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Bidirectional impact of covid-19, type II diabetes, and chronic kidney disease: A systematic review and its implications for metabolic control

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Abstract

From the perspective of clinical epidemiology, current evidence consolidates the existence of a bidirectional and synergistic relationship between COVID-19, Type 2 Diabetes Mellitus (T2DM), and chronic kidney disease (CKD). These comorbidities not only represent independent risk factors for the development of severe COVID-19, acute respiratory distress syndrome, and mortality (with significantly elevated odds ratios, as shown in international records), but SARS-CoV-2 infection also acts as a destabilizing factor, precipitating severe glycemic dysregulation, acute kidney injury, and accelerating the progression of both chronic conditions through direct pathophysiological mechanisms (linked to the high expression of ACE2 in the pancreas and kidneys, facilitating viral entry and cellular dysfunction) and indirect mechanisms (cytokine storm, hypercoagulability, and RAAS dysregulation).

This review, conducted using the PRISMA methodology and including 21 studies, highlights the urgent need for a comprehensive clinical management approach that prioritizes strict metabolic control and renal function monitoring—not only as baseline therapeutic goals but also as risk mitigation strategies against infection. It also emphasizes the importance of strengthening health systems to maintain continuity of chronic care during pandemics, given the profound prognostic impact this interaction has on patient morbidity and survival.

Keywords: COVID-19; SARS-CoV-2; Type 2 Diabetes Mellitus; Chronic Kidney Disease; Comorbidity; Bidirectional Relationship; Angiotensin-Converting Enzyme 2

1. Introduction

Coronaviruses belong to the Coronaviridae family, order Nidovirales, which are non-segmented positive-sense RNA viruses found in both humans and other mammals (1). Over the past two decades, infections from this virus family have caused pandemics with high infection rates, including severe acute respiratory syndrome (SARS) in 2002- 2003, Middle East Respiratory Syndrome (MERS) since 2012, and the most recent COVID-19 pandemic (2).

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The history of COVID-19 traces back to Wuhan, Hubei province, where the first cases of pneumonia of unknown origin were identified. After extensive investigations, the pathogen was identified as a novel enveloped beta-coronavirus, SARS-CoV-2, phylogenetically similar to SARS-CoV. Initially linked to zoonotic transmission in live animal and seafood markets, it soon became evident that efficient human-to-human transmission was occurring (3).

Due to its rapid spread, the World Health Organization (WHO) declared a pandemic on March 11, 2020 (4). As of the latest epidemiological report, Colombia has recorded 6,369,916 confirmed cases and 142,780 deaths (5).

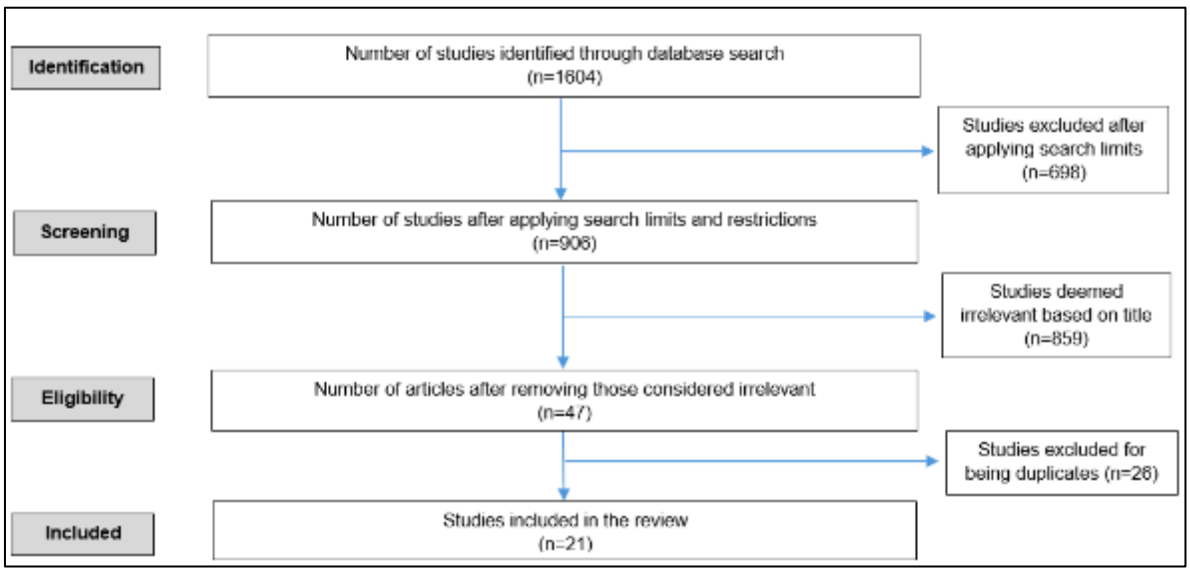
Type II Diabetes Mellitus (T2DM) and chronic kidney disease (CKD) are considered public health concerns in Colombia and globally (6,7), due to their clinical complexity, prevalence, and healthcare costs (8,9). During the COVID-19 pandemic, individuals with these chronic conditions were identified as high-risk due to increased complications and mortality (10).

Understanding the bidirectional relationship between SARS-CoV-2 and the pathophysiology of T2DM and CKD is crucial for medical intervention, ensuring precise application of treatment protocols recommended by national and international scientific organizations (11,12). Multiple studies highlight that maintaining adequate metabolic control in these diseases may serve as a protective mechanism, reducing localized inflammatory responses and blocking viral entry into cells (13,14).

2. Search methodology

A literature search was conducted from December 2022 to August 2023 in databases including PubMed/Medline, Redalyc, SciELO, LILACS, Embase, Scopus, and ScienceDirect using DeCS/MeSH terms: "Diabetes Mellitus, Type 2", "Renal Insufficiency, Chronic", "Severe Acute Respiratory Syndrome Coronavirus 2", and "Post-Acute COVID-19 Syndrome".

Primary and secondary studies were included, such as topic reviews, systematic reviews, original articles, brief originals, doctoral theses, and meta-analyses from the last five years. Duplicates and non-English/Spanish articles were excluded. Initially, 1604 articles were identified; after applying inclusion and exclusion criteria, 21 articles were selected for this review. (see figure 1)



Source: Authors

Figure 1 PRISMA flow diagram of study selection

2.1. Development

2.1.1. Pathophysiological Mechanism of the Disease

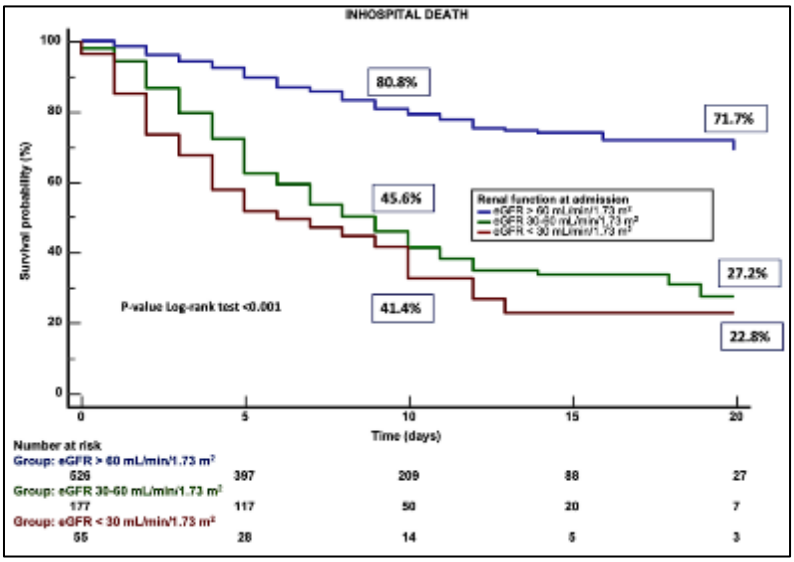
COVID-19 is characterized by a marked increase in inflammatory cytokines (IL-6, TNF-alpha), leading to systemic inflammation, hypercoagulability, and multiple organ dysfunction syndrome (15). These effects are based on both direct

and indirect mechanisms of SARS-CoV-2 infection, starting from viral entry into any organ with cells expressing Angiotensin-Converting Enzyme 2 (ACE2), to indirect effects such as immune response diffusion and dysregulation of the renin-angiotensin-aldosterone system (RAAS) (16). This explains the extensive multi-organ involvement of COVID-19 in the human body.

2.1.2. Bidirectional Association Between COVID-19 and chronic kidney disease

From a multi-organ involvement perspective, the kidney is one of the affected organs. Studies have shown direct damage to the kidney, with findings of coronavirus detected in kidneys and urine of COVID-19 patients, who presented with severe acute tubular necrosis and lymphocyte infiltration (17).

Beyond the damage caused by COVID-19 to the kidney, a direct relationship has also been established between mortality in COVID-19 patients with pre-existing CKD. This is supported by an analysis from the international HOPE COVID-19 Registry (Health Outcome Predictive Assessment for COVID-19), which categorized patients into three groups based on estimated glomerular filtration rate (eGFR) at admission (see figure 2). The study concluded that patients with lower eGFR received pharmacological treatment (e.g., hydroxychloroquine or antivirals) less frequently and experienced more complications such as sepsis (11.9% vs. 26.4% vs. 40.8%, $p < 0.001$) and respiratory failure (35.4% vs. 72.2% vs. 62.0%, $p < 0.001$), as well as higher in-hospital mortality rates (eGFR > 60 vs. 30–60 vs. < 30: 18.4% vs. 56.5% vs. 65.5%, $p < 0.001$) (18).



Source: Adapted from Uribarri A et al

Figure 2 Kaplan-Meier survival endpoint analysis according to glomerular filtration

2.1.3. Bidirectional Association Between COVID-19 and Type II Diabetes Mellitus

Diabetes mellitus is associated with a chronic low-grade inflammatory state that disrupts peripheral insulin sensitivity and systemic glucose regulation. Chronic hyperglycemia compromises both humoral and innate immunity, impairing the patient's ability to respond to infection (19). In SARS-CoV-2-infected patients with diabetes, elevated levels of C-reactive protein and interleukin-6 were observed, promoting cytokine storms and systemic inflammatory responses typical of acute respiratory distress syndrome in COVID-19 patients (20).

In patients with newly diagnosed diabetes following confirmed viral infection, the virus has been isolated in the pancreas, suggesting that some viruses may act as diabetogenic agents. It has been confirmed that ACE2 expression is higher in the pancreas than in the lungs, creating an entry point for SARS-CoV-2 into pancreatic β-cells, leading to cellular dysfunction and subsequent acute hyperglycemia (21).

3. Discussion

The evidence gathered in this review supports the notion of a bidirectional and synergistic relationship between COVID-19, Type 2 Diabetes Mellitus (T2DM), and chronic kidney disease (CKD). This interaction creates a vicious cycle that worsens adverse outcomes.

From an epidemiological perspective, it is clear that patients with pre-existing T2DM and CKD constitute a highly vulnerable group. They not only face a higher risk of severe SARS-CoV-2 infection but also a significantly increased likelihood of complications such as sepsis, respiratory failure, and death, as demonstrated by the HOPE COVID-19 registry (18). This poorer prognosis can be attributed to a compromised immune state, characterized by immunosenescence and an exaggerated and dysregulated inflammatory response. Chronic hyperglycemia in T2DM impairs neutrophil and T-cell function as well as innate immunity, creating a favorable environment for viral replication and the subsequent cytokine storm (19,20).

Conversely, SARS-CoV-2 acts as a direct aggressor on already fragile organ systems. The central pathophysiological mechanism is the virus's binding to Angiotensin-Converting Enzyme 2 (ACE2), which is abundantly expressed in the pancreas (β-cells) and kidneys (proximal tubules) (16,21). In the pancreas, viral invasion can induce β-cell dysfunction and apoptosis, leading to acute hyperglycemia or the onset of de novo diabetes (21). In the kidneys, direct infection of podocytes and tubular cells, combined with systemic inflammation, hypercoagulability, and RAAS dysregulation, precipitates acute-on-chronic kidney injury (AKD-on-CKD) and accelerates CKD progression (17).

A particularly concerning epidemiological finding is that during the pandemic, many patients experienced metabolic and renal decompensation—not only due to the infection itself but also because of disruptions in healthcare services, limited access to consultations, and medication shortages. This underscores the importance of strengthening health systems to ensure continuity of care for chronic diseases during health crises.

Evidence suggests that strict glycemic and renal control prior to infection may have a protective effect. It is hypothesized that better metabolic control mitigates the inflammatory response and may modulate ACE2 expression, reducing cellular susceptibility to the virus (13,14) Therefore, management strategies must be comprehensive, prioritizing optimal control of comorbidities as a fundamental part of preventing and treating severe COVID-19.

4. Conclusions

A well-established bidirectional relationship exists between COVID-19, T2DM, and CKD. Patients with these comorbidities are at greater risk of developing severe forms of COVID-19 and experiencing higher mortality, while SARS-CoV-2 infection can precipitate or worsen glycemic control and renal function.

The pathophysiological mechanisms explaining this interaction include cytokine storms, a hypercoagulable state, and, crucially, direct damage mediated by the virus binding to ACE2 expressed in pancreatic β-cells and renal tubular cells.

The pandemic's impact on the continuity of chronic disease care has been significant, highlighting the need to implement flexible and resilient care models, such as telemedicine, to maintain follow-up for patients with T2DM and CKD during health emergencies.

Strict metabolic control (glycemic and blood pressure) and close monitoring of renal function emerge not only as chronic management goals but also as key preventive strategies to improve outcomes in patients with T2DM and CKD who contract COVID-19.

4.1. Study limitations

Although this review was conducted using the PRISMA methodology, it is important to acknowledge certain limitations inherent to the field:

- The rapid evolution of the literature on COVID-19 may mean that new longitudinal studies published after the August 2023 cutoff were not included.
- The heterogeneity in the design of the primary studies reviewed (observational, retrospective cohorts) may limit the ability to establish definitive causality in all findings.
- More longitudinal studies will be required to fully understand the long-term sequelae of COVID-19 in the progression of T2DM and CKD.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Current ICTV Taxonomy Release | ICTV. Available at: https://ictv.global/taxonomy

[2] Paz Ibarra J. Management of diabetes mellitus in times of COVID-19. ACTA MEDICA Peru. July 1, 2020;37(2). Available at: https://amp.cmp.org.pe/index.php/AMP/article/view/962

[3] Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. N Engl J Med. March 26, 2020;382(13):1199–207.

[4] WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Available at: https://www.who.int/es/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020

[5] Coronavirus Colombia. Available at: https://www.ins.gov.co/Noticias/Paginas/Coronavirus.aspx

[6] Ginarte GM, Domínguez EG, Marín DP. Chronic kidney disease, some current considerations. MULTIMED. May 25, 2020;24(2). Available at: https://revmultimed.sld.cu/index.php/mtm/article/view/1929

[7] Basto-Abreu A, Barrientos-Gutiérrez T, Rojas-Martínez R, Aguilar-Salinas CA, López-Olmedo N, Cruz-Góngora VD la, et al. Prevalence of diabetes and glycemic control in Mexico: results from the Ensanut 2016. Salud Pública México. March 14, 2022;62:50–9.

[8] Sánchez-Cedillo A, Cruz-Santiago J, Mariño-Rojas FB, Hernández-Estrada S, García-Ramírez C. Disease burden: kidney failure, dialysis-hemodialysis and kidney transplant in Mexico. Cost of illness. Rev Mex Traspl. 2020;9(1):15–25.

[9] Estrada A, Reinaldo L. Economic impact of the disease burden of complications in type II diabetic patients among members of a health insurer in Colombia. Universidad Politécnica de València; 2020. Available at: https://riunet.upv.es/handle/10251/156195

[10] Ortiz A, Sanchez-Niño MD. Chronic kidney disease: the most prevalent risk factor and the risk factor that increases most the risk for lethal COVID-19. An RANM. December 30, 2020;137(137(03)):270–5.

[11] Lima-Martínez MM, Carrera Boada C, Madera-Silva MD, Marín W, Contreras M. COVID-19 and diabetes mellitus: a bidirectional relationship. Clínica E Investig En Arterioscler. May 2021;33(3):151–7.

[12] Pallarés Carratalá V, Górriz-Zambrano C, Morillas Ariño C, Llisterri Caro JL, Gorriz JL. COVID-19 and cardiovascular and renal disease: Where are we? Where are we going? Med Fam SEMERGEN. August 1, 2020;46:78–87.

[13] Bornstein SR, Dalan R, Hopkins D, Mingrone G, Boehm BO. Endocrine and metabolic link to coronavirus infection. Nat Rev Endocrinol. June 2020;16(6):297–8.

[14] Callapiña-De Paz M, Cisneros-Núñez YZ, Guillén-Ponce NR, De La Cruz-Vargas JA, Callapiña-De Paz M, Cisneros-Núñez YZ, et al. Lifestyle associated with the control of arterial hypertension and diabetes mellitus in a care center in Lima, during the Covid-19 pandemic. Rev Fac Med Humana. January 2022;22(1):79–88.

[15] Del Valle DM, Kim-Schulze S, Huang HH, Beckmann ND, Nirenberg S, Wang B, et al. An inflammatory cytokine signature predicts COVID-19 severity and survival. Nat Med. October 2020;26(10):1636–43.

[16] Sarkesh A, Daei Sorkhabi A, Sheykhsaran E, Alinezhad F, Mohammadzadeh N, Hemmat N, et al. Extrapulmonary Clinical Manifestations in COVID-19 Patients. Am J Trop Med Hyg. November 2020;103(5):1783–96.

[17] Diao B, Wang C, Wang R, Feng Z, Zhang J, Yang H, et al. Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 infection. Nat Commun. May 4, 2021;12:2506.

[18] Uribarri A, Núñez-Gil IJ, Aparisi A, Becerra-Muñoz VM, Feltes G, Trabattoni D, et al. Impact of renal function on admission in COVID-19 patients: an analysis of the international HOPE COVID-19 (Health Outcome Predictive Evaluation for COVID 19) Registry. J Nephrol. 2020;33(4):737–45.

[19] Iacobellis G. COVID-19 and diabetes: Can DPP4 inhibition play a role? Diabetes Res Clin Pract. April 1, 2020;162:108125.

[20] Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev. October 2020;36(7):e3319.

[21] Liu F, Long X, Zhang B, Zhang W, Chen X, Zhang Z. ACE2 Expression in Pancreas May Cause Pancreatic Damage After SARS-CoV-2 Infection. Clin Gastroenterol Hepatol. August 2020;18(9):2128-2130.e2.