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Brief report

Diabetes and COVID-19: A pooled analysis related to disease severity and mortality

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ABSTRACT

Globally, COVID-19 has become a major concern for the diabetic community. We conducted a pooled analysis and constructed a forest plot for the association between diabetes and COVID-19 progression in 47 studies. A random effects meta-analysis (Mantel–Haenszel method) was conducted to estimate the outcomes effect size as odds ratios (OR) and 95% confidence intervals (CI) using Review Manager Software version 5.3. COVID-19 patients with diabetes have a significantly higher risk of disease severity (OR = 2.20, 95% CI = 1.69–2.86, $p < 0.00001$) and associated mortality outcomes (OR = 2.52, 95% CI = 1.93–3.30, $p = < 0.00001$).

1. Introduction

Ever since the outbreak of coronavirus disease 2019 (COVID-19) due to a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the number of infected cases and associated mortalities due to COVID-19 are growing. Studies have linked fatal outcomes in COVID-19 to the associated comorbidities. Evidence reported in the Journal of Diabetes and Centers for Disease Control and Prevention (CDC) showed diabetes as the most important comorbidity associated with a 50% higher risk of fatal outcomes in COVID-19 cases with diabetes than their non-diabetic counterparts [1–3]. Considering the global concern for COVID-19 pandemic in the diabetes community, we aim to evaluate the risk of disease severity and mortality in association with diabetes in COVID-19 patients.

2. Methods

This meta-analysis was planned as a part of our PROSPERO registered protocol (CRD42020186661), and relevant studies were identified through searching PubMed, Cochrane, medRxiv and other databases. Studies reporting diabetic proportions in subgroups of COVID-19 patients (Severe vs. Non-severe & Mortal vs. Survival) were included. Other study types and reports with no data on diabetic numbers were excluded.

2.1. Outcomes

The proportions of COVID-19 patients with diabetes in severe/mortal & non-severe/survival groups were used to estimate the risk of disease progression associated with diabetes. Further, a separate outcome analysis was conducted to study the relationship of diabetes with disease severity (Severe vs. Non-severe) and mortality (Survival vs. Non-survival) in COVID-19

2.2. Statistical analysis

A random effects meta-analysis (Mantel-Haenszel method) was conducted to estimate the outcomes effect size as odds ratios (OR) and 95% confidence intervals (CI) using Review Manager Software version 5.3. The stability and publication bias were tested by a one-study leave-out sensitivity analysis and funnel plot asymmetry, respectively. Heterogeneity was assessed using the I^2 statistic. A p-value of < 0.05 was considered to be statistically significant. More information on literature search and results are presented in the Supplementary Material.

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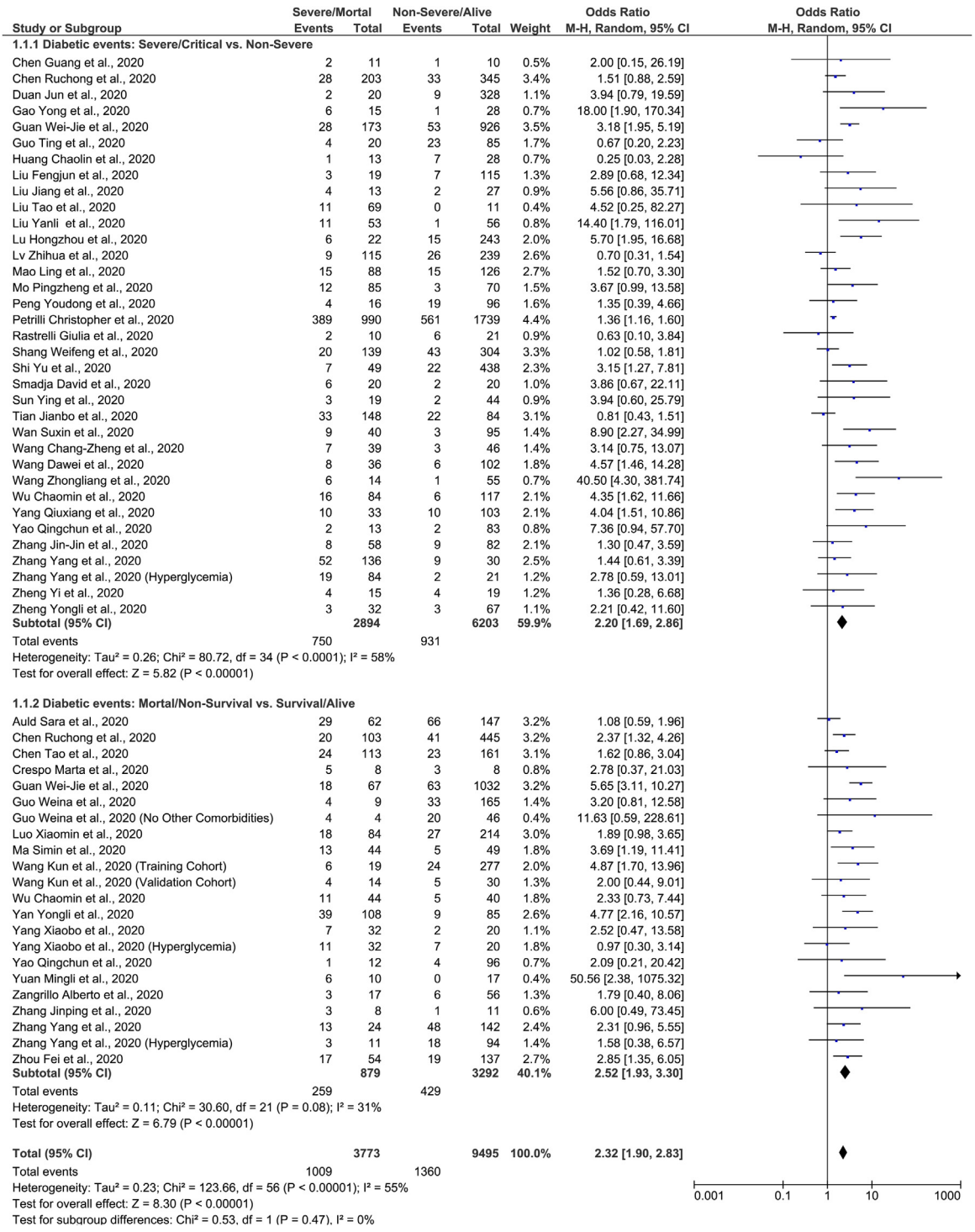

Fig. 1. Forest plot relating diabetes to disease severity and survival in COVID-19 patients from 47 studies.

3. Results

3.1. Subjects and pooled results

In this meta-analysis, a total of 47 relevant studies were included for the pooled outcome analysis [4–50]. All the studies confirmed diagnosis using the real-time reverse transcription polymerase chain reaction test. Overall, the diabetic proportions were 1009/3773 and 1360/9495 in severe/mortal and non-severe/survival groups of COVID-19 cases, respectively. The pooled outcome for the risk of disease progression indicated a significant impact of diabetes in COVID-19 cases (OR = 2.32, 95% CI = 1.90–2.83, $Z = 8.30$, $p < 0.00001$, $I^2 = 55\%$, $p < 0.0001$) (Fig. 1). The symmetrical funnel plot shown in Fig. 2 suggests no publication bias and sensitivity analysis indicated that the stability of overall result is not influenced by leaving-out any particular study. More information on search results, study characteristics and quality assessment are presented in the Supplementary Table 1.

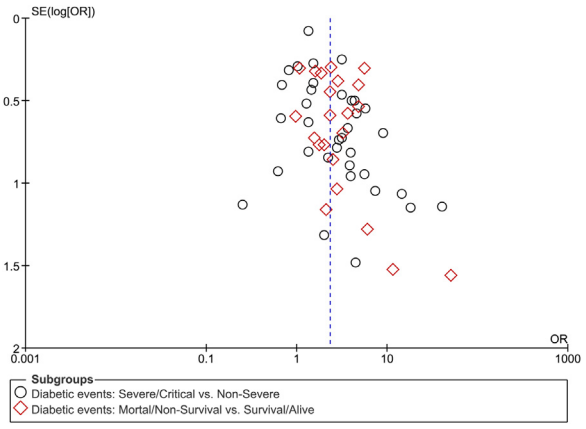

Fig. 2. The funnel plot of studies included in the analysis.

3.2. Diabetes and risk of severity and mortality

The diabetic proportions were 750/2894 and 931/6203 in severe and non-severe groups of COVID-19 cases, respectively. And, the respective diabetic proportions were 259/879 and 429/3292 in mortal and survival groups of COVID-19. As shown in Fig. 1, the subgroup analysis showed that diabetes related significantly with COVID-19 disease severity (OR = 2.20, 95% CI = 1.69–2.86, $Z = 5.82$, $p < 0.00001$, $I^2 = 58\%$, $p < 0.0001$) and mortality (OR = 2.52, 95% CI = 1.93–3.30, $Z = 6.79$, $p < 0.00001$, $I^2 = 31\%$, $p = 0.08$) as well. Though no significant heterogeneity was observed for the association of diabetes with mortality outcomes, the overall results should be viewed with caution to the heterogenous coexisting comorbidities across the included studies.

4. Discussion

Our results clearly indicate risk of disease progression and mortality is significantly high in COVID-19 patients with diabetes than in those without diabetes. It has been reported that individuals with impaired glucose tolerance or diabetes to have 50–60% higher risk of pulmonary infection [2,3]. Recent evidence suggests an increased risk of severe Adult Respiratory Distress Syndrome and multi-organ failure complications in diabetic patients. Globally, during the COVID-19 pandemic, diabetic cases consists of up to 50% COVID-19 cases [3].

As an important comorbid metabolic disorder, diabetes characterised by hyperglycemia has been reported to downregulate immune response and increased inflammation. It has also been proposed that coronavirus through angiotensin-converting enzyme 2 (ACE2) receptors may result in cell damage and disease progression [2,3]. The available evidence shows that the presence of diabetes in COVID-19 makes them more prone for disease progression and fatal outcomes. Our results are in support of the scientific/clinical opinion that COVID-19 patients with diabetes should be given much attention considering the associated higher risk of mortality in COVID-19 patients with diabetes. The recommendations and special considerations proposed for managing diabetic patients with COVID-19 are available elsewhere [1–3].

To summarise, this pooled analysis with a large sample size of 13,268 COVID-19 patients indicates significant association between diabetes and COVID-19 progression. COVID-19 patients with diabetes have a significantly higher risk of disease severity (OR = 2.20, 95% CI = 1.69–2.86, $p < 0.00001$) and associated mortality outcomes (OR = 2.52, 95% CI = 1.93–3.30, $p < 0.00001$). Considering the rapidly growing number of research reports, future meta-analyses with systematic review of literature are warranted to establish the independent associations of individual comorbidities for the risk of COVID-19 disease progression and mortality.

Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.pcd.2020.08.015.

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