REVIEW ARTICLE

Association Of Covid And Diabetes: A Systematic Review

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ABSTRACT
Background: Numerous reports have been published describing the presence of diabetes mellitus (DM) in COVID-19 patients, indicating a connection between the two conditions. In order to determine the clinical manifestations and outcomes in this patient cohort as well as to summarise the prevalence of DM in COVID-19 patients, we conducted this systematic review. **Materials and methods:** The electronic MEDLINE, Embase, Cochrane, and PubMed databases were searched. To make the search procedure more sensitive while finding research, the Medical Subject Heading (MeSH) terms were developed. Some of these words included "Diabetes Mellitus", "COVID-19," and "Association". **Results:** The qualitative analysis includes six studies. Studies that were cited provided information on both adult and paediatric patients. Between the studied populations, the investigated results varied greatly. **Conclusions:** Inclusion studies varied in how they reported the COVID-19 outcomes for length of hospital stay, hospitalisation, ICU admission, DKA rate, and severe hypoglycemia. In order to draw a firm conclusion, additional research is still necessary due to the varied study populations and the presence of numerous restrictions.
Keywords: Association, COVID-19, Diabetes, Systematic review

INTRODUCTION

The WHO declared coronavirus disease-2019 (COVID-19), a condition brought on by the SARS-CoV-2 coronavirus, a worldwide pandemic [1]. More than 1.2 million fatalities and more than 48.1 million instances of SARS-CoV2 infections have been recorded globally as of the 5th of November 2020 [2]. Diabetes has been recognised as a risk factor for a poor prognosis among people with COVID-19, along with other concurrent medical disorders (such as underlying CVD, respiratory illnesses, hypertension, and obesity) [3-6]. People with diabetes have an approximately two- to three-fold higher risk of dying from COVID-19 than people without diabetes, according to a number of systematic reviews and meta-analyses on the subject [6–14]. However, because diabetes is a complicated and heterogeneous condition, the disease have different associations with comorbidities and complications [15]. For COVID-19, endotracheal intubations, early death, and admission to intensive care units (ICUs) are all associated with more severe forms of diabetes, such as uncontrolled blood glucose, the presence of complications from diabetes, a higher BMI, and elevated biomarkers for liver damage and inflammation [16–18]. However,

some of the results are still ambiguous, rough estimates, or influenced by bias risk, like confounding. Therefore, it can be challenging to apply the results of a single study to clinical practice.

On the other hand, reports indicate that COVID-19 indirectly poses hazards for diabetic patients on a variety of levels; in some nations, it may make it more difficult for them to access sufficient medical care. The effective reaction to emergencies is also delayed since, according to reports, access to emergency rooms has significantly decreased, primarily due to infection-related anxiety [19]. Therefore, based on the findings of the available evidence, we conducted this systematic review to summarise the clinical findings, and outcomes of COVID-19 in patients with diabetes mellitus.

AIM
Association of COVID-19 and Diabetes mellitus.

OBJECTIVES
To assess:
1. Clinical Findings of COVID-19 in patients with Diabetes mellitus.

2. Outcomes of COVID-19 in patients with Diabetes mellitus.

METHODS

The electronic MEDLINE, Embase, Cochrane, and PubMed databases were searched. The bibliographies of all pertinent articles and books were also meticulously searched. According to the inclusion and exclusion criteria, the appropriate articles were picked. To make the search procedure more sensitive while finding research, the Medical Subject Heading (MeSH) terms were developed. Some of these words included "Diabetes Mellitus", "COVID-19," and "Association". Critical analysis was performed on studies that met these criteria. A recommended special quality rating scale was used to evaluate the qualities of the listed studies.

ELIGIBILITY CRITERIA AND STUDY SELECTION

Up to 2023, peer-reviewed studies on the relationship between COVID-19 and diabetes mellitus that appeared in English-language publications were taken into consideration. Diabetes and COVID-19 outcome definition studies were also included. Exclusion criteria included case reports, case series, cross-sectional studies, research using animals or lab animals, reviews, abstracts, articles with insufficient data, and patients who had any lesions. Further investigation was done on any studies that didn't fit the inclusion criteria as well as the references of the chosen articles.

DATA EXTRACTION AND SYNTHESIS

Three processes were taken in the selection of the research. The choice of research that complied with the inclusion and exclusion criteria was made possible by carefully examining each book's title. For each of the selected titles, abstracts were acquired, evaluated, and suitable abstracts were selected in accordance with the criteria. After retrieving, reading, and analysing the complete texts of all the selected abstracts, the selected articles were chosen while keeping in mind the selection criteria. In the end, 6 articles were chosen for the investigation.

The data extraction forms were used to extract the data. Authors, research year, design, patient count, gender, mean age, and intervention data on COVID-19 and diabetes were all taken from the data. If patients were followed up on, each article included information on the length of the follow-up and any recurrence.

Table 1:

Initial search	180
Duplicates and non-relevant	81
Case reports and series	13
Reviews	51
Abstract	14
Language other than English	15

RESULTS

180 articles were found after the original search. Six studies were considered for analysis out of a total of 180 articles that were found in the database after duplicates were removed and publications that didn't meet eligibility requirements were eliminated. Using the Cochrane collaborative approach for assessing risk of bias in RCTs, the studies' quality was evaluated. The Newcastle-Ottawa Quality Assessment Form for Cohort Studies, the Critical Appraisal Skills Programme, the Cochrane Collaboration's tool for assessing risk of bias, the Oxford Systematic Review Appraisal Sheet, and the Grading of Recommendations Assessment Development and Evaluation (GRADE) system for grading evidence were all used to ensure the accuracy of the data analysis for this systematic review. A narrative summary of the research's findings has been provided. The retrieved data has been displayed in tabular format. (Table no: 2)
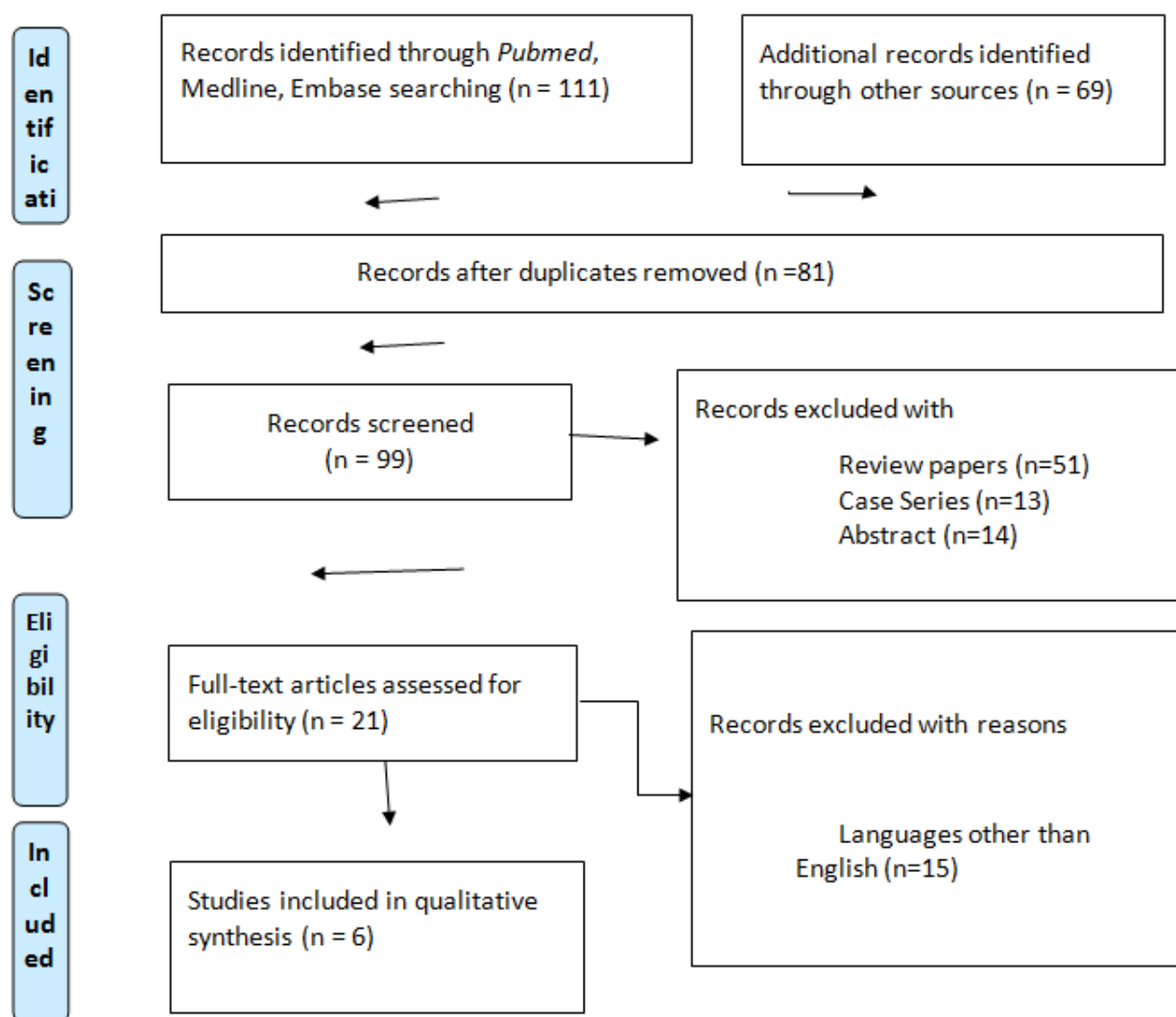
Identificati

Records identified through *Pubmed*, Medline, Embase searching (n = 111)

Additional records identified through other sources (n = 69)

Screening

Records after duplicates removed (n =81)

Records screened (n = 99)

Records excluded with

Review papers (n=51)
Case Series (n=13)
Abstract (n=14)

Eligibility

Full-text articles assessed for eligibility (n = 21)

Records excluded with reasons

Languages other than English (n=15)

Included

Studies included in qualitative synthesis (n = 6)

Table 2:

S no	Author, year and country	Type of Study	Patients	Outcome
1	Barron et al in 2020, UK [20]	Population based	23,698 COVID-19-related death cases	1.50% COVID-19 related death in diabetes patients
2	Vamvini et al in 2020, USA [21]	Commentary Retrospective case-control study	35 hospitalized patients with DM and COVID-19 vs. control (DM alone)	28.50% vs 14.30% composite outcome (ICU, intubation, or death in case and control group
3	Bhatti et al in 2020, UAE [22]	Cross-sectional study	103 COVID and DM patients	2.90% patients of DM have COVID-19
4	Al Hayek et al in 2020, Saudi Arabia [23]	Retrospective study	32 patients with COVID-19 and DM	21.90% hospitalization
5	Di Dalmazi et al in 2020, Italy [24]	Retrospective cohort study	130 patients with DM	0.77% had COVID-19
6	Rabbone et al in 2020, Italy [25]	Cross-sectional study	160 patients with DM	5% had COVID-19

Table 3: Assessment of quality of studies included in present systematic review

Authors name	Selection Bias Random sequence generation	Allocation Concealment	Reporting bias	Others	Performance bias Blinding participants and personnel	Blinding Outcome	Attrition bias
Barron et al in 2020, UK [20]	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	High risk
Vamvini et al in 2020, USA [21]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Bhatti et al in 2020, UAE [22]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Al Hayek et al in 2020, Saudi Arabia [23]	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk
Di Dalmazi et al in 2020, Italy [24]	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	Low risk
Rabbone et al in 2020, Italy [25]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

DISCUSSION

This is the first thorough review to systematically summarise the association between both conditions, the most typical presentation, and the clinical outcomes of patients with COVID-19 and DM, despite the fact that there have been numerous studies published that investigated the association between COVID-19 and DM, including systematic reviews and meta analyses. We included a total of 6 studies in our review.

A systematic review and meta-analysis of case-control studies were performed by Kumar et al. [26] to determine the prevalence of DM in patients with a COVID-19 diagnosis that was verified. After accounting for the observed heterogeneity, the authors' final meta-analysis, which included 33 papers, showed that the pooled prevalence of DM in patients with COVID-19 was 9.8% (95% confidence interval (CI) 14 8.7%е10.9%). The fact that these scientists looked at the prevalence of DM generally may be the reason why their results differ from ours. It's also likely that some of these researches were carried out in regions with high COVID-19 prevalence while it was less common in other nations.

Furthermore, it has been suggested that SARS-CoV-2 itself may contribute to diabetes. The earlier SARS-CoV-1 infection showed evidence of this [27]. Therefore, additional research in both adults and young children is still necessary to fully understand the relationship between COVID-19 and new-onset diabetes. However, only two studies reported the pertinent information, which prevented us from determining whether COVID-19 increased the incidence of newly diagnosed DM in this context. Patients with COVID-19 and DM were included in Ebekozien et al.'s study [28], and 15.6% (5/33) of them had newly developed diabetes. This prevalence rate, which was 1.77% (2/113) in the study by O'Malley et al. [29], was higher. On the other hand, Unsworth et al. [30] found that among 33 diabetic individuals, only 5 had a diagnosis of COVID-19, while the prevalence rate of new-onset diabetes was 90.1% (30/ 33). The small number of individuals included in each study, which could cause an overestimation or underestimation of the true burden of COVID-19 among patients with DM, could account for this significant variation.

According to O'Malley et al. [29], the rate was 4.0% (5/113). However, Holman et al.'s study [31] found that the rate of COVID-19-related deaths was extremely low, with a rate of 0.16% (432/264,391). Additionally, Ebekozien et al.'s study [28] found that the mortality rate was marginally lower in the case group (COVID-19 and DM, 3%) than in the control group (COVID19-like disease and DM, 3.3%).

Our study has a number of limitations, so it is important to use caution when interpreting the results. First, the dearth of pertinent data in the included studies prevented a meta-analysis from being done. The populations that were researched were also clinically diverse. Third, the variations in the reported findings due to the variations in the burden of COVID-

19 in different regions may be attributable to differences in the timing of conducting the study as well as the country in which the study was conducted. Finally, the quality of all included studies was low, and the radiographic findings of such patients are not adequately investigated in the available evidence. Therefore, additional research using larger sample sizes is still necessary to draw a firm conclusion.

CONCLUSIONS

According to the data that is currently available, the included studies' descriptions of the COVID-19's results in terms of length of hospital stay, hospitalisation, ICU admission, DKA rate, and severe hypoglycemia varied. In order to draw a firm conclusion, additional research is still necessary due to the varied study populations and the presence of numerous restrictions.

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