BMC Nephrology

RESEARCH

Open Access

Impact of COVID-19 on nephropathy in diabetes mellitus type–II patients: a systematic literature review and meta-analysis

Tabinda Azim[1,2*], Amer Hayat Khan[1*], Fouzia Sadiq[3], Syed Azhar Syed Sulaiman[1], Amjad Khan[4] and Quratul Ain[3]

Abstract

Background Recent reports have revealed that nephropathy leading to kidney injury (KI) is a prevalent complication of COVID-19 and is linked to high mortality and morbidity in diabetes mellitus type II (DM-T-II) patients. This systematic literature review and meta-analysis aimed to critically analyze existing studies and evidence on the impact of COVID-19 on nephropathy and kidney injury in diabetes mellitus type II (DM-T-II) patients.

Method A systematic search was conducted in the Web of Science (WoS), PubMed and Cochrane databases for relevant studies published between March 2020 and July 2023. To ensure the integrity of the systematic literature review and meta-analysis, observational studies that specifically reported post-COVID-19 kidney injury in DM-T2 patients were included, whereas we did not include articles in the press, meta-analyses, case reports, case series, Diabetes Type-I articles or non-English papers. The primary outcome was kidney injury in patients with type II diabetes after contracting COVID-19. The protocol for this study was published on PROSPERO (registration number CRD42023413887).

Results Initially, 6,339 articles were included in the search, from which only 6 observational studies were selected by following the 2020 PRISMA statement. The quality of the evidence was assessed by a tool provided by the National Institutes of Health (observational studies). The total number of participants included in the studies was 14,723. Our systematic literature review and meta-analysis provide compelling evidence that kidney injury is a prevalent complication of COVID-19 infection in the type II diabetes population, with a pooled odds ratio of 2.27 (95% CI: 2.05–2.51; $p < 0.00001$), often necessitating hospitalization and hemodialysis in severe cases.

Conclusion Covid-19 is associated with a two-fold increase in nephropathy and acute kidney injury in diabetes mellitus type 2 patients compared to non-diabetic patients. This implies that kidney injury is more likely to occur in diabetes mellitus type 2 patients post Covid infection.

Keywords Diabetes mellitus type 2, Diabetic kidney disease, Diabetic nephropathy, COVID-19 or coronavirus

*Correspondence:
Tabinda Azim
tabindaazim@student.usm.my; tabinda.azim@iqraisb.edu.pk
Amer Hayat Khan
dramer@usm.my

[1]School of Pharmaceutical Sciences, University Sains Malaysia, Penang 11800, Malaysia
[2]Iqra University, H-9 Campus, Islamabad 44000, Pakistan
[3]Directorate of Research, Shifa Tameer-e-Millat University, Islamabad, Pakistan
[4]Faculty of Pharmacy, Quaid-e-Azam University, Islamabad, Pakistan

Background

Coronavirus is a spherical, enveloped virus with single-stranded RNA, resembling previous coronaviruses such as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), which has caused widespread respiratory illnesses worldwide over the last two decades [1].

COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a global pandemic by the World Health Organization (WHO) on March 11, 2020, due to its rapid and widespread transmission. Currently, the number of globally reported cases has surpassed 774 million, and more than 7 million deaths have been reported [2]. The outbreak of COVID-19 has brought significant challenges to individuals living with diabetes mellitus Type-II (DM-T2). Recent research has indicated that people with DM-T2 who contract COVID-19 have a greater incidence of severe outcomes and mortality than those without diabetes Type-II [3, 4].

Diabetes mellitus type II poses a significant global health challenge that has escalated to pandemic levels. According to estimates from the International Diabetes Federation (IDF), nearly 537 million adults worldwide were found to be afflicted with diabetes in 2021. This number is projected to increase to 643 million by 2030 and a staggering 784 million by 2045. Almost 80% of the diabetes mellitus type II population (3 in 4 adults) lives in low- and middle-income countries (LMICs), where the prevalence of diabetes mellitus type II is increasing rapidly [5].

The corresponding global health expenditure for diabetes mellitus type II-related issues in 2021 was already a substantial 966 billion US dollars. In low-middle-income countries such as Pakistan, the total direct cost of DM-T2 management is reported to be USD 332, with medication costs comprising 60.4% [6].

The underlying mechanisms leading to poor outcomes in DM-T2 patients with COVID-19 are attributed to the SARS-CoV-2 virus binding to the angiotensin-converting enzyme 2 (ACE2) receptor, which leads to inflammation and cytokine storm [7]. Moreover, uncontrolled hyperglycemia leads to multiple microvascular complications in DM-T2 patients, including nephropathy, neuropathy and retinopathy [8–10].

Diabetic nephropathy is the primary cause of end-stage renal disease (ESRD) on a global scale, affecting approximately 40% of individuals diagnosed with DM-T2 [11], substantial data is available confirming that COVID-19 exacerbates renal function decline in DM patients, leading to higher rates of acute kidney injury (AKI), rapid progression of chronic kidney disease (CKD), and increased mortality. Furthermore, End-stage renal disease (ESRD) is also a risk factor for cardiovascular disease (CVD) as well as CVD mortality [12]. Recent studies have shown the complex pathophysiological association between diabetic nephropathy and COVID-19 as Narayan, K.V. and L.R. Staimez have reported that approximately 6.7% of patients afflicted by SARS-CoV-2 infections experienced the development of acute kidney injury (AKI) within a median period of 20 days, with approximately 30% necessitating renal replacement therapy [13].

Moreover, several other studies have revealed that approximately 70% of patients with AKI after COVID-19 infection did not survive [14]. Kolhe et al. have also reported a high incidence of AKI in patients with COVID-19 that was associated with a 3-fold higher odds of death than COVID-19 without AKI [15]. The elevated expression of angiotensin-converting enzyme 2 (ACE2) mRNA in the kidneys of DM-T2 patients may contribute to a higher severity risk of kidney injury and mortality with SARS-CoV-2 [16, 17]. Similar findings are reported by Menon, T., et al. revealing COVID-19 led to AKI in 50% of patients with Diabetes, contributing to a 30% higher mortality rate [18].

Renal histopathological features of deceased patients were analyzed by examining postmortem tissue samples from a cohort of COVID-19 patients ($n=85$). The findings revealed that 54% of these patients experienced severe acute kidney injury (AKI), while 27% showed evidence of diabetic nephropathy [19]. Additionally, in Germany, it has been reported that in a cohort of COVID-19 patients ($n=75$), obesity and diabetic nephropathy were linked to poor outcomes in 70% of patients who did not survive [20].

Despite abundant research on COVID-19 symptoms in hospitalized patients; there is a scarcity of studies investigating the clinical manifestations of DM-T2 patients post-COVID-19, particularly in terms of microvascular complications like diabetic nephropathy. A number of systematic reviews have provided evidence of nephropathy and acute kidney injury (AKI) occurring in the general population following COVID-19 infection [21–23]. However, there remains a significant knowledge gap regarding AKI, especially in patients with type 2 diabetes. Moreover, none of the existing studies have explored and compared the levels (stages) of kidney injury specifically in individuals with diabetes mellitus type 2 after contracting COVID-19. These studies, apart from being limited in number, have a small population size and mostly include case reports with insufficient clinical data. Furthermore, there is a scarcity of longitudinal studies that follow DM-T2 patients after COVID-19 with nephropathy over an extended period of time.

In light of this gap in knowledge, future research is necessary to investigate the incidence and severity of nephropathy/AKI in patients with DM-T2 following COVID-19 infection. Such studies would greatly

contribute to our knowledge and reform of clinical management strategies for this vulnerable population.

This systematic literature review (SLR) aimed to critically analyze existing studies and evidence on the impact of COVID-19 on nephropathy/kidney injury in DM-T2 patients. By synthesizing the available data, we sought to elucidate the potential effects of COVID-19 on the progression of nephropathy/acute kidney injury in individuals with DM-T2.

Methods

Systematic review and meta-analysis.

Search strategy and study selection

The protocol for this systematic literature review was developed following the guidelines provided by the Preferred Reporting Elements for Systematic Review and Meta-Analysis Protocols (PRISMA) (S1, provided as a supplementary file). The final results of the systematic review adhere to the preferred reporting items specified by the PRISMA 2020 guidelines [24, 25]. The identification of relevant articles was conducted through an electronic search using the 'search string (Supp file -S2) developed and validated by researchers. This approach ensured a systematic and rigorous process for identifying the most pertinent literature for the study. The population, exposure, outcome (PEO) framework was used for the search.

This study is registered on PROSPERO (Registration number CRD42023413887), and the register name is Azim Tabinda. The link to this systematic literature review is https://www.crd.york.ac.uk/prospero.

PRISMA Guidelines.

Keywords used:

The following keywords were used in the search:

"Diabetes Mellitus Type 2"; "Type 2 Diabetes"; Diabetes Type II, DM-T2; Diabetic Renal Disease, Diabetic nephropathy; Diabetic kidney disease; DKD, DN (Diabetic nephropathy); Kideny injury', COVID-19, coronavirus, or SARS-CoV-2.

Sources searched:

We searched the following databases for this systematic literature review:

The Cochrane Library, Web of Science and PubMed for articles with a publication date from

March 2020 to July 2023 with English language restriction.

A PubMed search was conducted on 1/4/2023, a Cochrane database search on 15/4/23 and a WoS search on 19/4/23.

Inclusion criteria Confirmed patients with COVID-19 and a pre-existing condition of DM-T2 were included in the study, labelled as experimental Group/population. The selection criteria did not impose restrictions based on geographic region, sex, or age. The operational definition of a confirmed case of COVID-19 provided by the World Health Organization's latest update was adopted as a reference for COVID-19 diagnosis in this study.

The standard operational definition of a confirmed diabetes mellitus case, as outlined by the American Diabetes Association [26], was utilized. The criteria for diabetes diagnosis, as referenced, were fasting plasma glucose levels ≥ 126 mg/dL (7.0 mmol/L), defined as no food intake for a minimum of 8 h. Additionally, a diagnosis may be made based on a 2-hour plasma glucose level ≥ 200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT) or a haemoglobin A1c level ≥ 6.5% (48 mmol/mol). It should be noted that in some primary studies, DM-T2 status identification may rely on medical history only [26]. We included cohort studies, cross-sectional studies, case-control studies, randomized control trials (RCTs), and nonrandomized control trials.

Comparator if possibly found in literature: Non-DM-T2 Covid patients (Control Group).

Exclusion criteria We excluded adolescents (under 18 years of age) and elderly people (over 70), patients with type I diabetes mellitus (DM-type 1), Gestational Diabetes, Keto-prone Diabetes and latent autoimmune Diabetes.

The main outcome was nephropathy/kidney injury in DM-T2 patients post-COVID-19.

Reviews, letters to editors, commentaries, and articles including Diabetes Type-I, Gestational Diabetes, and preprints were not considered. Irrelevant articles in terms of incorrect populations or outcomes as well as non-English articles were excluded.

Data extraction

Study selection Two independent researchers (Ms. AT and Ms. Q) reviewed the study titles and abstracts with previously established selection criteria, and studies meeting the inclusion criteria were retrieved for full-text assessment. Subsequently, the two researchers independently read the full texts of the selected articles. Both researchers utilized the same instrument (Data Extraction Template) previously validated in Excel, which adheres to predefined inclusion criteria. Citations were downloaded into Endnote X8. Duplicates were removed, and articles not matching the inclusion criteria were discarded. The Covidence tool was used for screening. Any disagreements were resolved by mutual discussion until a consensus was reached or by consulting a third investigator.

The latest version of the PRISMA Flowchart (2020) was used to describe the complete process for the identification, selection and inclusion of studies [24, 27].

Data synthesis and analysis:

For data extraction, the following data were extracted:

Basic literature information title, author and publishing year, study location, study type, sample size.

Basic research information participant demographics, grouping, age and sex of participants, duration of diabetes, diagnosis of COVID-19, percentage of patients with type- 2 diabetes, and percentage of DM-T2 patients who presented the outcomes (nephropathy, kidney injury, mortality).

Outcome indicators

The main outcome was nephropathy/kidney injury in diabetic patients (type II) post-COVID-19. The data extraction template was designed on a Microsoft Excel spreadsheet.

Quality assessment

Risk of bias in studies For observational studies such as cohort and cross-sectional studies, we used a study quality assessment tool provided by the National Institutes of Health (14 questions/domains). Both researchers worked independently. A summary of all the assessments is provided in Table S4 [28].

Two reviewers (TA and QA) worked independently to check the quality of the articles.

Statistical analysis

To study the association of COVID-19 with kidney injury in the DMT2 population, we performed a meta-analysis and computed the pooled odds ratio with a 95% confidence interval (CI) as the effect size. A p-value of <0.05 indicated a statistically significant association.

To assess the heterogeneity among studies, the I^2 statistic was calculated. Heterogeneity was considered to be low if I^2 was between 0% and 25%, moderate if I^2 was between 25% and 50%, or high if I^2 was greater than 75%. To address heterogeneity among the studies and to calculate a more conservative result, the odds ratios will be pooled using only the random effects model.

Egger's linear regression and Begg's rank tests were employed to quantitatively evaluate publication bias and qualitatively evaluate bias with a funnel plot. When the funnel plot is symmetrical and the p-value of the Begg and Egger tests is >0.05, no significant publication bias is considered to exist in the meta-analysis. Jamovi software and Excel were used for the meta-analysis and statistical analysis.

Results

Study selection and data collection

The total number of articles retrieved from different databases using the relevant keywords was 6,339 (PubMed = 1,061, Cochrane Library = 850, Web of Science (WoS) = 4,428 after using a filter for the year). After removing duplicates and screening titles, the total number of titles accepted was 152. After the abstract screening, the number of titles accepted was reduced to 54 for full-text screening. During the full-text screening, we excluded studies ($n=48$) based on irrelevancy, an incorrect patient population, or an incorrect outcome. The excluded studies are shown in the Supplementary file (S5).

The final records included the following:

After applying the selection criteria and quality assessment, we obtained a final set of 6 observational studies for analysis, S3. We adhered to reporting and guidance based on the preferred reporting items for systematic review and meta-analysis (PRISMA) statement [24] (Fig. 1).

Study characteristics

The 6 included studies were published between December 2020 and 2022. Except for one prospective study [29], five studies were retrospective [30–34]. The total reported patients were 14,723, with a study sample size ranging from 154 [33] to 6078 [29]. Table S3 lists all the characteristics of the included studies.

Characteristics of the included studies

The six included studies (S3) explored the complex relationship between COVID-19, and acute kidney injury (AKI) in individuals with Type 2 Diabetes (DM-T2).

The included studies were carried out in different countries, including the United States ($n=3$) and one each in Pakistan, Malaysia and Iran. All studies focused on multiple hospitals or clusters of hospitals.

The demographic characteristics of the study populations varied; they typically included individuals spanning a wide age range, from 18 to 70 years. Only two studies received funding from institutional Research Foundations; the funding bodies included the Ruth L. Kirchstein National Research Service Award program [30] and the US Department of Veterans Affairs [31]. The rest of the studies did not receive any funding.

The central focus of these studies was the potential association between COVID-19 infection and the occurrence of nephropathy/AKI in patients with DM-T2 disease. In the analysis of six studies, the following important themes were identified:

Increased risk of kidney injury in DM-T2 patients post-COVID-19 and increased mortality rates

Despite the scarcity of information on COVID-19-related kidney damage, AKI appears to be a multifaceted process influenced by virus-mediated tubular injury, cytokine storm, Angiotensin II pathway activation, complement

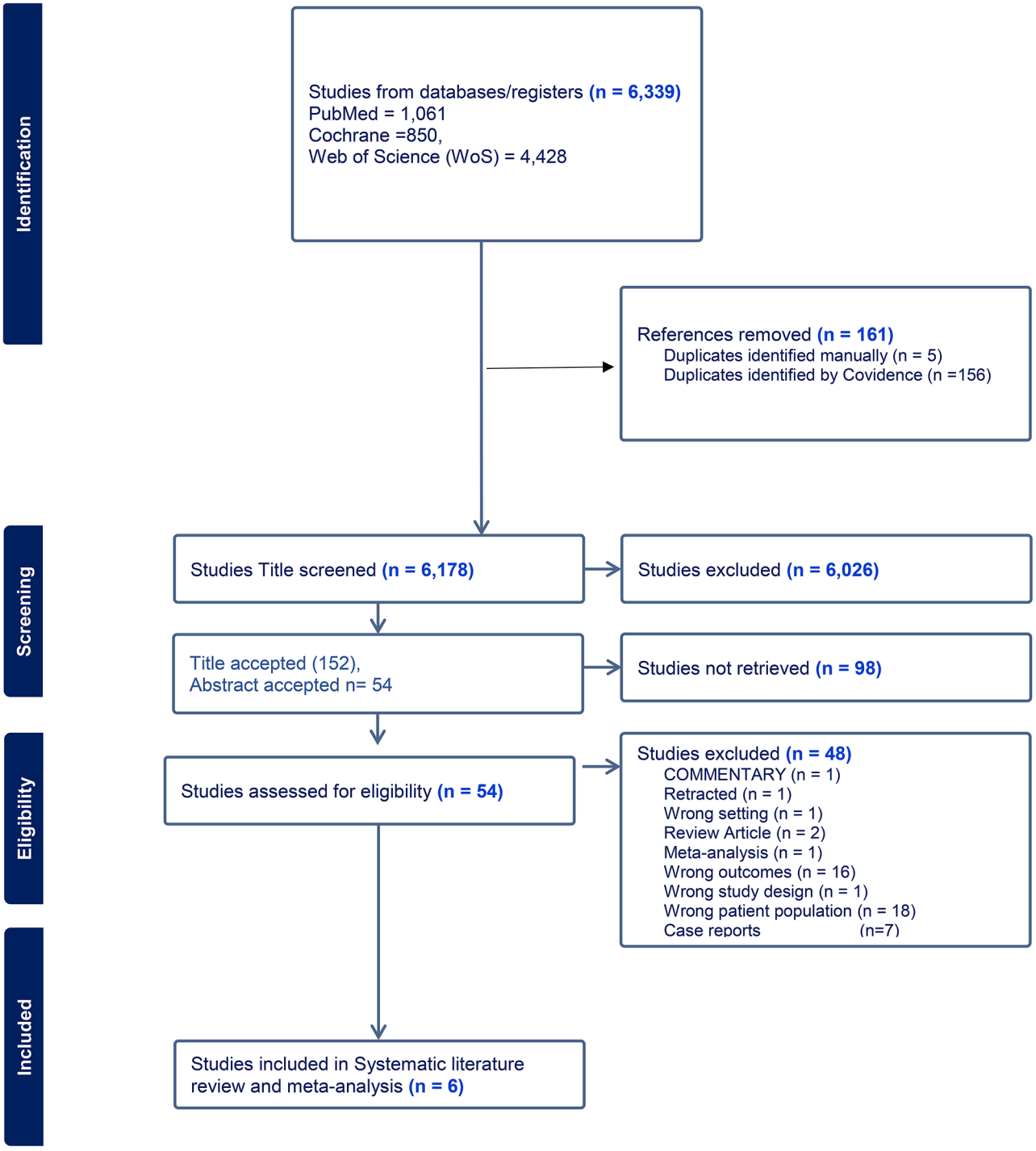

Fig. 1 PRISMA Flow diagram

system dysregulation and hyper-coagulation, all of which can exacerbate AKI risk in individuals with known risk factors like DM-T2 [17]. Studies have reported significantly higher mortality rates among COVID-19 patients with DM-T2 who develop acute kidney injury (AKI) [35]. This highlights the severity of kidney complications in this subgroup and its impact on overall outcomes. A study included in this systematic Literature review (SLR and Meta-analysis) conducted by Bowe [31] has reported that patients with DM-T2 are at increased risk of developing AKI during hospitalization for COVID-19; notably, 47% of AKI patients did not return to their baseline serum creatinine levels at discharge. Moreover, the researchers have revealed that the majority of

participants (80%) had no previous history of diabetic nephropathy and developed acute kidney injury (AKI) on the first day of hospitalization, indicating that the coronavirus directly affected the kidneys [31].

Similarly, the results of another included study conducted by Bandelac et al. reported that 608 patients (39.3%) without any prior history of Diabetic nephropathy developed AKI either on admission or during their admission to the hospital [32]. Furthermore, Khalili et al. [34] revealed that DM-T2 patients with COVID-19 had a greater risk of renal impairment than those without DM-T2.

The interpretation of the results of the meta-analysis process can be seen in the forest plot (Fig. 2). COVID-19 was significantly associated with acute kidney injury (AKI) in the DM-T2 population. The pooled odds ratio (OR) was 2.27 (95% Confidence Interval [CI]: 2.05–2.50; $p<0.00001$), indicating that DM-T2 patients with COVID-19 have more than twice the odds of developing AKI compared to non-diabetic patients. The test for overall effect ($Z=15.85$, $p<0.00001$) strongly supports the statistical significance of the association. However, it's important to note the substantial heterogeneity among the studies ($I^2 = 92\%$, $Chi^2 = 61.17$, $df=5$, $p<0.00001$). This high heterogeneity suggests considerable variability in the effect sizes across studies, which may be due to differences in study populations or other methodological factors.

All six included studies demonstrated a consistent direction of effect, with ORs ranging from 1.80 to 5.33, all favouring an increased risk of AKI in the COVID-19-exposed DM-T2 group. The study by Goh et al. (2022) reported the highest OR of 5.33 (95% CI: 4.21–6.74), while Bandalac et al. (2022) showed the lowest OR of 1.80 (95% CI: 1.47–2.22). Despite the variability among the studies, the consistent increase in AKI risk observed in all studies, along with the narrow confidence interval of the pooled estimate, strongly supports the association between COVID-19 and AKI in DM-T2 patients. These findings emphasize the need for close monitoring and preventive measures for efficient kidney function in this vulnerable population after COVID-19 infection.

Forest plot for the association of COVID-19 with Nephropathy/kidney injury in Diabetes Type-2 patients. Squares and the corresponding lines are the point estimates of individual studies and 95% confidence intervals (95% CI). The pooled odds ratio (OR) was 2.27 (95% [CI]: 2.05–2.50; $p<0.00001$.

Hyperglycemia as a risk factor

Hyperglycemia upon admission is identified as a significant risk factor for AKI in COVID-19 patients with DMT2. Poor Diabetes control and elevated blood glucose levels appear to contribute to the development of kidney injury. Charoenngam [30] revealed that hyperglycemia upon admission in DM-T2 patients suffering from COVID-19 was significantly associated with acute kidney injury (AKI).

Publication bias and heterogeneity

For the main outcome of this meta-analysis, i.e., the association of Covid-19 with nephropathy/acute kidney injury (AKI) in DM-T2 patients, publication bias was evaluated through visual inspection of the funnel plot (Figure S3) and Begg's and Egger's tests. Neither the rank correlation nor the regression test indicated any funnel plot asymmetry ($p=0.4694$ and $p=0.8201$, respectively).

Discussion

This meta-analysis examined the association between kidney injury and COVID-19 in DM-T2 patients. Our results revealed a significant association between COVID-19 and kidney injury in DM-T2 patients without any history of Diabetic nephropathy. This suggests that kidney injury is a prevalent complication of COVID-19 infection in the type II diabetes population, which often requires hospitalization and even hemodialysis in severe cases.

Acute kidney injury (AKI) is a significant complication associated with COVID-19 and contributes to high morbidity and mortality rates. Early and aggressive

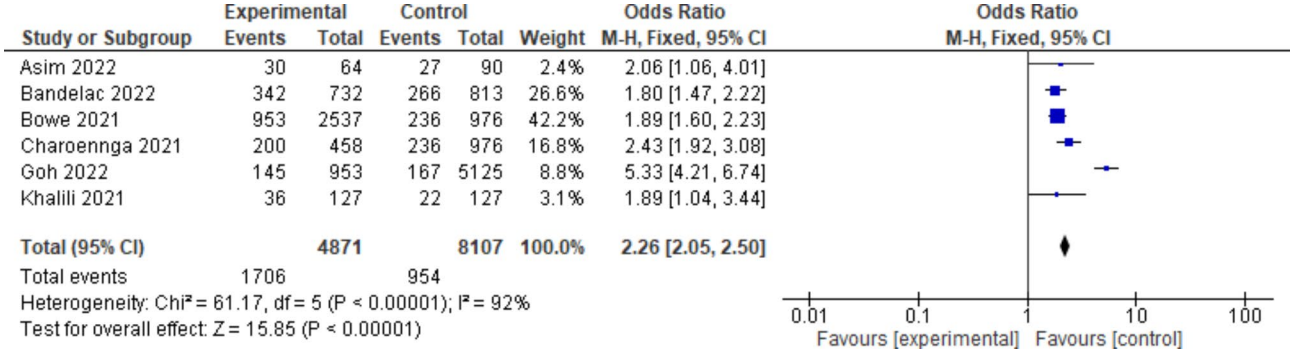

Fig. 2 Forest Plot

fluid therapy can prevent AKI in DM-T2 patients post-COVID-19. Effective management requires the early identification and differentiation of patients at risk from those not at risk [36].

Studies have suggested that a substantial number of COVID-19 patients also have DM-T2 as a common comorbidity [37]. The primary mechanism responsible for the poor prognosis in individuals with both conditions involves the binding of the Covid-19 virus to the angiotensin-converting enzyme 2 (ACE2) receptor. This interaction leads to an acute inflammatory response and cytokine release. In the case of DM-T2 patients, this exacerbates preexisting immune system challenges, heightening the risk of a cytokine storm and causing a pro-inflammatory and pro-coagulative state [38].

Research suggests that there is an intricate relationship between diabetic nephropathy (DN) and COVID-19, this complication after SARS-CoV-2 infection was initially identified in 2003 [39]. The SARS-CoV-2 virus responsible for COVID-19 infection has been found to directly infect renal cells, leading to acute kidney injury (AKI) [40, 41]. Furthermore, in addition to direct entry into cells, the virus has indirect effects, including inflammation, hypoxia, and cytokine storms, which further contribute to the progression of nephropathy in DM-T2 patients. The pro-inflammatory state induced by COVID-19 can lead to endothelial dysfunction, oxidative stress, and microvascular damage, all of which are known to worsen renal function [42, 43].

This connection between COVID-19 and diabetic nephropathy highlights the complex pathophysiology involved, and understanding this relationship is crucial for effective management and prevention strategies for the DM-T2 population.

Other published reviews support the results we have presented in this research. A narrative review by Sonkar [44] indicated the impact of COVID-19 on patients with DM-T2 with respect to the development of nephropathy and acute kidney injury. Another study conducted by McGurnaghan et al. in Scotland (n=5,463,300) revealed that individuals with DM-T2 who contracted COVID-19 were more likely to experience severe outcomes, such as the need for critical care treatment, including dialysis, or even death [45]. Similarly, a study conducted by Rivero et al. in Mexico, which evaluated postmortem kidney biopsies, revealed that 54% of patients exhibited severe acute kidney injury (AKI), 27% of whom also exhibited signs of diabetic nephropathy [20]. This finding is consistent with our findings, which were reported in a study conducted by Bandelac, L., et al. revealing that in approximately 1500 COVID-19 patients, 39% developed AKI, including 342 with DM-T2, without any prior diabetic nephropathy. Among those with AKI, 58.2% did not survive their hospital stay, and the AKI rate was notably higher than the global rate but aligned with local studies [32]. The pathogenesis of acute kidney injury (AKI) in DM-T2 patients after COVID-19 is complex and involves multiple factors. The primary cause of AKI in COVID-19 patients is acute tubular injury, which is attributed to direct viral infection and replication in podocytes and renal tubule cells, leading to tubular damage [46]. SARS-CoV-2, the virus responsible for COVID-19, has been found to directly infect renal cells, leading to acute kidney injury (AKI). The virus enters the kidney cells through the angiotensin-converting enzyme 2 (ACE2) receptor, which is highly expressed in the renal tubules. This direct viral injury can exacerbate nephropathy and acute kidney injury in DMT2 patients, leading to a decline in renal function [47].

Furthermore, a systematic review reported that nearly one-third of patients hospitalized with COVID-19 developed acute kidney injury (AKI) [48], reinforcing the evidence that COVID-19 may impact the kidneys through direct virus-mediated injury, cytokine storms, complement system dysregulation, and hypercoagulability.

In support of these findings, a study utilizing data from the Mexican Open Registry of COVID-19 revealed that individuals with diabetic nephropathy had a 5% greater chance of being admitted to the hospital, a 101.7% greater chance of requiring intubation, and a 20.8% greater chance of experiencing a fatal outcome. These results were statistically significant ($p<0.01$), highlighting the heightened risk faced by individuals with diabetic nephropathy when infected with COVID-19 [49].

COVID-19 has had a significant impact on individuals, especially those with pre-existing diseases, society and, as a whole, the global economy. It has profoundly affected the DM-T2 population since both pandemics have common pathologies and poor glycemic control leads to worse outcomes in this population.

Conclusion

In conclusion, our systematic review and meta-analysis offer compelling evidence of the significant impact of COVID-19 on causing acute kidney injury in individuals with DM-T2 patients without any history of diabetic nephropathy. This complication often necessitates hospitalization and, in severe cases, requires hemodialysis.

When treating DM-T2 patients with renal injury, it is essential to focus on maintaining the balance of acids, bases, electrolytes, and body fluids, as well as managing diet and nitrogen balance. Continuous renal replacement therapy (CRRT) may be necessary for critically ill patients. Continuous renal replacement therapy (CRRT) is recommended in situations such as acidosis, pulmonary edema or fluid overload, hyperkalemia, and fluid management in cases of multiple organ dysfunction in DMT-2 patients suffering from COVID-19.

The findings of this SLR can contribute to the existing knowledge and help healthcare professionals, researchers, and policymakers develop preventive strategies, clinical management approaches, and resource allocation to mitigate the adverse outcomes associated with the intersection of COVID-19 and kidney injury in individuals with DM-T2 without any prior history of diabetic nephropathy.

To further advance our understanding, future prospective studies on a substantial scale with extended and comprehensive follow-up periods are required to assess kidney function using novel kidney markers, urine analysis and biopsy studies. Moreover, post-COVID-19 care should also focus on renal function in this population.

Limitations

The included studies have certain limitations, including small sample sizes, retrospective study designs, and missing clinical data.

Although our search was unbiased and we tried to follow a proper strategy for searching the literature that has assessed both DM-T2 and COVID-19, some unpublished data might have been missing.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12882-024-03821-6.

Supplementary Material 1

Acknowledgements
We are thankful to Mr Amjad from Shifa Tameer-e-Millat University for his guidance in statistical analysis.

Author contributions
T.A formulated the research question, designed the study, searched the published articles, extracted and selected articles, extracted and analysed data, drafted and revised the Systematic literature review. QA helped to design the study, selected articles, extracted data and commented on drafts. A.H, F.S, S.S and A.K commented on versions of the manuscript. H.A, and S.F resolved conflicts and provided supervision during the screening of articles.

Funding
There was no funding source for this study.

Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request (tabinda.azim@iqraisb.edu.pk).

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Clinical trial number
Not applicable.

Received: 3 June 2024 / Accepted: 14 October 2024
Published online: 06 November 2024

References

1. Zu ZY et al. *Coronavirus disease 2019 (COVID-19): a perspective from China.* 2020. 296(2): pp. E15-E25.
2. Organization WHO. COVID-19 epidemiological update – 19 January 2024. 2024; https://www.who.int/publications/m/item/covid-19-epidemiological-update-19-January-2024
3. Kania M et al. *Characteristics, mortality, and clinical outcomes of hospitalized patients with COVID-19 and diabetes: a reference single-center cohort study from Poland.* International Journal of Endocrinology, 2023. 2023.
4. Tarawade AS, Mane AB, Chawla P. *COVID-19 outcome among diabetic patients admitted in a tertiary care hospital: An observational study.*
5. Magliano DJ, Boyko EJ, Atlas ID. *What is diabetes?* in *IDF DIABETES ATLAS [Internet]. 10th edition*. 2021, International Diabetes Federation.
6. Butt MD et al. *Cost of illness analysis of type 2 diabetes mellitus: the findings from a lower-middle income country.* 2022. 19(19): p. 12611.
7. Sandooja R, Vura NVRK. and M.J.I.J.o.E. Morocco, *heightened ACE activity and unfavorable consequences in COVID-19 Diabetic subjects*. 2020. 2020(1): p. 7847526.
8. Gude-Sampedro F et al. Development and validation of a prognostic model based on comorbidities to predict COVID-19 severity: a population-based study. 2021. 50(1): pp. 64–74.
9. da Silva PH et al. *COVID-19 and Diabetes Mellitus: Potential Metabolic Associations.* 2021. 21(11): pp. 929–936.
10. Zhu L et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. 2020. 31(6): pp. 1068–77. e3.
11. Yuan CM, et al. Diabetic nephropathy as the cause of end-stage kidney disease reported on the medical evidence form CMS2728 at a single center. Clin Kidney J. 2017;10(2):257–62.
12. Silver SA et al. *The prevalence of acute kidney injury in patients hospitalized with COVID-19 infection: a systematic review and meta-analysis.* 2021. 3(1): pp. 83–98. e1.
13. Narayan KV, L.R.J.T.L D, Staimez, Endocrinology. Rising Diabetes Diagnosis long COVID. 2022;10(5):298–9.
14. Rivero J et al. Association between postmortem kidney biopsy findings and acute kidney injury from patients with SARS-CoV-2 (COVID-19). 2021. 16(5): pp. 685–93.
15. Kolhe NV, et al. Acute kidney injury associated with COVID-19: a retrospective cohort study. PLoS Med. 2020;17(10):e1003406.
16. Gilbert RE et al. Overexpression of the severe acute respiratory syndrome coronavirus-2 receptor, angiotensin-converting enzyme 2, in diabetic kidney disease: implications for kidney injury in novel coronavirus disease 2019. 2021. 45(2): pp. 162–6. e1.
17. Batlle D et al. Acute kidney Injury in COVID-19: emerging evidence of a distinct pathophysiology. 2020. 31(7): pp. 1380–3.
18. Menon T et al. The association of acute kidney injury with disease severity and mortality in COVID-19: a systematic review and meta-analysis. 2021. 13(3).
19. Santoriello D et al. Postmortem kidney pathology findings in patients with COVID-19. 2020. 31(9): pp. 2158–67.
20. Rivero J, et al. Association between postmortem kidney biopsy findings and acute kidney injury from patients with SARS-CoV-2 (COVID-19). Clin J Am Soc Nephrology: CJASN. 2021;16(5):685.
21. Sabaghian T et al. *COVID-19 and acute kidney injury: a systematic review.* 2022. 9: p. 705908.
22. Fabrizi F et al. *COVID-19 and acute kidney injury: a systematic review and meta-analysis.* 2020. 9(12): p. 1052.
23. Chen Y-T et al. Incidence of acute kidney injury in COVID-19 infection: a systematic review and meta-analysis. 2020. 24: pp. 1–4.
24. Moher D, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Reviews. 2015;4(1):1–9.
25. Page MJ, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg. 2021;88:105906.
26. Care DJD. c., *Care in diabetes—2022.* 2022. 45: p. S17.

27. Page MJ, et al. Updating guidance for reporting systematic reviews: development of the PRISMA 2020 statement. J Clin Epidemiol. 2021;134:103–12.
28. National Heart. Lung, a.B.I., *Study quality assessment tools.* 2023.
29. Goh BL, et al. COVID-19 death and kidney disease in a multiracial Asian country. Nephrology. 2022;27(7):566–76.
30. Charoenngam N, et al. Association between hyperglycemia at hospital presentation and hospital outcomes in COVID-19 patients with and without type 2 diabetes: a retrospective cohort study of hospitalized inner-city COVID-19 patients. Nutrients. 2021;13(7):2199.
31. Bowe B, et al. Acute kidney injury in a national cohort of hospitalized US veterans with COVID-19. Clin J Am Soc Nephrol. 2021;16(1):14–25.
32. Bandelac L et al. Acute kidney injury incidence, stage, and recovery in patients with COVID-19. Int J Nephrol Renovascular Disease, 2022: pp. 77–83.
33. Asim M, et al. Acute kidney injury in hospitalized covid-19 patients: a retrospective observational study. J Ayub Med Coll Abbottabad. 2022;34(3 Suppl 1):661–6.
34. Khalili S et al. *Prevalence, risk factors and outcomes associated with acute kidney injury in patients hospitalized for COVID-19: a comparative study between diabetic and nondiabetic patients.* Journal of diabetes research, 2021. 2021.
35. Chen J, et al. Inflammatory stress in SARS-COV-2 associated acute kidney injury. Int J Biol Sci. 2021;17(6):1497.
36. Ronco C, Reis T, Husain-Syed F. Management of acute kidney injury in patients with COVID-19. Lancet Respir Med. 2020;8(7):738–42.
37. Mithal A, et al. High prevalence of diabetes and other comorbidities in hospitalized patients with COVID-19 in Delhi, India, and their association with outcomes. Volume 15. Diabetes & Metabolic Syndrome: Clinical Research & Reviews; 2021. pp. 169–75. 1.
38. Nataraj M. Devising solutions for COVID-19 fear in type 2 diabetes Mellitus. Volume 87. OMEGA-JOURNAL OF DEATH AND DYING; 2023. pp. 765–8. 3.
39. Chenna A et al. *Acute kidney injury in a case series of patients with confirmed COVID-19 (coronavirus disease 2019): role of angiotensin-converting enzyme 2 and renin-angiotensin system blockade.* Case reports in nephrology, 2020. 2020.
40. Su H et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. 2020. 98(1): pp. 219–27.
41. Mohamed NE, et al. Association between chronic kidney disease and COVID-19-related mortality in New York. World journal of urology; 2021. pp. 1–7.
42. Zaghloul H, Malik RA. COVID-19 and the hidden threat of diabetic microvascular complications. Therapeutic Adv Endocrinol Metabolism. 2022;13:20420188221110708.
43. Kant S, et al. The COVID-19 nephrology compendium: AKI, CKD, ESKD and transplantation. BMC Nephrol. 2020;21(1):1–13.
44. Sonkar GK, Singh S, Sonkar SK. A systematic review approach in understanding the COVID-19 mechanism in diabetes and its progression to diabetic microvascular complications. J Diabetol. 2022;13(4):322–30.
45. McGurnaghan SJ, et al. Risks of and risk factors for COVID-19 disease in people with diabetes: a cohort study of the total population of Scotland. Volume 9. The lancet Diabetes & endocrinology; 2021. pp. 82–93. 2.
46. Chen S, et al. Are glucagon-like peptide 1 analogues effective and safe in severe COVID-19 patients with type 2 diabetes?-a case report. Volume 10. ANNALS OF PALLIATIVE MEDICINE; 2021. pp. 7057–61. 6.
47. Su H, et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. Kidney Int. 2020;98(1):219–27.
48. Silver SA, et al. The prevalence of acute kidney injury in patients hospitalized with COVID-19 infection: a systematic review and meta-analysis. Kidney Med. 2021;3(1):83–98. e1.
49. Leon-Abarca JA et al. The impact of COVID-19 in diabetic kidney disease and chronic kidney disease: a population-based study. 2020. 91(4).

Publisher's note