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Impact of COVID-19 infection on mortality, diabetic complications and haematological parameters in patients with diabetes mellitus: a systematic review and meta-analysis

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ABSTRACT

Objectives SARS-CoV-2 poses significant challenges to people living with diabetes (PLWD). This systematic review aimed to explore the impact of COVID-19 on mortality, complications associated with diabetes and haematological parameters among PLWD.

Design Systematic review and meta-analysis using the Grading of Recommendations Assessment, Development and Evaluation (GRADE).

Data sources EMBASE, MEDLINE, Cochrane Central Register of Controlled Trials and LILACS were searched between 1 December 2019 and 14 January 2025.

Eligibility criteria for selecting studies Eligible studies included case-control and cohort studies involving PLWD categorised into two groups: those with confirmed SARS-CoV-2 infection and those without.

Data extraction and synthesis Meta-analyses estimated the odds ratios (ORs) and mean differences (MDs) of outcomes including mortality, intensive care unit (ICU) admission, diabetic ketoacidosis (DKA), acute kidney injury, hospitalisation length and haematological parameters. We pooled results using random-effects models and assessed study quality with the Newcastle-Ottawa Scale. A funnel plot was used to detect potential publication bias. The overall certainty of evidence was assessed using GRADE.

Results 25 of 7266 unique studies were eligible, including 1 154674 PLWD (561 558 with COVID-19 and 593 116 without COVID-19). SARS-CoV-2 infection in PLWD was associated with significantly increased mortality (OR 2.52, 95% CI 1.45 to 4.36, I^2=99%), acute kidney injury (3.69, 95% CI 2.75 to 4.94, I^2=0%), random plasma glucose in subjects with type 1 diabetes (MD 20.38 mg/dL, 95% CI 7.39 to 33.36, I^2=0%), haemoglobin A1C in subjects with type 2 diabetes (0.21%, 95% CI 0.05 to 0.38, I^2=13%), creatinine (0.12 mg/dL, 95% CI 0.04 to 0.19, I^2=0%), C reactive protein (38.30 mg/L, 95% CI 4.79 to 71.82, I^2=82%) and D-dimer (1.52 µg/mL, 95% CI 0.73 to 2.31, I^2=0%). No significant differences were observed in the incidence of ICU admission and DKA, hospitalisation length, haemoglobin, leucocyte, lymphocyte, neutrophil to lymphocyte ratio, platelet, blood urea nitrogen, estimated glomerular filtration rate, procalcitonin, albumin, ferritin and bilirubin among PLWD with and without SARS-CoV-2 infection.

Conclusions SARS-CoV-2 infection is associated with elevated risks of mortality and acute kidney injury and poor glycaemic control in PLWD, alongside increased levels of inflammatory and coagulation biomarkers. These findings underscore the urgent need for tailored clinical management strategies for PLWD with COVID-19.

PROSPERO registration number CRD42023418039.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This systematic review and meta-analysis synthesises data from 25 observational studies, offering comprehensive insights into the impact of COVID-19 on mortality, complications and haematological parameters in people living with diabetes.
⇒ Subgroup analyses stratified by diabetes type, diabetic emergencies, age and study design enhance clinical applicability.
⇒ Methodological heterogeneity across the studies necessitates cautious interpretation of pooled estimates.
⇒ The overall certainty of evidence is low due to observational study limitations, heterogeneity and imprecision.

INTRODUCTION

Diabetes mellitus (DM) is one of the major global public health concerns, imposing a huge global burden on public health and socioeconomic development. In 2021, DM affected an estimated 537 million adults worldwide, with a projected increase to 783 million by 2045 if no effective prevention methods are adopted.[1] COVID-19 was declared a public health emergency by WHO on 30 January 2020. As of 29 December 2024, COVID-19 has infected 770 million individuals worldwide, resulting in 7.07 million deaths.[2] The association between DM and adverse

outcomes of COVID-19 has been recognised. People living with diabetes (PLWD) face an approximately threefold increased mortality rate and a twofold higher risk of severe COVID-19 outcomes, with dysglycaemia further linked to higher mortality and medical interventions in PLWD infected with COVID-19.[3–5] COVID-19 could result in endocrine dysfunction and glycaemic dysregulation, triggering transient or persistent DM in people without a history of diabetes and severe metabolic complications in PLWD.[6–8] The bidirectional relationship between DM and COVID-19 has prompted increasing studies to investigate the impact of COVID-19 on mortality and complications associated with diabetes in PLWD.

The impact of COVID-19 on haematological parameters, such as plasma glucose, has garnered significant attention in both research and clinical practice. While some studies have reported a positive association between COVID-19 and hyperglycaemia in PLWD,[9 10] one study found no significant changes in fasting glucose and haemoglobin A1C (HbA1C) levels among PLWD before and after COVID-19, even at a median follow-up of 215 days postinfection.[11] The association between COVID-19 and dysglycaemia in PLWD remains inconclusive, and whether the infection itself exacerbates dysglycaemia in this population is unresolved. Potential contributing factors include reduced access to diabetes care services, lifestyle modifications and disturbances in emotional well-being due to recurring lockdowns and public health measures, as well as the direct or indirect effects of SARS-CoV-2.[12 13] Additionally, the effects of COVID-19 on other haematological parameters in PLWD are unclear. A comprehensive understanding of the impact of COVID-19 on haematological parameters in PLWD is therefore warranted. In this systematic review, we aim, for the first time, to provide a pooled estimate of the impact of COVID-19 on mortality, complications associated with diabetes and haematological parameters in PLWD.

METHODS

Search strategy and selection criteria

The review was registered on PROSPERO (CRD42023418039) and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guideline.[14] The research question followed the Population, Exposure, Comparison and Outcome (PECO) framework: in PLWD (P), did COVID-19 infection (E) increase the risk of incidence of mortality, complications associated with diabetes or glycaemic outcomes (O) compared with PLWD without COVID-19 infection (C)?

Studies meeting the following criteria were included:

- Population: PLWD, including type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM). Participants were categorised into those with confirmed SARS-CoV-2 infection and those without evidence of infection. Studies involving participants of all ages and from any setting were eligible.
- Study type: cohort studies and case-control studies. We excluded case reports, case series, commentaries, books, editorials, opinion pieces, posters, conference abstracts, qualitative studies, in vitro studies, animal studies and preprint papers (ie, non-peer-reviewed).
- Outcomes: comparative data on diabetes-related indicators or outcomes between PLWD with and without COVID-19 infection.

The search strategy (online supplemental table 1) was applied to EMBASE (Ovid), MEDLINE (Ovid), Cochrane Central Register of Controlled Trials (Ovid) and LILACS, covering the period from 1 December 2019 to 14 January 2025 (the initial search was conducted on 23 March 2023 and an updated search took place on 14 January 2025). Search terms included medical subject headings, keywords and variants of COVID-19 and diabetes. No language restrictions were applied. Grey literature was not searched. Google Translate was used to translate non-English publications. EndNote V.20 (Clarivate, Philadelphia, Pennsylvania) was used for deduplication, and Rayyan facilitated blinded title and abstract screening.[15] Three pairs of reviewers (JZ and WLT, JZ and SC, HTT and HKW) independently screened the titles, abstracts and full texts of the identified studies. Disagreements over title and abstract screening, full-text review and reasons for exclusion were resolved through consensus.

Data analysis

Two pairs of reviewers (JZ and YM, JZ and WLT) extracted the data independently with a predesigned standardised Microsoft Excel form. Disagreements were resolved by consensus. Extracted data included the following: (1) general information (eg, title, authors, country and publication year); (2) study design and participants (eg, design, study period, study population, demographics, inclusion and exclusion criteria, sample size and DM duration); (3) details of the exposure and control (eg, characteristics of the subjects and diagnosis and severity of COVID-19 infection); and (4) outcomes of interest, including primary outcomes (mortality and complications associated with diabetes: intensive care unit (ICU) admission, diabetic ketoacidosis (DKA), acute kidney injury and hospitalisation length) and haematological parameters (glycaemic control, blood cells, renal function, inflammation and other indicators).

The quality of the included studies was independently assessed by two pairs of assessors (JZ and YM, JZ and WLT) using the Newcastle-Ottawa Scale (NOS) on three broad characteristics: selection of study groups, comparability of groups and ascertainment of the outcome of interest.[16] Disagreements were resolved by consensus. Studies were considered low risk if they scored ≥7 and high risk if they scored ≤6.

Quantitative meta-analysis was performed using Review Manager V.5.4 (RevMan). Dichotomous outcomes were pooled via the Mantel-Haenszel method, reported as OR with 95% CI. Continuous outcomes were analysed using sample size-weighted mean differences (MDs) under

random-effects models. Medians and quartiles were converted to means and SDs using the formula developed by Wan *et al*.[17]

Units of glucose, creatinine, C reactive protein (CRP), blood urea nitrogen (BUN) and bilirubin were converted to mg/dL; HbA1C levels were expressed as percentage; estimated glomerular filtration rate (eGFR) was reported in mL/min/m^2; procalcitonin and ferritin levels were converted to ng/dL; erythrocyte sedimentation rate (ESR) was measured in mm/hour; D-dimer levels were reported in µg/mL; albumin and haemoglobin were expressed in g/dL; leucocyte counts were converted to $\times 10^9$/L; and lymphocyte and platelet counts were reported in $\times 10^9$/L. Heterogeneity was assessed with the Cochran Q test ($p<0.10$) and I^2 statistic ($I^2>50\%$=substantial). Subgroup analyses examined diabetes type (T1DM vs T2DM), DKA comorbidity, age (adults ≥18 years vs adolescents) and study design (cohort vs case-control). Funnel plots assessed publication bias (n >10). Sensitivity analyses tested robustness (if n ≥3) by iteratively excluding studies and including high-quality studies (low risk).

The overall certainty of evidence was assessed by two assessors (JZ and YM) using the Grading of Recommendations Assessment, Development and Evaluation (GRADE).[18] The certainty of evidence was downgraded based on the following factors: risk of bias, inconsistency, imprecision, indirectness and publication bias. It was upgraded if (1) the effect size was large (without substantial imprecision, although small effect sizes remained plausible); (2) a dose–response gradient was present; or (3) plausible residual confounding would reduce a demonstrated effect or suggest a spurious effect when the observed effect was neutral. The certainty of evidence was categorised as high, moderate, low or very low certainty.

Patient and public involvement

Patients and the public were not involved in the design, conduct, reporting or dissemination of this study.

RESULTS

Study selection and characteristics

As shown in figure 1, a total of 13 732 records were identified through database searching. After removing 6466 duplicate records, the titles and abstracts of 7266 records were screened and 7234 records were excluded. We evaluated the full texts of 32 potentially eligible studies and included 25 studies in the review (online supplemental table 2), which involved 1154674 PLWD (561 558 with and 593 116 without COVID-19).[9 19–42] A list of the excluded full-text studies with reasons for exclusion is provided in online supplemental table 3.

All studies were published between 2020 and 2025 and included participants from 13 countries across Europe, Asia and North America, including Turkey, Georgia, the UK, Italy, Sweden, Germany, Romania, India, Indonesia, Israel, China, Pakistan and the USA. Twenty-one studies had a comparison group from the equivalent study period

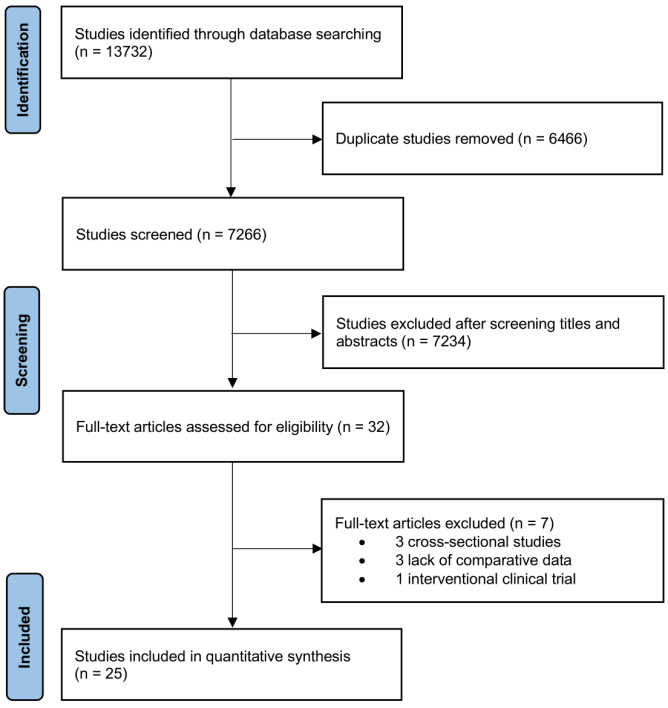

Figure 1 Flow diagram of the screening process and the papers excluded at each stage.

(the year preceding the pandemic).[9 19–28 30–32 34–36 38 39 41 42] Four studies were of case-control design[9 21 27 33] and the rest were cohort studies.[19 20 22–26 28–32 34–42] Five studies were prospective observational.[23 33–35 39] Seventeen studies analysed data from hospitals or research institutes,[9 19 21 23–29 31–34 37 38 41] and eight used regional or national databases/registries.[20 22 30 35 36 39 40 42] Of the studies, 6 reported the clinical features of subjects with T1DM,[9 20 26 28 41 42] 4 focused on T2DM[21 33–35] and 15 reported mixed DM types or unspecified DM classifications.[19 22–25 27 29–32 36–40] Twenty-one studies recruited adult subjects,[9 19–25 27 29–40] three studies enrolled adolescents[26 28 41] and one study included both adults and adolescents.[42] Sample sizes ranged from 20 to 1031880 subjects (online supplemental table 2). Meta-analysis was performed for 22 outcomes.

Quality assessment

The majority of the included studies (80%, 20/25) demonstrated moderate to high methodological rigour (scored ≥7 on the NOS; online supplemental table 4). The main limitations were incomparability in study design/analysis, inconsistent definitions and reporting of outcomes, variability in control group selection and retrospective study design. For example, although 13 papers reported mortality, incomparability in design/analysis resulted in insufficient control of confounding factors, limiting the credibility of the results.

Meta-analysis

Mortality

Thirteen studies, including a total of 1086757 PLWD (543 983 with COVID-19 and 542 774 controls), reported

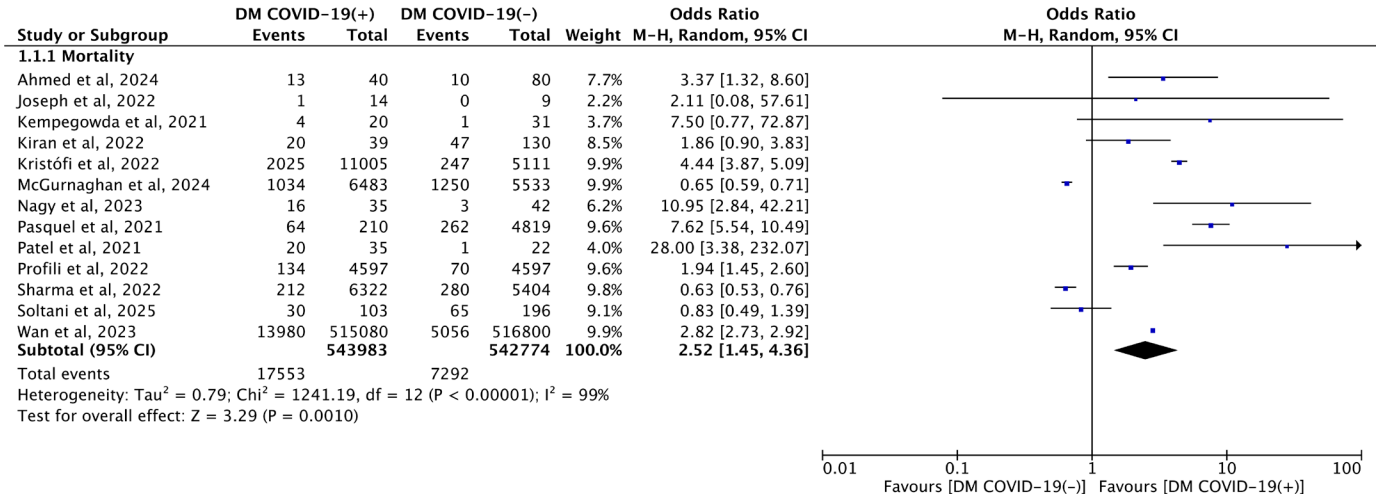

Figure 2 Comparison of risk differences in mortality: PLWD with COVID-19 versus PLWD without COVID-19. DM, diabetes mellitus; PLWD, people living with diabetes; M-H, Mantel-Haenszel.

on mortality[22 23 25 27 29–31 35–40] and found a significant increase in mortality among PLWD infected with COVID-19 (OR 2.52, 95% CI 1.45 to 4.36, I^2=99%; figure 2). The pooled OR remained robust in the leave-one-out analysis (online supplemental table 5). The sensitivity analysis restricted to high-quality studies revealed a significant increase in mortality among PLWD with COVID-19 compared with those without (2.72, 95% CI 1.50 to 4.94, I^2=99%). Subgroup analyses revealed significantly higher mortality in subjects with T1DM (5.68, 95% CI 2.90 to 11.12, I^2=0%), those presenting DKA (5.55, 95% CI 2.68 to 11.48, I^2=70%) and adults (2.52, 95% CI 1.45 to 4.36, I^2=99%; online supplemental figure 1a) infected with COVID-19, compared with those without COVID-19. The overall certainty was 'very low' (online supplemental table 6). The funnel plot exhibited asymmetry, suggesting potential publication bias (online supplemental figure 1b).

ICU admission

Four studies, involving 274 PLWD (109 with COVID-19 and 165 controls), were eligible for inclusion in the meta-analysis for ICU admission.[24 25 27 29] No significant difference in ICU admission rates was observed between PLWD infected with COVID-19 and non-COVID-19 controls (OR 0.89, 95% CI 0.37 to 2.21, I^2=0%; online supplemental figure 2). The pooled OR remained robust in the leave-one-out analysis (online supplemental table 5). The sensitivity analysis of high-quality studies showed no significant difference in ICU admission between PLWD with COVID-19 and non-COVID-19 controls (0.90, 95% CI 0.33 to 2.41, I^2=0%). The overall certainty was 'very low' (online supplemental table 6).

Diabetic ketoacidosis

Four studies, involving 24794 PLWD (9782 with COVID-19 and 15102 controls), were included in the analysis of DKA.[27 36 41 42] The overall analysis found no significant difference in DKA occurrence between PLWD with and without COVID-19 (OR 0.72, 95% CI 0.32 to 1.62, I^2=80%; online supplemental figure 3). The pooled OR was robust according to the leave-one-out analysis (online supplemental table 5). Similarly, no significant difference in DKA occurrence was observed among PLWD with COVID-19 compared with those without in the high-quality studies (1.18, 95% CI 0.83 to 1.69, I^2=0%). The overall certainty was 'very low' (online supplemental table 6).

Acute kidney injury

Two studies were included in the analysis of acute kidney injury.[22 38] The synthesis of the data from 5106 subjects demonstrated a significantly increased rate of acute kidney injury among PLWD with COVID-19 compared with those without COVID-19 (OR 3.69, 95% CI 2.75 to 4.94, I^2=0%; online supplemental figure 4). The overall certainty was 'moderate' (online supplemental table 6).

Hospitalisation length

The data from 16810 subjects across eight studies showed no significant difference in hospitalisation length (days) between PLWD with and without COVID-19 (MD −1.31, 95% CI −9.77 to 7.14, I^2=99%).[23–26 28 29 38 40] The sensitivity analysis, which included high-quality studies, revealed no significant difference in hospitalisation length between PLWD infected with COVID-19 and non-COVID-19 controls (−1.70, 95% CI −12.49 to 7.09, I^2=100%). The pooled OR was robust according to the leave-one-out analysis (online supplemental table 5). Similar results were found in the subgroup analyses (online supplemental figure 5). The overall certainty was 'very low' (online supplemental table 6).

Random plasma glucose

Thirteen studies, involving 15686 subjects, were included in the meta-analysis of random plasma glucose, revealing no significant difference in glucose levels between PLWD with COVID-19 and those without COVID-19 (MD 3.30 mg/dL, 95% CI −7.78 to 14.37, I^2=75%;

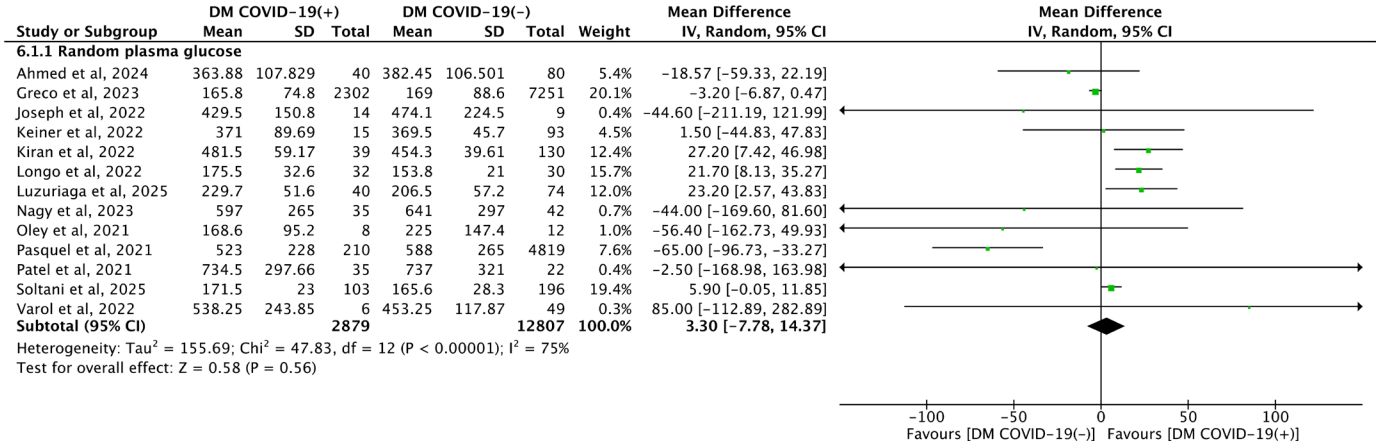

Figure 3 Comparison of differences in random plasma glucose (mg/dL): PLWD with COVID-19 versus PLWD without COVID-19. DM, diabetes mellitus; PLWD, people living with diabetes; IV, inverse variance.

figure 3).[9 22–28 31 32 34 37 38] The pooled estimate remained robust in the leave-one-out analysis (online supplemental table 5) and in the analysis that included only low-risk studies (−0.33, 95% CI −17.29 to 16.62, I^2=79%). Among subjects with T1DM, COVID-19 infection significantly increased random plasma glucose compared with uninfected individuals (20.38, 95% CI 7.39 to 33.36, I^2=0%). No significant differences were observed in subgroups presenting with DKA (−11.45, 95% CI −51.56 to 28.67, I^2=76%) and those without DKA (8.11, 95% CI −2.40 to 18.62, I^2=78%), as well as in adults (2.99, 95% CI −8.56 to 14.54, I^2=79%) and adolescents (5.84, 95% CI −39.27 to 50.95, I^2=0%; online supplemental figure 6). The funnel plot exhibited asymmetry, suggesting potential publication bias (online supplemental figure 7). The overall certainty was 'very low' (online supplemental table 6).

Other haematological outcomes

Seventeen studies, including 85 300 subjects, showed no significant difference in HbA1C between PLWD with and without COVID-19 (MD 0.14%, 95% CI −0.07 to 0.34, I^2=92%; online supplemental figure 8).[9 19–24 26–28 31–33 35 38 41 42] However, COVID-19 infection significantly increased HbA1C in subjects with T2DM (0.21, 95% CI 0.05 to 0.38, I^2=13%). Additionally, pooled data revealed no significant differences in haemoglobin (4 studies, 288 subjects; −0.78 g/dL, 95% CI −1.74 to 0.18, I^2=61%),[19 23 27 34] leucocyte count (2 studies, 189 subjects; -0.45×10^9/L, 95% CI −4.34 to 3.43, I^2=13%),[23 34] lymphocyte count (2 studies, 99 subjects; -0.20×10^9/L, 95% CI −0.51 to 0.11, I^2=0%),[19 27] neutrophil to lymphocyte ratio (2 studies, 229 subjects; 1.38, 95% CI −0.28 to 3.04, I^2=0%)[21 34] and platelet count (2 studies, 192 subjects; 23.22×10^9/L, 95% CI −20.73 to 67.16, I^2=12%)[23 27] among PLWD with and without COVID-19 (online supplemental figure 9). Synthesis of six studies (5411 subjects) showed significantly higher creatinine levels in PLWD with COVID-19 (0.12 mg/dL, 95% CI 0.04 to 0.19, I^2=0%).[9 22 23 26 27 34] However, no significant differences were observed in BUN (2 studies,[26 38] 138 subjects; 2.69 mg/dL, 95% CI −4.17 to 9.55, I^2=6%) and eGFR (5 studies,[9 21 26 27 35] 12 418 subjects; 2.91 mL/min/m^2, 95% CI −3.03 to 8.84, I^2=65%) between PLWD with and without COVID-19 (online supplemental figure 10).

COVID-19 significantly increased CRP levels in PLWD (4 studies, 342 subjects; 38.30 mg/dL, 95% CI 4.79 to 71.82, I^2=82%; online supplemental figure 11),[19 21 27 38] as well as D-dimer levels (2 studies, 106 subjects; 1.52, 95% CI 0.73 to 2.31, I^2=0%).[19 38] No significant differences were found in procalcitonin (2 studies, 112 subjects; 112.42 ng/dL, 95% CI −167.33 to 392.16, I^2=44%),[19 38] albumin (3 studies, 337 subjects; 0.09 g/dL, 95% CI −0.23 to 0.41, I^2=81%),[21 33 34] ferritin (2 studies, 105 subjects; 0.70 ng/L, 95% CI −0.15 to 1.55, I^2=90%)[19 38] and bilirubin (2 studies, 192 subjects; 0.02 mg/dL, 95% CI −0.05 to 0.99, I^2=0%)[23 27] (online supplemental figures 11 and 12). One study compared ESR but insufficient data precluded synthesis.[19]

GRADE certainty of the body of evidence

The GRADE evidence profile for the summary of findings is presented in online supplemental table 6. The analyses showed COVID-19 infection significantly increased the rate of mortality (the overall certainty was 'very low') and acute kidney injury ('moderate') among PLWD. However, COVID-19 did not have significant impacts on ICU admission ('very low'), rate of DKA ('very low'), hospitalisation length ('very low') and glucose ('very low') in the included studies. The overall certainty was low due to the nature of the observational studies included, the quality of the studies, considerable heterogeneity and imprecision.

DISCUSSION

This meta-analysis summarised the available data of 25 observational studies on the impact of COVID-19 on mortality, complications associated with diabetes and glycaemic and haematological parameters. We found that COVID-19 was associated with an increased risk of mortality and acute kidney injury and elevated plasma glucose (in T1DM), HbA1C (in T2DM), creatinine, CRP and D-dimer in PLWD. There was no difference in ICU

admission, DKA, hospitalisation length, haemoglobin, leucocyte, lymphocyte, neutrophil to lymphocyte ratio, platelets, BUN, eGFR, procalcitonin, albumin, ferritin and bilirubin among PLWD with and without COVID-19.

Current literature predominantly investigates the association between the presence or absence of DM and the risk of mortality and poor outcomes following COVID-19 infection. A meta-analysis comprising 6452 subjects from 30 studies revealed that DM was associated with a twofold increased risk of mortality and poor outcomes in individuals with COVID-19, compared with those without a history of diabetes and infected with COVID-19.[43] In a review encompassing 42 779 subjects across 38 studies, the presence of DM emerged as an independent risk factor for acute kidney injury after COVID-19, yielding an OR of 1.71 (95% CI 1.59 to 1.84), as compared with subjects without a history of diabetes and infected with COVID-19.[44] A systematic review including 15 282 subjects from 29 studies found that PLWD showed higher levels of serum CRP (standard mean difference (SMD) 0.41 mg/L, 95% CI 0.21 to 0.60 mg/L) and D-dimer (SMD 0.32 mg/L, 95% CI 0.17 to 0.47 mg/L) after COVID-19 than subjects without a history of diabetes.[45] Notably, our study contributes a distinct perspective by specifically investigating the impact of COVID-19 on the progression of pre-existing DM. By comparing clinical parameters between PLWD with and without COVID-19, our review further supports that COVID-19 is linked to higher mortality rates, elevated incidence of acute kidney injury and increased serum CRP, D-dimer and creatinine in PLWD. These findings contribute to a more comprehensive understanding of the complex interplay between COVID-19 and DM.

In terms of glycaemic control, our study aligns with previous research by observing a substantial increase in random plasma glucose levels among PLWD, particularly among those with T1DM.[9 10 46] This is consistent with the understanding that hyperglycaemia is a significant risk factor for adverse outcomes in COVID-19 infection.[47] Notably, a previous study reported no significant change in HbA1C levels before and after COVID-19 infection.[11] Consistent with this, our review also identified no difference in HbA1C levels between PLWD with and without COVID-19 when diabetes type was not differentiated. One plausible explanation is that HbA1C reflects long-term glycaemic control over 2–3 months, and the duration of the included studies may have been insufficient to observe changes.[48] Additionally, the absence of significant differences in ICU admission, DKA, hospitalisation length, blood cell parameters, renal function and other indicators may reflect limited statistical power due to the small number of studies. Further research with a larger sample size and comprehensive assessment is warranted to provide a thorough understanding of the potential impact of SARS-CoV-2 infection among PLWD.

COVID-19 infection exerts multifaceted systemic impacts on PLWD. The increased rates of mortality and acute kidney injury, along with poor glycaemic control and elevated creatinine, CRP and D-dimer levels, observed in PLWD and COVID-19 likely arise from multifactorial mechanisms. First, the chronic inflammatory state associated with DM may lead to an exaggerated cytokine response, potentially leading to the widespread tissue damage and severe consequences of COVID-19, including mortality and acute kidney injury.[49 50] Second, hyperglycaemia is associated with increased SARS-CoV-2 replication and heightened inflammation, potentially exacerbating disease severity in PLWD and COVID-19.[51 52] Additionally, the interaction between SARS-CoV-2 and ACE2 receptor, predominantly expressed on the surface of endothelial cells, can result in endothelial dysfunction, microvascular thrombosis and vascular inflammation.[53 54] This interplay, coupled with dysglycaemia, may also contribute to a weakened immunological response to anti-SARS-CoV-2 vaccination.[55] These pathological processes contribute to elevated levels of creatinine, CRP and D-dimer in PLWD. The presence of comorbidities commonly observed in PLWD, such as hypertension and cardiovascular disease, which are established risk factors for severe COVID-19, can further amplify the detrimental impacts of SARS-CoV-2 infection.[56] Further research is crucial to gain a comprehensive understanding of the multifactorial nature of adverse outcomes in PLWD and COVID-19.

Our study has several strengths. First, we examined a wide range of outcomes, including mortality, ICU admission, serious complications, glycaemic control, blood cells, renal function and inflammation, as well as other indicators such as D-dimer, albumin, ferritin and bilirubin. To our knowledge, this is the first systematic review and meta-analysis to comprehensively assess the impact of COVID-19 on disease progression of pre-existing DM, by comparing clinical parameters between PLWD with and without COVID-19. Second, our team assessed the impact across different groups of DM, age and with or without DKA. The study also has some limitations. First, geographical and temporal variability in dominant SARS-CoV-2 strains may have diverse impacts on PLWD, potentially influencing the outcomes observed in this review. However, it is important to note that the included studies did not report the specific dominant SARS-CoV-2 strains, which restricts our understanding of their potential influence on the outcomes. Second, the findings should be interpreted with caution due to methodological heterogeneity across the included studies. Among the 25 studies analysed, 5 were rated to have a high risk of bias (eg, variability in case and control population sources, incomplete adjustment for confounders). These variabilities may introduce bias into the pooled estimates and reduce the generalisability of the findings. Third, the potential for publication bias in outcomes with fewer than 10 studies remains uncertain. In these instances, a formal assessment of publication bias using funnel plots was not feasible. This limitation may lead to inaccuracies in the results by over-representing studies that report extreme effects, which could inflate the apparent magnitude of associations. Fourth, the long-term impacts of COVID-19

on the aforementioned outcomes in PLWD remain uncertain due to the scarcity of available post-COVID-19 follow-up data. The need for further exploration is therefore imperative.

CONCLUSIONS

SARS-CoV-2 poses particular challenges to PLWD, including increased mortality and acute kidney injury, poor glycaemic control and elevated creatinine, CRP and D-dimer levels. Given these risks, prioritising vaccination of PLWD emerges as a critical preventive measure to mitigate the severe COVID-19 outcomes in this high-risk population. These findings also underscore the critical need for tailored treatment strategies and clinical management for COVID-19 patients with diabetes.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data used to support the findings of this study are available from the corresponding author upon request.

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