. The combination of genetic information, biomarkers, and clinical data has enabled more specific treatments tailored to the individual needs of patients. Additionally, the multidisciplinary approach to treatment has improved comprehensive care, addressing risk factors such as hypertension and obesity. The use of SGLT2 inhibitors and other emerging medications has proven essential in slowing disease progression, while advancements in kidney transplantation and surgical techniques have significantly improved outcomes and quality of life for patients with advanced chronic kidney failure.

IV. CONCLUSIONS

- Diabetic nephropathy was identified as a specific complication of diabetes. Markers such as microalbuminuria and techniques such as renal biopsy were highlighted, laying the foundation for early diagnosis.
- Advances in molecular understanding and genetic factors related to the progression of diabetic nephropathy, along with intensive glycemic control and ACE inhibitors, revolutionized its clinical management.
- Predictive markers such as microalbuminuria were consolidated, and new treatments, such as ARBs and SGLT2 inhibitors, offered renal and cardiovascular protection.
- Personalized medicine, biomarkers, and gene editing opened doors to more specific diagnostics and treatments, while pharmacological advancements and transplants significantly improved the prognosis of patients.

REFERENCES

[1]. Terista Nelly Garcia JCCHL. Hipoglucemiantes orales y seguridad cardioovascular. Relacion con la nefropatia diabetica. revista federacion cardiologia. 2016; 46(1): p. 3-9.
[2]. B. FUPyCC. Nefropatía Diabética. Revista chilena de pediatría. 2002; 75(3).
[3]. Javier Donate-Correa CMFFSQAPCAGLEMNCMFJFNG. Inflammatory Cytokines in Diabetic Kidney Disease: Pathophysiologic and Therapeutic Implications. Frontiers in Medicine. 2021; 7.
[4]. Organización Mundial de la Salud. who.int. [Online]; 2024. Acceso 21 de 12de 2024. Disponible en: https://www.who.int/es/news-room/fact-sheets/detail/diabetes.
[5]. Villa BMU. Universidad Catolica de Cuenca. [Online].; 2023. Acceso 16 de Diciembre de 2024. Disponible en: https://dspace.ucacue.edu.ec/browse/author?value=Urquizo%20Villa,%20Brayan%20Marcelo.
[6]. Paula Cordero-Péreza CSMPAGHALS. Metabolómica de la nefropatía diabética: tras la huella deindicadores de desarrollo y progresión. 2020; 40(6): p. 585-596.
[7]. Díez J, Ibarrola AS, Monfa JM, Purroy A. Revista de Medicina de la Universidad de Navarra. [Online].; 1980. Acceso 17 de Diciembre de 2024. Disponible en: https://revistas.unav.edu/index.php/revista-de-medicina/article/view/5619.
[8]. Gabrielle Azevedo JRFMPMDCS. Fisiopatologia e diagnóstico da nefropatia diabética: uma revisão integrativa. Brazilian Journal of Health Review. 2022; 5(1).
[9]. Huidobro JP, Guzmán AM, Tagle R. Uso de la cistatina C como biomarcador para estimar la tasa de filtración glomerular. Revista médica de Chile. 2021; 149(1).
[10]. Prado MMC, Granados KPM, Carrera MAV, Correa SMV. Insuficiencia reanal cronica en pacientes con diabétes mellitus. RECIIAMUC. 2020; 4(1).
[11]. Sánchez ABM, Veloz APM. Emerging biomarkers in gestational diabetes: perspectives for improving diagnosis and prognoses. Salu, Ciencia y Tecnología. 2024; 4.
[12]. Rivera GS. HISTORIA DE LA DIABETES. Gaceta Médica Boliviana. 2007; 30(2): p. 74-78.
[13]. Luque FMM. Nefropatía diabética. Intervenciones para su tratamiento. Revisión Narrativ. Revista Médica y de Enfermería Ocronos. 2021; 4(11).
[14]. Karen Julecxi Porras-Reyes JFNC. Efectividad del uso de inhibidores del cotransportador de sodio-glucosa 2. Journal Scientific MQRInvestigar. 2023; 7(4).
[15]. Stewart GL. Nueva clasificación y criterios. Revista médica de Chile. 1998; 126(7).
[16]. B. Bouça1 APBAA. Nefropatia Diabética. Revista Portuguesa de Diabetes. 2021; 16(2): p. 90-89.
[17]. Sánchez CDP. Identificación de marcadores tempranos metabolómicos en el desarrollo de daño renal en pacientes con diabetes mellitus tipo 2 mediante la aplicación de la minería de datos usando R. Revista Jóvenes en la Ciencia. 2021; 10.
[18]. Lina María Serna Higuita NPTAMGCMACJMAVVBGJJV. Nefropatía diabética. MEDICINA UPB. 2009; 28(1): p. 42-53.
[19]. M. L. Amoedo MJPEFJMPJRyJM. Glomerulosclerosis nodular diabética. NEFROLOGIA. 1994; 14(5).

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603632

[20]. Organización Panamericana de la Salud. paho.org. [Online]; 2023. Acceso 17 de Diciembrede 2024. Disponible en: https://www.paho.org/es/documentos/perfil-carga-enfermedad-por-diabetes-2023-estado-plurinacional-bolivia.

[21]. Orellana AEA, Bernat CAL, Rojas DOR. Comparación estadística de nefropatía diabética en Bolivia, en relación a Sud América y países desarrollados. Revistas Bolivianas. 2006;(3).