COVID-19 and diabetes mellitus: A need for prudence in elderly patients from a pooled analysis

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ARTICLE INFO

ABSTRACT

Objective: The objective of this study was to evaluate the pooled estimate of diabetes prevalence in young (<50 years) versus elderly (>50 years) COVID-19 cohorts.
Methods: Studies published between December-2019 and March-2020 reporting demographic and clinical characteristics of COVID-19 cases were identified. A total of 11 studies included accounting for 2084 COVID-19 patients.
Results: The overall prevalence of diabetes in COVID-19 patients with a mean age>50 years was 13.2%, whereas studies with relatively younger patients (mean age <50 years) had a pooled prevalence of 9.0%
Conclusion: The overall prevalence of diabetes in COVID-19 patients was found to be 13.2% with studies including relatively elderly patients showing higher rates of diabetes. The intermingled effects of diabetes with other cardiovascular comorbidities warrant age-specific outcomes data including the impact of ongoing antidiabetic treatment.

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1. Introduction

As of April 28, 2020, novel coronavirus disease 2019 (COVID-19) has accounted for the death of around 217,000 people worldwide. Upcoming reports have suggested that patients with COVID-19 infection have a high burden of complications [1], and underlying comorbidities like cardiovascular conditions, diabetes, and hypertension, and cancer [2]. A recent meta-analysis of studies published in China reported a pooled diabetes prevalence of 10.3% among patients infected with Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [3]. Furthermore, COVID-19 patients with adverse outcomes have a diabetes rate ratio of 2.26 (95% CI 1.47–3.49) compared to those with a favorable outcome [3]. Age has been suggested to be one of the important drivers of COVID-19 related mortality with a rate of 7.8% among elderly (>80 years)

versus 0.0016% in children (aged $\leq$ 9 years) [4]. These figures suggest that the presence of diabetes in the elderly COVID-19 population could add-up to the worse outcomes. However, data on age-specific diabetes prevalence in COVID-19 patients remains unknown. Therefore, we sought to evaluate the pooled estimate of diabetes prevalence in young (<50 years) versus elderly (>50 years) COVID-19 cohorts.

2. Methods

From a literature review using PubMed, Scopus and Web of Science until March 2020, all eligible studies reporting frequency of diabetes mellitus were included. Random effects models were obtained, and I^2 statistics were used to analyze heterogeneity. $I^2 > 50\%$ was considered moderate heterogeneity. A total of 11 studies included accounting for 2084 COVID-19 patients. Of these, the studies with a mean age of less than 50-years consisted of 1365 patients while cohorts with a mean age of>50-years included 107 patients.

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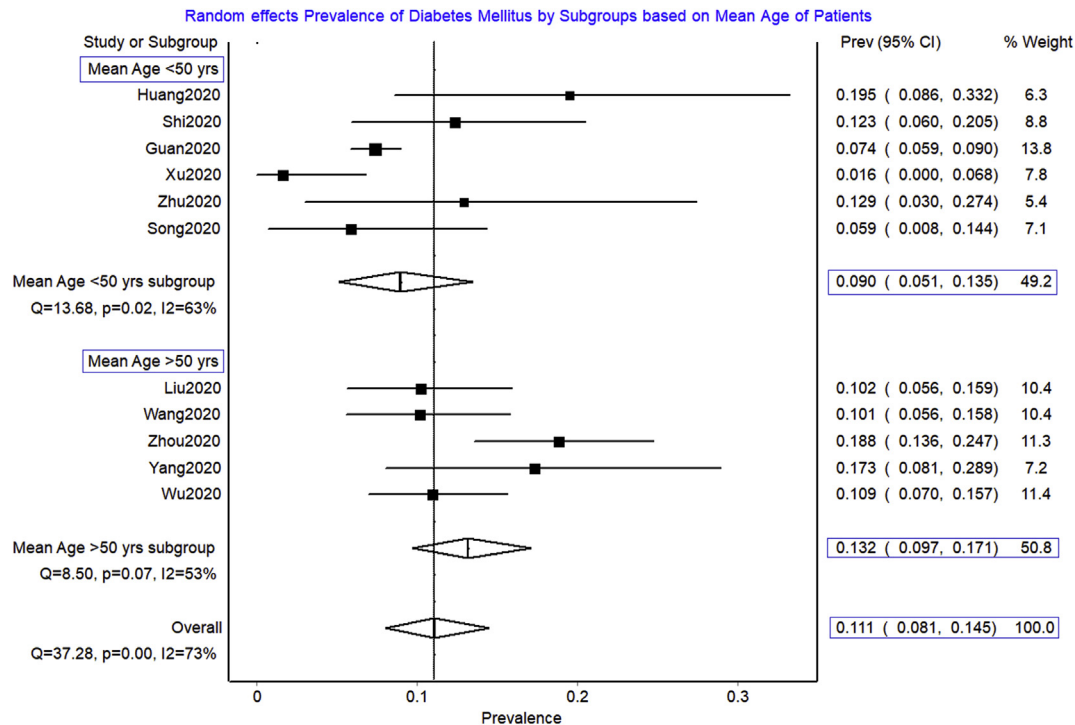E-mail addresses: drrupakdesai@gmail.com, rdesa30@emory.edu (R. Desai).

Fig. 1. Pooled prevalence of diabetes mellitus in COVID-19.

3. Results

The overall prevalence of diabetes in studies including COVID-19 patients with a mean age >50 years was 13.2% [95% CI 9.7%–17.1%, $I^2 = 53\%$], whereas studies with relatively younger patients (mean age <50 years) had pooled prevalence of 9.0% [95% CI 5.1%–13.5%, $I^2 = 63\%$] (p < 0.001) (Fig. 1). This meta-analysis revealed that the elderly COVID-19 population had a significantly higher burden of diabetes than the younger cohort (13.2% vs. 9.0%). This rate remains higher than the overall rate earlier studies have estimated (13.2% vs. 10.3%).

4. Discussion

Studies from China and Italy have suggested older age and underlying health conditions to be major risk factors for severe COVID-19 disease. Consistently, a report from the United States also revealed that among 457 intensive care unit admissions, a majority (78%) of them occurred in older patients or patients with pre-existing comorbidities [5]. Previous studies on SARS-CoV reported that the presence of cardiac disease and diabetes could increase the risk of death by two folds as much as other risk factors [6]. Elderly patients with a high burden of diabetes may also have other underlying cardiovascular conditions. A study by Shi et al. suggested that COVID-19 patients with the underlying cardiovascular disease might also be susceptible to acute cardiac injury that could potentially increase the risk of in-hospital mortality [7]. Furthermore, older age is a major risk factor for the occurrence of arrhythmias, which could have an additive worse effect with the presence of diabetes, a chronic inflammatory state.

It has been noted that COVID-19 patients have hyperinflammatory syndrome characterized by fulminant and fatal hypercytokinaemia [8], which could predispose elderly patients with diabetes towards malignant arrhythmias. Elderly with diabetes often have concomitant hypertension which could require Angiotensin-converting enzyme-2 (ACE2) inhibitors (ACEIs) and angiotensin receptor blockers (ARBs). These medications have a debatable role in increasing the susceptibility for COVID-19 infection and related outcomes. ACE2 has been identified as one of the major receptors for SARS-Cov-2, which is also widely expressed in the pancreas [9]. Similarly, Dipeptidyl peptidase-4 (DPP-4) is reported as a primary receptor in MERS-CoV, however, its role in SARS-CoV-2 has not yet established [9]. With such limited knowledge, it is imperative to identify whether patients with diabetes who are on ARBs/ACEIs or any other anti-diabetic drugs exacerbate COVID-19 prognosis.

While we are still searching for drugs to cure COVID-19, one controversial treatment option relevant to patients with diabetes is hydroxychloroquine, which is widely used for malaria and auto-immune diseases. Several trials have shown that hydroxychloroquine decreased HbA1c level in decompensated diabetes patients [10], although, the exact mechanism remains unclear. Given the indirect effect of hydroxychloroquine in diabetes, and the possible role of ACE2 and DPP-4 in SARS-CoV2, caution is warranted when treating COVID-19 patients with diabetes. It is also conceivable that acute decompensated diabetes would severely hinder COVID-19 care and prognosis, especially among the geriatric population.

5. Conclusion

Concisely, it is essential to acknowledge that the prevalence of diabetes in elderly COVID-19 patients remain significantly higher. Considering the intermingled effects of diabetes with other cardiovascular comorbidities, age-specific outcomes data are warranted including the impact of underlying cardiovascular conditions and ongoing antidiabetic treatment on COVID-19 prognosis.

Declaration of competing interest

The authors report no relationships that could be construed as a conflict of interest.

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