ISSN (P) : 2589-9120 / (O) : 2589-9139
PubMed-National Library of Medicine - ID: 101773527

International Journal of Medical Science and Applied Research (IJMSAR)

Available Online at: https://www.ijmsar.com

Volume – 4, Issue – 6, November – 2021, Page No. : 42 – 49

A Metaanalysis Related To Severity and Mortality in Diabetic COVID-19 Patients

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Citation of this Article: Dr. Prathusha Nerella, Dr. Mohammed Jaffer Pinjar, Dr. Keshav Kumar Majjari, Dr. Mujahid Mohammed, Dr. Shobha Mohammed, "A Metaanalysis Related To Severity and Mortality in Diabetic COVID-19 Patients,'' IJMSAR – November – 2021, Vol. – 4, Issue - 6, P. No. 42-49.

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Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

The aim of the study is to evaluate the impact of diabetes on severity and mortality in COVID-19. Events of diabetes analysed for the severity out of 35 studies, with a total no of 13268 patients with 2369 diabetics were analysed, the random effect of metanalysis estimated a pooled odds ratio (OR) of 2.175 (95% CI 1.641 to 2.88) Z value 5.409 with p<0.001. In this analysis mild heterogeneity in severity and non-severity, with I^2 = 61.26; p=0.0001, (95%CI for I^2 - 42-74.12), with no significant bias (Egger's) Test interpret 1.19, 95% CI 0.42-1.95, p=0.003 were found. The analysis of mortality was done by including 22research studies, random effect showed a pooled OR of 2.524 (95% CI 1.932-3.298) Z=6.788, p<0.001, with moderate heterogeneity I^2 31.38, (95% CI for I^2 0.00-59.19), with no publication bias (Egger's) test intercept was 0.65, (95% CI 0.57-1.87), p value=0.27. To conclude diabetes maybe a culprit for increase in

severity and mortality in CVOID-19 infections.

Keywords

COVID-19**,** Diabetes, SARS-CoV-2, Severity and Mortality

Introduction

Ever since the outbreak of Coronavirus disease (COVID-19) due to a novel severe acute respiratory syndrome Coronavirus (SARS-CoV-2) the number of infected patients and mortalities are growing due to COVID-19. The World health organisation (WHO) declared COVID-19 as pandemic on 11th of March 2020, it affected 114 countries and was responsible for 51, 30,689 deaths around world. Studies have linked the fatal outcome of COVID-19 to the associated comorbidities. Journals on diabetes and centres for disease control showed diabetes as one of the important comorbidities associated with a 50% higher risk of fatal outcomes in COVID-19 cases. As the increased rate of those suffering from diabetes is increasing, the prevalence of COVID-19in diabetics suggests that the care for diabetic patients must be increased in order to reduce any further complications and the risk of death. Due to the lack of studies on relationship between COVID-19 severity and mortality in diabetics, it is difficult to suggests how exactly the care show be taken. In view of global concern for COVID-19 pandemic, we aimed to evaluate the risk of severity and mortality in association with diabetes in this metaanalysis.

Materials and Methods

Protocol and Registration

A protocol for this metaanalysis was registered with institutional ethical committee. The focus of the review was narrowed to diabetes patient's status in COVID-19 pandemic.

Eligibility Criteria

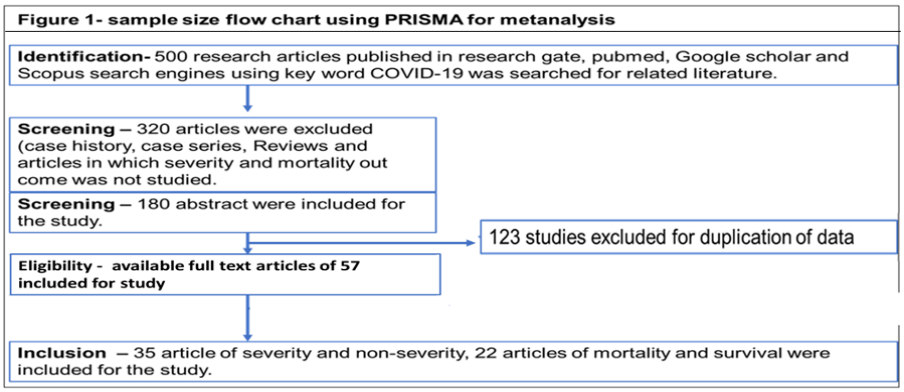
Inclusion of publications that were observational studies, such as cohort and case-control research. The editorials or review studies that just summarize other studies were excluded. Studies considered focused on those that reported diabetes in COVID-19 patients.

Search Strategy

An unrestricted search upto September 2021 in Scopus, PubMed, Google scholar, Research gate and Web of science were searched. We developed search strategies using keywords of diabetic severity, diabetic mortality, corona, COVID-19 and SARS-CoV2.

Search Validation and Data Selection

All Articles Were Discovered By using the key words and those that were available on the indicated databases during the period of this review were included. All articles which were not matching the inclusion criteria were discarded and potentially eligible manuscripts were exported. At this stage, exported papers were screened again to identify articles relevant to diabetes andCOVID-19 and eliminated duplicates. Results were compared and any controversies surrounding any particular included or excluded paper were resolved by discussion with co-authors. Data extraction was performed independently using a standard extraction form. The studies were subsequently screened for reporting diabetes and COVID-19 (Figure 1).



Results

Events of diabetes analysed for the severity in 35 studies, with a total no of 13,268 patients with 2,369 diabetics showed random effect of metaanalysis estimated a pooled odds ratio (OR) of 2.175 (95% CI 1.641 to 2.88) Z value 5.409 with p<0.001(Table 1, Figure 2,3). In this analysis mild heterogeneity in severity and non-severity, with I^2 = 61.26; p=0.0001, 95%CI for I^2- 42-74.12, with no significant publication bias (Egger's) test interpret 1.19, 95% CI 0.42-1.95, p=0.003 was found. The analysis of mortality in 22 studies showed random effect of pooled OR of 2.524(95% CI 1.932 -3.298), Z=6.788, p<0.001 with moderate heterogeneity I^2 31.38, (95% CI for I^2 0.00-59.19) with no publication bias (Egger's) test intercept was 0.65, (95% CI 0.57-1.87), p value=0.27 was found (Table 2, Figure 4, 5).

Table 1- Diabetics events of Severity and non-severity in COVID-19

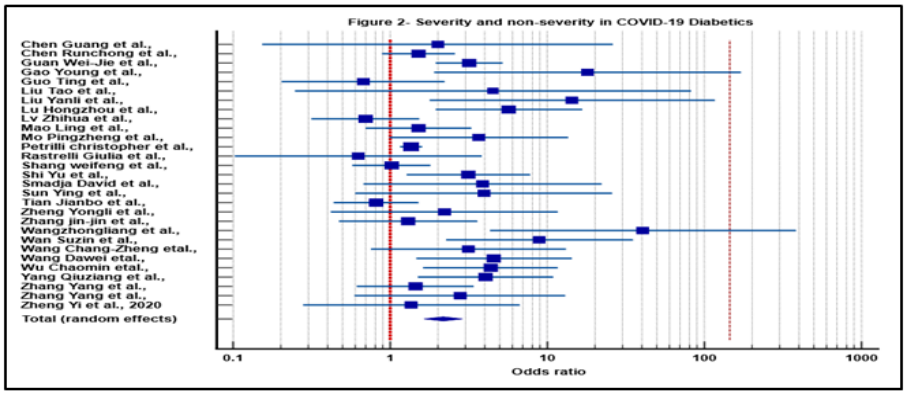
Study	Odds ratio	95% CI	z	P	Weight (%) Random
Chen Guang et al.,	2	0.153 to 26.189			1.04
Chen Runchong et al.,	1.513	0.885 to 2.587			6.19
Guan Wei-Jie et al.,	3.181	1.948 to 5.195			6.43
Gao Young et al.,	18	1.902 to 170.343			1.31
Guo Ting et al.,	0.674	0.204 to 2.228			3.27
Liu Tao et al.,	4.521	0.248 to 82.271			0.84
Liu Yanli et al.,	14.405	1.789 to 116.017			1.48
Lu Hongzhou et al.,	5.7	1.947 to 16.683			3.7
Lv Zhihua et al.,	0.696	0.315 to 1.537			4.89
Mao Ling et al.,	1.521	0.701 to 3.298			4.98
Mo Pingzheng et al.,	3.671	0.993 to 13.578			2.93
Petrilli christopher et al.,	1.359	1.155 to 1.599			7.78
Rastrelli Giulia et al.,	0.625	0.102 to 3.842			1.85
Shang weifeng et al.,	1.02	0.575 to 1.809			6
Shi Yu et al.,	3.152	1.271 to 7.812			4.36
Smadja David et al.,	3.857	0.673 to 22.110			1.96
Sun Ying et al.,	3.938	0.601 to 25.794			1.75
Tian Jianbo et al.,	0.809	0.434 to 1.506			5.75
Zheng Yongli et al.,	2.207	0.420 to 11.600			2.12
Zhang jin-jin et al.,	1.298	0.469 to 3.592			3.91
Wangzhongliang et al.,	40.5	4.297 to 381.757			1.32
Wan Suzin et al.,	8.903	2.266 to 34.988			2.77
Wang Chang-Zheng et.al,	3.135	0.752 to 13.074			2.62
Wang Dawei etal.,	4.571	1.463 to 14.282			3.46
Wu Chaomin etal.,	4.353	1.625 to 11.664			4.04
Yang Qiuziang et al.,	4.043	1.505 to 10.863			4.03
Zhang Yang et al.,	1.444	0.615 to 3.393			4.61
Zhang Yang et al.,	2.777	0.593 to 13.007			2.35
Zheng Yi et al., 2020	1.364	0.278 to 6.683			2.25
Total (random effects)	2.175	1.641 to 2.883	5.409	<0.001	100

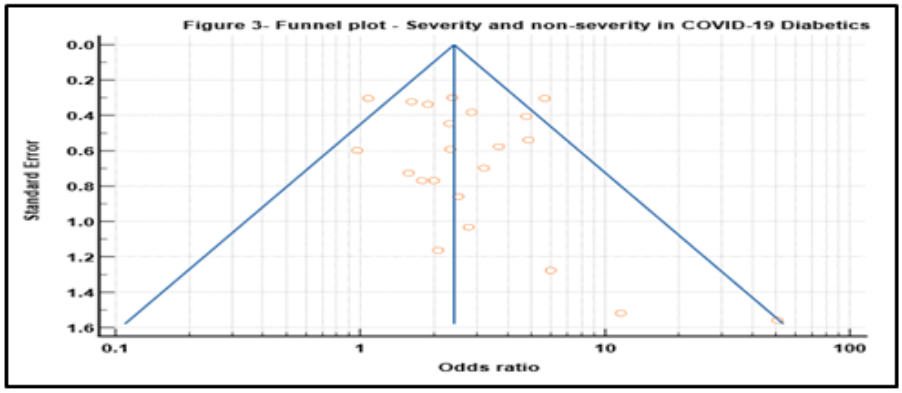
Data presented for Heterogeneity severity and non-severity, with I^2 = 61.26; p, 0.0001, 95%CI for I^2- 42-74.12, with no significant bias (Egger's) Test interpret 1.19, 95% CI 0.42-1.95, p=0.003.

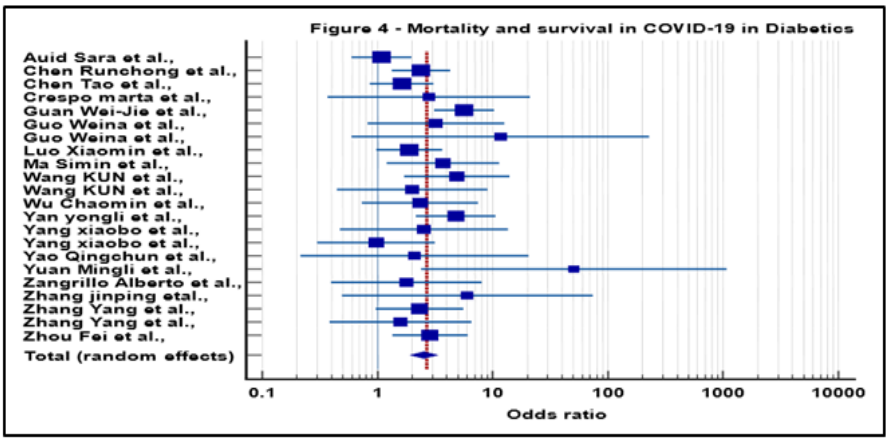
Table 2- Diabetics events of mortality and survival in COVID-19

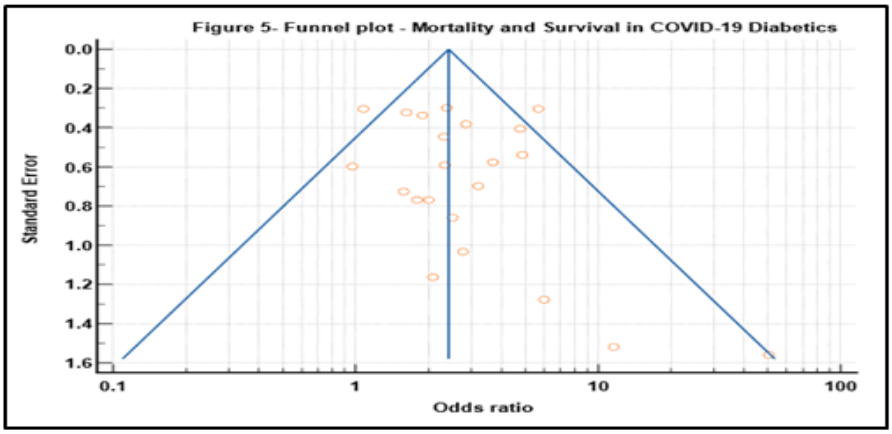
Study	Odds ratio	95% CI	z	P	Weight (%) Random
Auid Sara et al.,	1.079	0.595 to 1.956			9.11
Chen Runchong et al.,	2.374	1.324 to 4.260			9.26
Chen Tao et al.,	1.618	0.861 to 3.041			8.63
Crespo marta et al.,	2.778	0.367 to 21.030			1.58
Guan Wei-Jie et al.,	5.65	3.109 to 10.267			9.09
Guo Weina et al.,	3.2	0.814 to 12.581			3.1
Guo Weina et al.,	11.634	0.592 to 228.623			0.77
Luo Xiaomin et al.,	1.889	0.977 to 3.651			8.27
Ma Simin et al.,	3.69	1.193 to 11.415			4.19
Wang KUN et al.,	4.865	1.696 to 13.960			4.64
Wang KUN et al.,	2	0.444 to 9.013			2.65
Wu Chaomin et al.,	2.333	0.732 to 7.437			4.03
Yan yongli et al.,	4.773	2.156 to 10.566			6.73
Yang xiaobo et al.,	2.52	0.468 to 13.579			2.19
Yang xiaobo et al.,	0.973	0.301 to 3.144			3.96
Yao Qingchun et al.,	2.091	0.214 to 20.418			1.27
Yuan Mingli et al.,	50.556	2.377 to 1075.379			0.73
Zangrillo Alberto et al.,	1.786	0.396 to 8.062			2.65
Zhang jinping etal.,	6	0.490 to 73.455			1.07
Zhang Yang et al.,	2.314	0.965 to 5.552			5.98
Zhang Yang et al.,	1.583	0.382 to 6.570			2.91
Zhou Fei et al.,	2.853	1.346 to 6.049			7.19
Total (random effects)	2.524	1.932 to 3.298	6.788	<0.001	100

Data presented for Heterogeneity I^2 31.38, 95% CI for I^2 0.00- 59.19, with no publication bias (Egger's) test intercept was 0.65, 95% CI 0.57-1.87, p value=0.27.









Discussion

We performed metanalysis by including 57 articles associated with diabetes with COVID-19 outcome. Total no of 13265 patients who were tested positive for COVID-19 were included with 2369 diabetics. We identified a strong positive association between diabetes and COVID-19. Diabetes is an important comorbid metabolic disorder, is characterised by hyperglycaemia has been reported to down regulate 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 [1]. 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 [2,3].The association of diabetes and COVID-19 and its outcome was previously studied by other researchers in a metaanalysis with small number of studies [4-6]. In a previous metaanalysis 7 studies were analysed with 1592 confirmed COVID-19patients, 138 being diabetics and they associated diabetes is an important risk factor for COVID-19 severity OR-3.53 (1.48-8.93)in this study there was a high heterogeneity that was addressed by random effect

analysis and meta-regression using the mean age as a covariate, with no impact on results, indicating that diabetes risk was independent of age [7].Another study identified 1.5-fold increase in the risk of severity and 1.2fold increase in mortality in COVID-19 patients with diabetes[7], our data is in compromise with these authors. another metanalysis included 30 studies, each study was performed aiming to investigate the association between diabetes with severity and mortality of COVID-19[8]. This study is in compromise with our study. Authors also associated diabetic mortality in severe acute respiratory syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS-Cov) in previous studies [7-10].

Conclusion

To conclude, this metaanaly is with a large sample size of 13,268 COVID-19 patients showed significant association between diabetes and progression of COVID-19. Diabetic COVID-19 patients have significantly higher risk of disease severity(OR = 2.1, 95% CI = 1.641–2.883,p< 0.001) and associated mortalityoutcomes (OR = 2.5, 95% CI = 1.93–3.29, p < 0.001). Consideringthe rapidly growing disease severity and mortality number research reports, future meta analysisis warranted with larger systematic review of literature on uncontrolled diabetes and CVOID-19 and their associated factors to evaluate the progression of severity and mortality in COVID-19.

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