ORIGINAL ARTICLE

Impact of diabetes mellitus on in-hospital mortality in adult patients with COVID-19: a systematic review and meta-analysis

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Abstract

Background The novel coronavirus disease 2019 (COVID-19) has spread worldwide since the beginning of 2020, placing the heavy burden on the health systems all over the world. The population that particularly has been affected by the pandemic is the group of patients suffering from diabetes mellitus. Having taken the public health in considerations, we have decided to perform a systematic review and meta-analysis of diabetes mellitus on in-hospital mortality in patients with COVID-19.

Methods A systematic literature review (MEDLINE, EMBASE, Web of Science, Scopus, Cochrane) including all published clinical trials or observational studies published till December 10, 2020, was performed using following terms "diabetes mellitus" OR "diabetes" OR "DM" AND "survival" OR "mortality" AND "SARS-CoV-2" OR "COVID-19".

Results Nineteen studies were included out of the 7327 initially identified studies. Mortality of DM patients vs non-DM patients was 21.3 versus 6.1%, respectively (OR = 2.39; 95%CI: 1.65, 3.64; $P < 0.001$), while severe disease in DM and non-DM group varied and amounted to 34.8% versus 22.8% (OR = 1.43; 95%CI: 0.82, 2.50; $P = 0.20$). In the DM group, the complications were observed far more often when compared with non-DM group, both in acute respiratory distress (31.4 vs. 17.2%; OR = 2.38; 95%CI:1.80, 3.13; $P < 0.001$), acute cardiac injury (22.0% vs. 12.8%; OR = 2.59; 95%CI: 1.81, 3.73; $P < 0.001$), and acute kidney injury (19.1 vs. 10.2%; OR = 1.97; 95%CI: 1.36, 2.85; $P < 0.001$).

Conclusions Based on the findings, we shall conclude that diabetes is an independent risk factor of the severity of COVID-19 in-hospital settings; therefore, patients with diabetes shall aim to reduce the exposure to the potential infection of COVID-19.

Keywords Diabetes mellitus · COVID-19 · SARS-CoV-2 · Systematic review · Meta-analysis · Mortality · Hospitalization

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Introduction

In 2020, world has been facing 2 pandemics. The new one has started in January 2020 with the outbreak of coronavirus disease 2019 (COVID-19) caused by a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The COVID-19 started in Wuhan, China as has rapidly spread through the whole globe causing patients to suffer viral pneumonia like symptoms [2]. No specific treatment has been found so far; however, a treatment with antiviral agents has been proposed, yet with no efficiency [3]. Currently, the only way to truly limit the spread of the disease is the widespread use of vaccinations [4]. On the other hand, the pandemic that the world is fighting every year is the diabetes, which is the only non-infectious disease declared pandemic by the United Nations [5]. Diabetes causes the immunosuppression which leaves patients more prone to the infectious complications [6]. Those two pandemics go hand to hand as literature confirms that most people who suffer from COVID-19 also have comorbidities, most common being diabetes, cardiovascular disease, and hypertension [7]. Additionally, diabetes has been found to increase complications and mortality rate in COVID-19 infected patients [8]. Taking the aforementioned arguments regarding public health, we have decided to perform systematic review and meta-analysis aim to summarize and synthesize the evidence published about the impact of diabetes mellitus on in-hospital mortality in patients with COVID-19.

This systematic review and meta-analysis aim to summarize and synthesize the evidence published about the impact of diabetes mellitus on in-hospital mortality in patients with COVID-19.

Methods

The Systematic Review and Meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [9].

Search strategy

Two investigators (H.K. and M.P.) independently searched for published clinical trials or observational studies indexed in MEDLINE, EMBASE, Web of Science, Scopus and the Cochrane databases from inception to December 10, 2020, using the following terms: "diabetes mellitus" OR "diabetes" OR "DM" AND "survival" OR "mortality" AND "SARS-CoV-2" OR "COVID-19". We limited the search to English-language studies. A manual search for additional pertinent studies and review articles using references from the retrieved articles was also completed.

Inclusion criteria and exclusion criteria

The PECOS strategy consisting of patient, exposure, comparison, and outcome was used as a tool to ensure focused clinical questions. The prespecified criteria for studies included in the meta-analysis were original papers of RCTs or cohort studies with minimum 10 patients in each group of (P) participants, adult patients with diabetes mellitus; (E) COVID-19 disease; (C) patients without diabetes mellitus; (O) outcomes, detailed information for survival, complications and length of hospital stay; (S) study design, randomized controlled trials, quazi-randomized or observational studies comparing resuscitation effects in patients with cardiac arrest.

Studies were excluded if they were reviews, case reports, conference or poster abstracts or articles not containing original data or comparator group.

Data extraction

The titles and abstracts were screened for relevance by 2 of the authors (L.S. and H.K.) independently. Any disagreement was resolved by discussion with third investigator (M.J.J.).

The manuscripts of selected titles/abstracts were assessed for inclusion, and the authors were contacted if further information was required.

Using the selection criteria enlisted above, the three reviewers (L.S., H.K. and W.W.) independently identified the papers to be included and excluded, and data from the included papers were extracted using predefined extraction flow sheets, and discrepancies were resolved through consensus with another reviewer (M.J.J.).

Quality assessment

Two investigators (H.K. and L.S.) independently extracted individual study data and evaluated studies for risk of bias using a previously piloted standardized form and the Newcastle–Ottawa scale [10]. The three major domains of quality of a study covered by this tool were selection of participants, comparability of cohorts, and outcome assessment against a total score of 9. Any disagreement was resolved by discussion with third investigator (J.S.).

Statistical analysis

Statistical analysis was performed with Review Manager (RevMan) software, version 5.4 (Cochrane Collaboration, Oxford, UK). The Mantel–Haenszel method was used to analyze dichotomous outcomes, and results are reported as odds ratios (ODs) with 95% confidence interval (CI) and two tailed p values. Continuous outcome differences were analyzed using an inverse variance model with a 95%CI, and values are reported as mean difference (MD). Results are presented as risk ratios (RR) with 95% confidence intervals (CI) for dichotomous measures. When the continuous outcome was reported in a study as median, range, and interquartile range, we estimated means and standard deviations using the formula described by Hozo et al. [11]. We quantified heterogeneity in each analysis by the tau-squared and I-squared statistics. Heterogeneity was detected with the chi-squared test with n—1 degrees of freedom, which was expressed as I^2. Values of $I^2 > 50\%$ and $> 75\%$ were considered to indicate moderate and significant heterogeneity among studies, respectively. A P value less than 0.05 was judged statistically significant.

Role of the funding source

Results

Description of studies included in the analysis

We identified 7,327 records through the literature search and 1 record from the reference list of relevant articles. Among them, 19 studies fulfilled our inclusion and exclusion criteria [12–31]. The identification procedure of these eligible articles is described in Fig. 1. The studies examined 10,801 patients.

Characteristics of selected studies

Table 1 gives details of the study characteristics. All studies were retrospective studies. Fourteen studies reported the outcome of mortality, and seven studies reported the outcome of length of hospital stay. Of the 19 studies, 10

Fig. 1 Flow diagram showing stages of database searching and study selection as per PRISMA guidelines
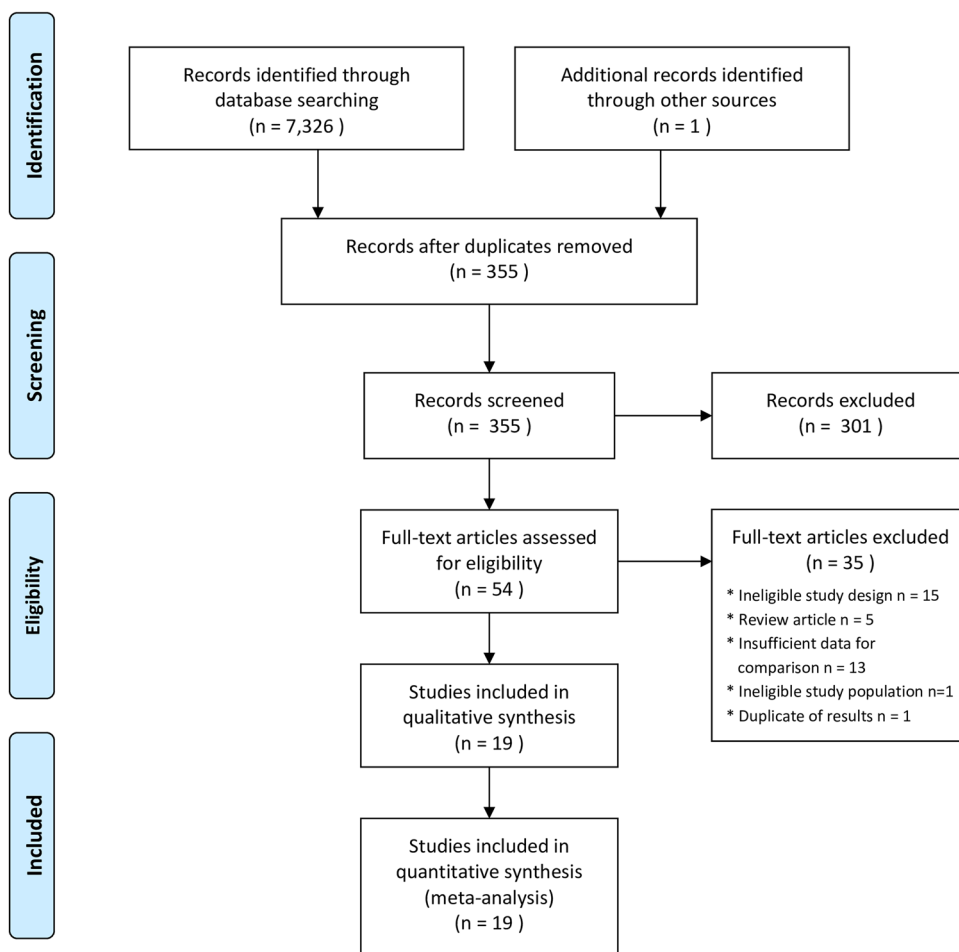
Table 1 Characteristics of included studies

Study	Country	Study design	DM group			Non-DM group		
			No	Age	Sex, male	No	Age	Sex, male
Acharya D et al. [12]	Korea	Multi-center cross-sectional study	55	69.8 ± 13.5	20 (36.4%)	269	51.9 ± 21.4	115 (42.8%)
Al-Salame et al. [13]	France	Observational cohort	115	72.6 ± 3.3	73 (62.6%)	317	72.3 ± 4.2	165 (52.1%)
Alzaid et al. [14]	France	Observational cohort	30	64.8 ± 6.6	23 (76.7%)	15	63.3 ± 7.2	8 (53.3%)
Chung SM. et al. [15]	South Korea	Retrospective cohort study	29	66.3 ± 8.9	14 (48.3%)	81	53.5 ± 17.9	34 (24.0%)
Conway J. et al. [16]	UK	Retrospective case series	16	NS	9 (56.3%)	55	NS	32 (58.2%)
Fox T. et al. [17]	USA	Retrospective observational study	166	66.42 ± 12.67	86 (51.8%)	189	66.03 ± 15.46	88 (46.6%)
Guan Wj. et al. [18]	China	Multi-center retrospective case study	130	61.2 ± 13.4	76/129 (58.9%)	1460	47.8 ± 16.1	828/1449 (57.1%)
Kim MK. et al. [19]	Korea	Multi-center, retrospective, observational study	235	68.3 ± 11.9	106 (45.1%)	235	69.7 ± 12.4	95 (40.4%)
Liang JJ. et al. [20]	China	Retrospective study	55	62.4 ± 7.7	27 (49.1%)	76	63.3 ± 8.3	43 (56.6%)
Liu D. et al. [21]	China	Retrospective observational study	19	60.3 ± 11.9	10 (52.6%)	76	46.5 ± 17.2	36 (47.4%)
Liu Z. et al. [22]	China	Retrospective observational study	139	64.5 ± 10.0	66 (47.5%)	795	61.6 ± 14.5	388 (48.8%)
Saeed O. et al. [23]	USA	Retrospective study	2266	67.9 ± 12.8	1189 (52.5%)	1986	61.1 ± 17.6	1066 (53.7%)
Shang J. et al. [24]	China	Retrospective, single-center cohort study	84	NS	42 (50.0%)	500	NS	235 (47.0%)
Soliman A. et al. [25]	Qatar	Retrospective study	56	52.1 ± 12.67	NS	243	36.22 ± 11.43	NS
Wu D. et al. [26]	China	Retrospective study	16	43.5 ± 17.8	8 (50.0%)	47	51.0 ± 12.6	25 (53.1%)
Wu J. et al. [27]	China	Retrospective study	22	52.55 ± 13.70	16 (72.73)	44	47.98 ± 15.11	28 (63.64%)
Xu Z. et al. [28]	China	Retrospective study	114	65.5 ± 2.7	62 (54.4%)	250	63.3 ± 3.5	144 (57.6%)
Zhang Y. et al. [29]a	China	Retrospective study	63	64.5 ± 4.0	38 (60.3%)	195	63.3 ± 2.5	100 (51.3%)
Zhang Y. et al. [30]b	China	Retrospective study	61	65.6 ± 11.4	33 (54.1%)	84	59.4 ± 16.0	41 (48.8%)
Summary characteristics			3671	66.9 ± 12.5	1898/3614 (52.5%)	6917	67.5 ± 17.5	3471/6663 (52.1%)

DM Diabetes mellitus; *NS* Not specified

studies were performed in China [18, 20–22, 24, 26–31], two in USA [17, 23], two in France [13, 14], two in Korea [12, 19], one in each of the following countries: UK [16], Qatar [25], and South Korea [15]. Detailed characteristics of the patients included in the meta-analysis are presented in Supplementary Digital File. The detailed risk of bias abuts the methodological quality of the included studies that are elaborated and summarized, respectively, in Table 1.

Meta-analysis results

Fourteen studies reported in-hospital mortality [12, 13, 15–19, 21, 22, 24, 25, 28–30]. The mortality of DM vs non-DM patients was 21.3 versus 6.1%, respectively (OR = 2.39; 95%CI: 1.65, 3.46; I^2 = 62%; $P < 0.001$; Fig. 2). We find

medium effect of power analysis of in-hospital mortality (d Cohena = 0.68, 95%CI: 0.51, 0.72).

Severe disease between DM and non-DM groups was reported in six studies [18, 19, 22, 27, 29, 30]. Severe disease in DM and non-DM group varied and amounted to 34.8 versus 22.8% (OR = 1.43; 95%CI: 0.82, 2.50; I^2 = 85%; $P = 0.20$). Clinical condition in DM group was observed in 18.4% and was higher than in non-DM group (6.9%; OR = 2.56; 95%CI: 1.77, 3.68; I^2 = 0%; $P < 0.001$; Fig. 3).

In the DM group, the complications were observed more often when compared with non-DM group (Fig. 4), both in acute respiratory distress (31.4 vs. 17.2%; OR = 2.38; 95%CI: 1.80, 3.13; I^2 = 40%; $P < 0.001$), acute cardiac injury (22.0 vs. 12.8%; OR = 2.59; 95%CI: 1.81, 3.73; I^2 = 57%; $P < 0.001$), as well as acute kidney injury (19.1 vs. 10.2%;

| Study or Subgroup | DM | | Non–DM | | | Odds Ratio | Odds Ratio |
	Events	Total	Events	Total	Weight	M–H, Random, 95% CI	M–H, Random, 95% CI
Acharya D 2020	11	55	13	269	7.9%	4.92 [2.07, 11.68]	
Al–Salameh A 2020	20	115	68	317	10.5%	0.77 [0.44, 1.34]	
Chung SM 2020	5	29	1	81	2.4%	16.67 [1.86, 149.66]	
Conway J 2020	4	16	19	55	5.3%	0.63 [0.18, 2.23]	
Fox T 2020	45	166	35	189	11.0%	1.64 [0.99, 2.70]	
Guan WJ 2020	13	130	37	1460	9.6%	4.27 [2.21, 8.26]	
Kim MK 2020	44	235	18	235	10.3%	2.78 [1.55, 4.97]	
Liu D 2020	1	19	2	76	2.0%	2.06 [0.18, 23.94]	
Liu Z 2020	4	139	9	795	5.7%	2.59 [0.79, 8.52]	
Shang J 2020	17	84	40	500	9.9%	2.92 [1.57, 5.44]	
Soliman A 2020	2	56	0	243	1.3%	22.34 [1.06, 471.96]	
Xu Z 2020	27	114	32	250	10.4%	2.11 [1.20, 3.74]	
Zhang Y 2020 (a)	7	63	8	195	6.5%	2.92 [1.01, 8.41]	
Zhang Y 2020 (b)	13	61	8	84	7.2%	2.57 [0.99, 6.67]	
Total (95% CI)		**1282**		**4749**	**100.0%**	**2.39 [1.65, 3.46]**	
Total events	213		290				

Heterogeneity: Tau^2 = 0.26; Chi^2 = 33.78, df = 13 (P = 0.001); I^2 = 62%
Test for overall effect: Z = 4.59 (P < 0.00001)

Fig. 2 Forest plot of In-hospital mortality in DM versus non-DM group. The center of each square represents the weighted odds ratios for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results. *DM* Diabetes mellitus; *CI* Confidence interval; *M–H* Mantel–Haenszel model

OR = 1.97; 95%CI: 1.36, 2.85; I^2 = 0%; P < 0.001). Additionally, in the study by Chung et al. [15] the authors observed a higher frequency of septic shock occurrence in DM group when compared to non-DM group (24.1 vs. 1.2%; OR = 25.45; 95%CI: 2.97, 218.03; P = 0.003).

Detailed procedures which were performed in DM and non-DM groups are presented in Table 2.

Length of hospital stay was reported in seven studies [12, 13, 17, 19, 25, 26, 30]. Polled analysis showed statistically significant longer length of hospital stay with DM than with non-DM group (MD = 1.36; 95%CI: 1.09, 1.63; I^2 = 95%; P < 0.001; Fig. 5).

Discussion

Our study is a systematic review and meta-analysis aimed at the association between diabetes and mortality in adult hospitalized patients with COVID-19. The findings may summarize as follows: overall death is more likely to occur in hospitalized patients with diabetes compared to those who are diabetes free 21.3 versus 6.1%, diabetes increases the risk of organ damage including septic shock, diabetes increases hospital stay.

Diabetes is an extremely widespread disease, which causes multiple expensive complications [31]. These findings are highlighted in the COVID-19 era. As although the symptoms of COVID-19 in patients suffering from diabetes do not differ from those suffered by general population [32], however, the hospitalized patients suffer far more
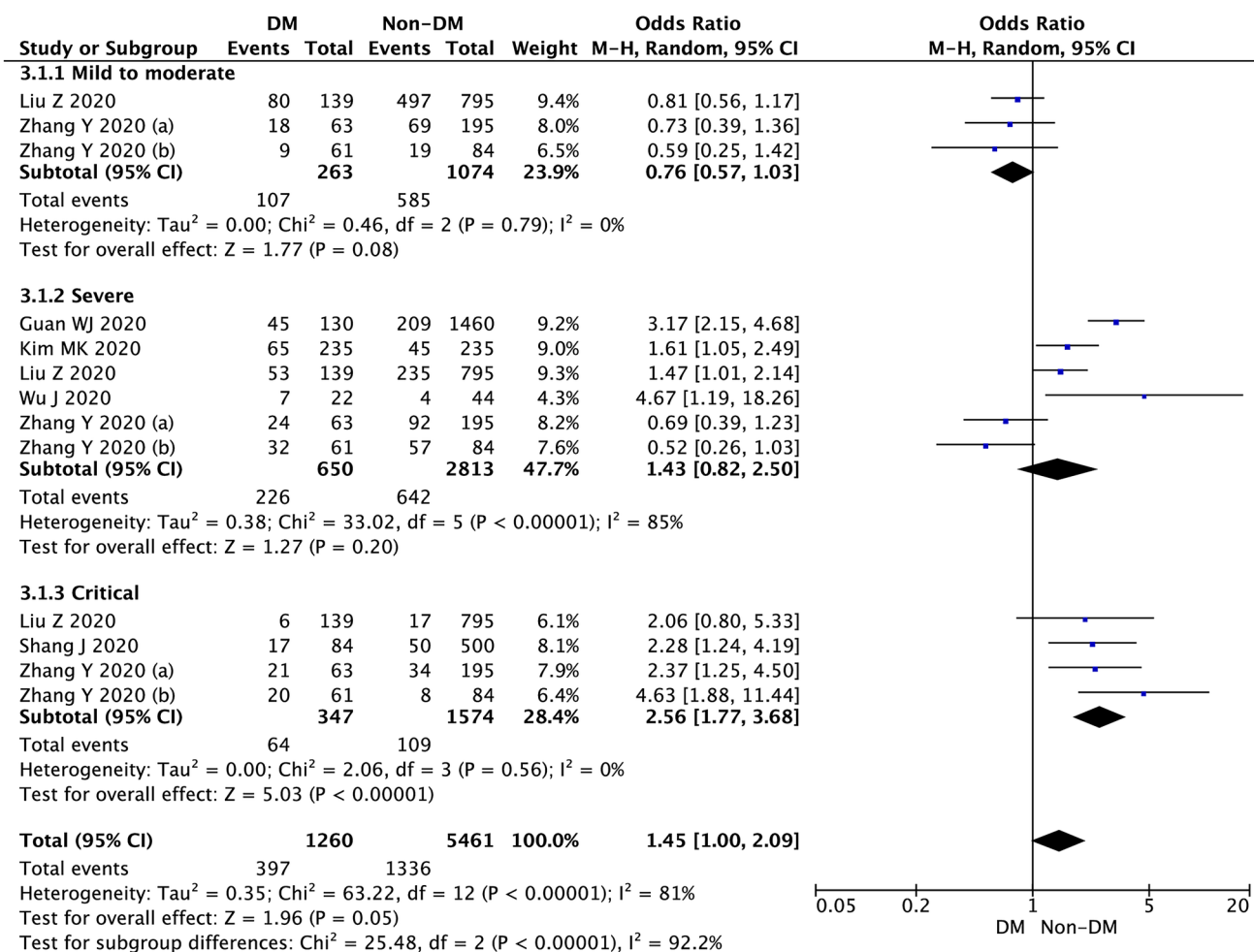
complications and require more interventions including respiratory support.

Although most patients infected with COVID-19 are asymptomatic or develop only mild symptoms [33], some patients require hospitalization and even treatment in the Intensive Care Unit conditions. Diabetes has been found to be a fairly comorbidity in patients requiring ICU support ranging from 17 [34] to 32% [35], indicating the need for a diligent blood glucose monitoring [36].

Diabetes induces immunosuppression which leaves patients susceptible to develop far more severe course of infection [6]. In the cohort study by Kim et al. [37], patients who suffered from diabetes had a considerably higher incidence of infection-related hospitalizations and deaths than the general population. Similarly, in a cohort study from Saudi Arabia, patients with diabetes had a corresponding increasingly increased risk of complicated clinical course and death [38].

Importantly when discussing complication, one cannot forget that as the number of complications increases so does the financial burden of the treatment [39]. Taking into the account that the total cost of the COVID-19 management amounts to over 1.6 trillion US dollars [40], it is important to identify the factors that increase the cost of treatment in order to reduce them. The risk of admission to the ICU for the diabetic patients relies heavily on the glycemic control. For DM1 patients who achieve good control, the risk increases almost threefold, while for the patients who achieve poor control, the relative risk increases almost fivefold. The numbers are lower for the DM2 patients, and the risk increases twofold for the good

Study or Subgroup	DM Events	Total	Non-DM Events	Total	Weight	Odds Ratio M–H, Random, 95% CI	Odds Ratio M–H, Random, 95% CI
3.1.1 Mild to moderate							
Liu Z 2020	80	139	497	795	9.4%	0.81 [0.56, 1.17]	
Zhang Y 2020 (a)	18	63	69	195	8.0%	0.73 [0.39, 1.36]	
Zhang Y 2020 (b)	9	61	19	84	6.5%	0.59 [0.25, 1.42]	
Subtotal (95% CI)		263		1074	23.9%	0.76 [0.57, 1.03]	
Total events	107		585				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.46$, $df = 2$ ($P = 0.79$); $I^2 = 0\%$
Test for overall effect: $Z = 1.77$ ($P = 0.08$)

Study or Subgroup	DM Events	Total	Non-DM Events	Total	Weight	Odds Ratio M–H, Random, 95% CI	
3.1.2 Severe							
Guan WJ 2020	45	130	209	1460	9.2%	3.17 [2.15, 4.68]	
Kim MK 2020	65	235	45	235	9.0%	1.61 [1.05, 2.49]	
Liu Z 2020	53	139	235	795	9.3%	1.47 [1.01, 2.14]	
Wu J 2020	7	22	4	44	4.3%	4.67 [1.19, 18.26]	
Zhang Y 2020 (a)	24	63	92	195	8.2%	0.69 [0.39, 1.23]	
Zhang Y 2020 (b)	32	61	57	84	7.6%	0.52 [0.26, 1.03]	
Subtotal (95% CI)		650		2813	47.7%	1.43 [0.82, 2.50]	
Total events	226		642				

Heterogeneity: $Tau^2 = 0.38$; $Chi^2 = 33.02$, $df = 5$ ($P < 0.00001$); $I^2 = 85\%$
Test for overall effect: $Z = 1.27$ ($P = 0.20$)

Study or Subgroup	DM Events	Total	Non-DM Events	Total	Weight	Odds Ratio M–H, Random, 95% CI	
3.1.3 Critical							
Liu Z 2020	6	139	17	795	6.1%	2.06 [0.80, 5.33]	
Shang J 2020	17	84	50	500	8.1%	2.28 [1.24, 4.19]	
Zhang Y 2020 (a)	21	63	34	195	7.9%	2.37 [1.25, 4.50]	
Zhang Y 2020 (b)	20	61	8	84	6.4%	4.63 [1.88, 11.44]	
Subtotal (95% CI)		347		1574	28.4%	2.56 [1.77, 3.68]	
Total events	64		109				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.06$, $df = 3$ ($P = 0.56$); $I^2 = 0\%$
Test for overall effect: $Z = 5.03$ ($P < 0.00001$)

	DM	Non-DM					
Total (95% CI)		1260		5461	100.0%	1.45 [1.00, 2.09]	
Total events	397		1336				

Heterogeneity: $Tau^2 = 0.35$; $Chi^2 = 63.22$, $df = 12$ ($P < 0.00001$); $I^2 = 81\%$
Test for overall effect: $Z = 1.96$ ($P = 0.05$)
Test for subgroup differences: $Chi^2 = 25.48$, $df = 2$ ($P < 0.00001$), $I^2 = 92.2\%$
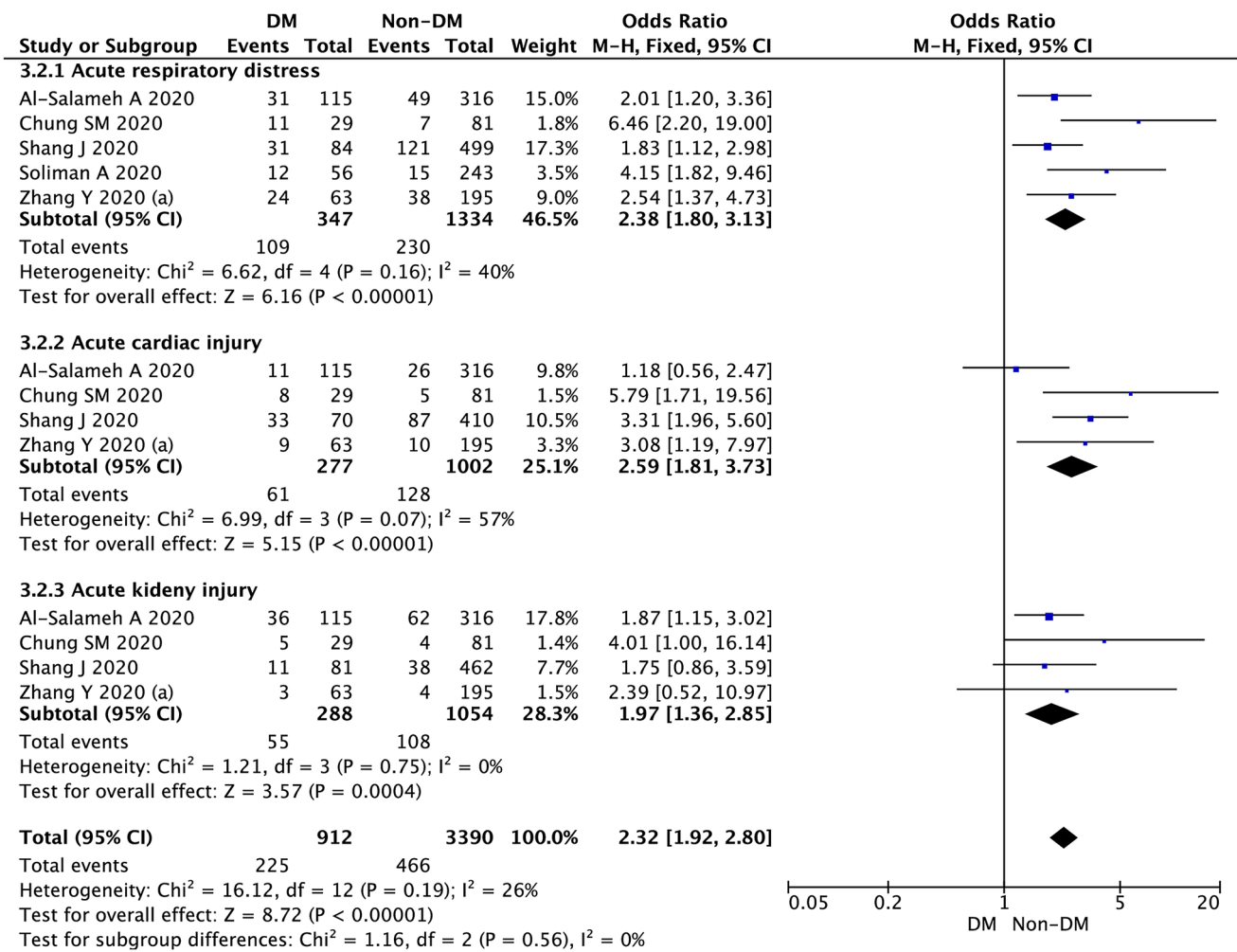
Fig. 3 Forest plot of clinical conditions in DM versus non-DM group. The center of each square represents the weighted odds ratios for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results. *DM* Diabetes mellitus; *CI* Confidence interval; *M–H* Mantel–Haenszel model

control and fourfold for the poor control. [41, 42]. The average cost for the DM patients as calculated by Bain et al. [43] was EUR 25,018 among people with type 2 diabetes in good glycemic control to EUR 57,244 among people with type 1 diabetes in poor glycemic control, reflecting higher risk of intensive care, ventilator support and longer hospital stay according to diabetes category, while the corresponding cost for people without diabetes was estimated at EUR 16,993, indicating the need for closer management in terms of monitoring the glucose levels of the patients. However, due to pandemic the routine follow-up course has been disrupted and the number of visits drastically reduced [44]. Therefore, the remote visits have emerged as a mean to replace the need for face-to-face visits [45]. Interestingly, although initiated in the "time of the crisis", it allowed for an introduction of the mechanisms that does not require personal contact and interestingly even in high-risk patients reduce the probability of experiencing acute complications, resulting in lower numbers of hospitalizations and intensive treatment. [46]

A review by Klekotka et al. proved that diabetes not only increases the risk of acquiring respiratory tract infection but also leads to higher incidence of hospitalizations [47]. The main marker that is continuously tracked during treatment of diabetes is blood glucose level [48]. The number of excursions both in terms of hypo- and hyperglycemia correlates with the increased risk of complications and mortality in the patients who do not suffer from infectious disease [49]. In turn, the presence of increased fasting blood glucose level > 126 mg/dl during the SARS infection was correlated with the increase in risk of death more than threefold [50]. The population particularly affected by the COVID-19 hyperglycemia are older people as demonstrated by Xue et al. [51] as it seems that this population has an increased risk of hyperglycemia occurrence overall. Interestingly, a meta-analysis by

Study or Subgroup	DM Events	Total	Non-DM Events	Total	Weight	Odds Ratio M–H, Fixed, 95% CI
3.2.1 Acute respiratory distress						
Al–Salameh A 2020	31	115	49	316	15.0%	2.01 [1.20, 3.36]
Chung SM 2020	11	29	7	81	1.8%	6.46 [2.20, 19.00]
Shang J 2020	31	84	121	499	17.3%	1.83 [1.12, 2.98]
Soliman A 2020	12	56	15	243	3.5%	4.15 [1.82, 9.46]
Zhang Y 2020 (a)	24	63	38	195	9.0%	2.54 [1.37, 4.73]
Subtotal (95% CI)		**347**		**1334**	**46.5%**	**2.38 [1.80, 3.13]**
Total events	109		230			
Heterogeneity: Chi² = 6.62, df = 4 (P = 0.16); I² = 40%						
Test for overall effect: Z = 6.16 (P < 0.00001)						
3.2.2 Acute cardiac injury						
Al–Salameh A 2020	11	115	26	316	9.8%	1.18 [0.56, 2.47]
Chung SM 2020	8	29	5	81	1.5%	5.79 [1.71, 19.56]
Shang J 2020	33	70	87	410	10.5%	3.31 [1.96, 5.60]
Zhang Y 2020 (a)	9	63	10	195	3.3%	3.08 [1.19, 7.97]
Subtotal (95% CI)		**277**		**1002**	**25.1%**	**2.59 [1.81, 3.73]**
Total events	61		128			
Heterogeneity: Chi² = 6.99, df = 3 (P = 0.07); I² = 57%						
Test for overall effect: Z = 5.15 (P < 0.00001)						
3.2.3 Acute kideny injury						
Al–Salameh A 2020	36	115	62	316	17.8%	1.87 [1.15, 3.02]
Chung SM 2020	5	29	4	81	1.4%	4.01 [1.00, 16.14]
Shang J 2020	11	81	38	462	7.7%	1.75 [0.86, 3.59]
Zhang Y 2020 (a)	3	63	4	195	1.5%	2.39 [0.52, 10.97]
Subtotal (95% CI)		**288**		**1054**	**28.3%**	**1.97 [1.36, 2.85]**
Total events	55		108			
Heterogeneity: Chi² = 1.21, df = 3 (P = 0.75); I² = 0%						
Test for overall effect: Z = 3.57 (P = 0.0004)						
Total (95% CI)		**912**		**3390**	**100.0%**	**2.32 [1.92, 2.80]**
Total events	225		466			
Heterogeneity: Chi² = 16.12, df = 12 (P = 0.19); I² = 26%						
Test for overall effect: Z = 8.72 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.16, df = 2 (P = 0.56), I² = 0%						

Fig. 4 Forest plot of adverse events in DM versus non-DM group. The center of each square represents the weighted odds ratios for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results. *DM* Diabetes mellitus; *CI* Confidence interval; *M–H* Mantel–Haenszel model
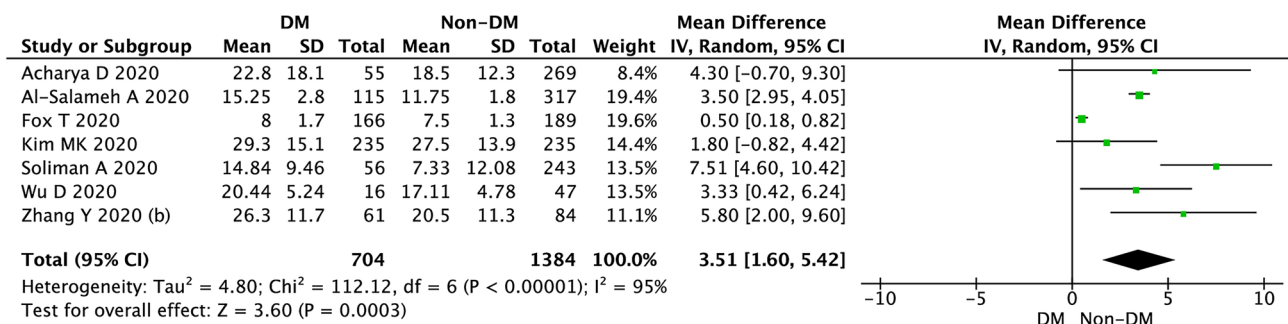
Table 2 Treatment characteristics in patients with diabetes versus patients without diabetes

Parameter	Number of studies	Incidence ratio DM	non-DM	OR (95%CI)	*P*-value	I²statistic
High-flow oxygen	3	47/327 (14.4%)	53/511 (10.4%)	1.47 (0.94, 2.28)	0.09	0
Noninvasive ventilation	2	18/124 (14.5%)	23/279 (8.2%)	1.92 (0.99, 3.74)	0.05	0
Invasive mechanical ventilation	8	148/824 (17.9%)	164/2987 (5.5%)	3.13 (1.96, 5.00)	<0.001	62
ECMO	3	14/327 (4.3%)	4/511 (0.8%)	4.75 (1.63, 13.85)	0.004	0
Continous renal replacement therapy	3	19/325 (5.8%)	4/400 (1.0%)	5.58 (1.96, 15.90)	0.001	0

CI Confidence interval*; DM* Diabetes mellitus*; ECMO* Extracorporeal membrane oxygenation*; OR* Odds ratio

Miller et al. [52] revealed that the prevalence of diabetes increases the mortality, while comorbidities do not affect the overall number of deaths. The same findings have been observed by Shang [53], whose team goes as far as to conclude that not only the diabetic patients shall avoid exposure to COVID-19 but also when treated they should be monitored more closely with special attention to improve prognosis.

Study or Subgroup	DM			Non–DM			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Acharya D 2020	22.8	18.1	55	18.5	12.3	269	8.4%	4.30 [−0.70, 9.30]	
Al–Salameh A 2020	15.25	2.8	115	11.75	1.8	317	19.4%	3.50 [2.95, 4.05]	
Fox T 2020	8	1.7	166	7.5	1.3	189	19.6%	0.50 [0.18, 0.82]	
Kim MK 2020	29.3	15.1	235	27.5	13.9	235	14.4%	1.80 [−0.82, 4.42]	
Soliman A 2020	14.84	9.46	56	7.33	12.08	243	13.5%	7.51 [4.60, 10.42]	
Wu D 2020	20.44	5.24	16	17.11	4.78	47	13.5%	3.33 [0.42, 6.24]	
Zhang Y 2020 (b)	26.3	11.7	61	20.5	11.3	84	11.1%	5.80 [2.00, 9.60]	
Total (95% CI)			**704**			**1384**	**100.0%**	**3.51 [1.60, 5.42]**	

Heterogeneity: Tau² = 4.80; Chi² = 112.12, df = 6 (P < 0.00001); I² = 95%
Test for overall effect: Z = 3.60 (P = 0.0003)

Fig. 5 Forest plot of length of hospital stay in DM versus non-DM group. The center of each square represents the weighted mean differences for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results. *DM* Diabetes mellitus; *CI* Confidence interval; *M–H* Mantel–Haenszel model

Conclusions

Based on the findings, we shall conclude that diabetes is an independent risk factor of the severity of COVID-19 in-hospital settings; therefore, patients with diabetes shall aim to reduce the exposure to the potential infection of COVID-19.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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