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Evaluating the Effects of Diabetes on Severity of COVID-19: A Meta-Analysis

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Abstract - *Underlying medical conditions including age and gender have been identified as main risk factors for COVID-19. Common comorbidities in COVID-19 patients include hypertension, diabetes, and cardiovascular diseases. Current research has identified diabetes as one of the risk factors for the severity of COVID-19. While there has been extensive research showing the correlation of diabetes and severity of COVID-19, there is a lack of research evaluating the extent of the risk diabetes presents to infected patients. In this research, we aim to investigate to what degree diabetes may affect the severity of COVID-19. We perform meta-analysis through data extraction to evaluate the relationship between diabetes and severity in contrast to non-diabetes groups. We reviewed recently published literature databases, including PubMed, ResearchGate, and NCBI, until July 16, 2020. The quality of the papers was evaluated through the Newcastle-Ottawa Scale and converted into the AHRQ scale to classify the papers into good, fair, and poor quality. Data regarding ICU admission, mortality rates, and percentage of patients in severe and critical conditions comparing diabetics and non-diabetics were collected to assess the extent of the risk that diabetes poses to the prognosis of the virus. A meta-analysis model was established to compare the diabetics and non-diabetics subgroups. Our meta-analysis showed a strong correlation between diabetes and severity of COVID-19. Diabetics were 2.377 times more likely to deteriorate to severe conditions than non-diabetics as they are likely to have more than one comorbidity and display higher inflammatory responses. Therefore, this study recommends the use of diabetes history to allocate adequate treatments for diabetics infected with COVID-19.*

***Key Words*: COVID-19, coronavirus, diabetes, severity, comorbidity**

1. INTRODUCTION

Many reports have shown different clinical characteristics in patients infected by COVID-19. While patients show common symptoms of fever, cough, and difficulties in breathing, they have shown varying prognosis of the virus. While it has been reported that most patients recover from the virus without special treatment in a recovery time of approximately two weeks, approximately 20% of those infected by COVID-19 require hospital care and undergo severe conditions. Common risk factors to COVID-19 include age and underlying medical conditions. Studies have identified comorbidities as risk factors to severity of the virus, indicated by higher ICU admission rates, mortality, and percentage of patients in severe and critical conditions. Some common comorbidities observed in severe populations include hypertension, diabetes, cardiovascular diseases, chronic kidney, liver, and pulmonary diseases. Among these comorbidities, hypertension and diabetes have been identified as the most common comorbidities observed in severe patients. Patients with diabetes have been reported to have greater inflammatory responses with higher possibility of infection from other pathogens. Yet, it is unclear whether how much risk diabetes poses to the severity of the virus especially compared to those who do not have the comorbidity. In this research, we aim to investigate the correlation between diabetes and severity of COVID-19 and its comparison to patients without the comorbidity.

2. METHOD

The method of this research was based on first developing a search protocol. Keywords included "COVID-19", "coronavirus", "severity", "comorbidity", "diabetes", and "clinical". Papers that were found based on these search keywords were included in this study if they involved the outcome of patients with diabetes and COVID-19, were cohort studies, based on multi-center or single-center clinical records, included sample size greater than 30, and discussed the admission of severe patients into intensive care unit (ICU).

Papers were then determined of its quality and relevance to this study. Criteria were created for extracting data and relevant data was recorded using an external software Google Sheets. In order to determine the relevance of a paper, the Newcastle-Ottawa scale was used to evaluate the quality of each paper. Papers were assessed based on three domains: selection, comparability, and outcome. For the selection criteria, the papers were examined on its representativeness, selection of the non-exposed cohort, ascertainment of exposure, and demonstration of outcome of interest. Outcome was evaluated based on assessment of the outcome and the adequacy of follow-up. The median duration of follow-up was established at one month due to the rapid progression of the virus observed in diabetes patients infected by COVID-19. A star was awarded for each criterion it met. The Newcastle-Ottawa scale was converted into the AHRQ scales of good, fair, and poor quality based on the number of stars received for each domain.

Papers that were determined to have good or fair quality advanced to the data extraction stage where the sample size, percentage of patients with diabetes, and number of patients discharged, admitted into intensive care units, or died. To evaluate the correlation between pre-existing diabetes and severity of COVID-19 infection, data on the number of

patients with diabetes, admitted to intensive care, or death were considered along with hazard ratios. Mean values and ratios of diabetes and non-diabetes patients were used to reach a conclusion.

Papers have utilized different markers to describe the severity of the virus in diabetics. These methods included comparisons of number and percentage of patients admitted to ICU, classification of patients into mild, severe, and critical conditions, mortality, and use of treatment methods such as mechanical ventilation. In order to create unified parameters that would compare the severity of the virus in diabetics and non-diabetics, these markers have been narrowed down into conditions and mortality. Admission to ICU, use of ventilator supports, and severe and critical conditions were combined to describe the severity of the virus. Mortality values were averaged to be compared to the control group.

3. RESULTS

Twenty-six (26) papers were collected and their quality was assessed through the Newcastle-Ottawa scale. When converted into the AHRQ scale, 15 papers were classified as good quality, 2 papers were of fair quality, and 9 papers were of poor quality. Among poor quality papers, many of them collected data from a nationwide database, which had its strengths in representativeness but lacked adequacy of follow-ups for missing data due to its large sample size. Some of these papers did not have a control group which made it difficult to compare the severity of COVID-19 patients that had diabetes with those that did not.

Compared to patients without diabetes, common baseline characteristics of diabetics involved older age and history of multiple comorbidities along with diabetes, with hypertension being one of the main comorbidities in these patients. Laboratory tests showed that patients with diabetes had severe inflammation with weak immune responses that had reduced functions.

Fifteen (15) papers have shown association between diabetes with severity of COVID-19. In order to investigate the extent of how diabetes affects the severity of the virus, three markers were utilized: ICU admission rates, mortality, and demographics of severe and critical condition patients. As seen on Table 1, data comparing the rates of ICU admission in diabetics and non-diabetics have been analyzed to deduce the ratio of diabetics admitted to ICU compared to non-diabetics. The following equation (a) has been used and the comparison values have been averaged to deduce the mean value. As a result, this data showed that diabetes patients are 2.785 times more likely to be admitted to ICU than non-diabetes patients.

$$\text{Equation (a):} \quad \frac{Rate\ of\ diabetes\ patients}{Rate\ of\ non-diabetes\ patients}$$

As shown on Table 2, when comparing the mortality of diabetics and non-diabetics, the same method was used to compare how the comorbidity can affect mortality from COVID-19. Equation (a) was used to deduce the stark differences in two groups. In this particular data, Cummings et al. paper used hazard ratios for mortality and this value was added as input data for the comparison column. Out of 11 papers that used mortality as a marker for indicating severity, data from 8 papers was used to deduce the mean value for the comparison between mortality in diabetes and non-diabetes patients. Results have shown that mortality is higher by 2.379 times for diabetes patients than those without the comorbidity.

The third marker in evaluating the extent of severity in the diabetes and non-diabetes population was using the number of patients in severe or critical condition. Patients were evaluated in these conditions based on their vital signs. Similar to the two data sets above, this data was analyzed by comparing the percentage of diabetes and non-diabetes deteriorating to severe or critical conditions as illustrated in Table 3. Based on the analysis, diabetes patients were more likely to fall into severe conditions by 1.885 times and fall into critical conditions by 2.459 times.

When averaging the comparison ratios of each marker, diabetes patients are more likely to go through severe conditions when infected by 2.377 times than non-diabetes patients.

Table -1: Comparison of Severity of Diabetes and Non-diabetes Patient Based on ICU Admission

Paper	Diabetes	non-Diabetes	Comparison
Argenziano et al.[1]	0.428	-	-
Chen et al.[2]	0.052	0.027	1.941
Guan et al.[4]	0.146	0.055	2.665
Ortiz Brizuela et al.[7]	0.414	0.180	2.297
Shang et al.[8]	0.107	0.058	1.847
Shi et al.[9]	0.176	0.078	2.250
Suleyman et al.[10]	0.388	-	-
Yan et al.[12]	0.667	0.414	1.612
Zhang et al.[15]	0.082	0.012	6.885
Mean	0.273	0.118	2.785

Table -2: Comparison of Mortality of Diabetics and Non-diabetics

Paper	Diabetes	non-Diabetes	Comparison
Chen et al.[2]	0.063	0.027	2.333
Cummings et al.[3]	-	-	1.650

Guan et al.[4]	0.100	0.025	3.946
Guo et al.[5]	0.108	0.036	2.962
Shang et al.[8]	0.181	0.080	2.261
Shi et al.[9]	0.203	0.105	1.938
Wang et al.[11]	0.857	-	-
Yu et al.[13]	0.327	-	-
Zhang et al.[14]	0.813	0.476	1.707
Zhang et al.[15]	0.213	0.095	2.238
Zhou et al.[16]	0.472	-	-
Mean			2.379

Table -3: Comparison of Severity of COVID-19 Infection in Diabetics and Non-diabetics Based on Condition

Severe Condition			
Paper	Diabetes	non-Diabetes	Comparison
Guan et al. [4]	0.346	0.143	2.418
Jang et al.[6]	0.609	0.172	3.541
Shang et al.[8]	-	-	-
Zhang et al.[14]	0.381	0.472	0.807
Zhang et al.[15]	0.525	0.679	0.773
Mean	0.465	0.366	1.885
Critical Condition			
Paper	Diabetes	non-Diabetes	Comparison
Guan et al. [4]	-	0.100	-
Jang et al. [6]	-	0.174	-
Shang et al.[8]	0.202	0.095	2.024
Zhang et al.[14]	0.333	0.123	1.912
Zhang et al.[15]	0.328	0.095	3.443
Mean	0.288	0.123	2.459

4. CONCLUSIONS

Results show that there is a strong correlation between the severity of COVID-19 in patients with diabetes. In terms of mortality, diabetics have 2.379 times higher mortality than non-diabetics. Diabetes patients are more likely to fall into severe and critical conditions than non-diabetes patients by 1.885 times and 2.459 times respectively. Another marker, ICU admission rates, also show that diabetics are more likely to be admitted to the facility than non-diabetics by 2.785 times. These markers can be combined to a conclusion that diabetics are more likely to fall into severe conditions by 2.377 times than non-diabetics when infected by COVID-19.

Numerous papers have pointed out two main reasons for the high severity in diabetes patients. First of all, diabetes is a comorbidity that usually comes with aging, which has also been identified as one of the risk factors for COVID-19. Furthermore, patients with diabetes are likely to have pre-existing comorbidities other than diabetes, such as hypertension. Hypertension has also been identified as one of the risk factors for the virus and having multiple comorbidities is likely to increase the risks for diabetics.

Another mechanism behind the high severity links to severe inflammatory responses in diabetes patients. Radiological and clinical data show that diabetics had high levels of neutrophils, c-reactive protein and procalcitonin, and a lower level of lymphocytes than patients without the comorbidity, indicating that diabetes patients have severe inflammatory responses when infected by COVID-19.

These factors combined to result in a severe inflammatory storm deteriorating the conditions of diabetic patients, which led to greater severity and poor prognosis of the virus.

REFERENCES

[1] Argenziano, M. G., Bruce, S. L., Slater, C. L., Tiao, J. R., Baldwin, M. R., Barr, R. G., ... & Goyal, P. (2020). Characterization and Clinical Course of 1000 Patients with COVID-19 in New York: retrospective case series. medRxiv.

[2] Chen, Y., Chen, J., Gong, X., Rong, X., Ye, D., Jin, Y., ... & Guo, J. (2020). Clinical Characteristics and Outcomes of Type 2 Diabetes Patients Infected with COVID-19: A Retrospective Study. Engineering.

[3] Cummings, M. J., Baldwin, M. R., Abrams, D., Jacobson, S. D., Meyer, B. J., Balough, E. M., ... & Hochman, B. R. (2020). Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. The Lancet.

[4] Guan, W. J., Liang, W. H., Zhao, Y., Liang, H. R., Chen, Z. S., Li, Y. M., Liu, X. Q., Chen, R. C., Tang, C. L., Wang, T., Ou, C. Q., Li, L., Chen, P. Y., Sang, L., Wang, W., Li, J. F., Li, C. C., Ou, L. M., Cheng, B., Xiong, S., ... China Medical Treatment Expert Group for COVID-19 (2020). Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. The European respiratory journal, 55(5), 2000547. https://doi.org/10.1183/13993003.00547-2020

[5] Guo, W., Li, M., Dong, Y., Zhou, H., Zhang, Z., Tian, C., ... & Zhao, L. (2020). Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes/metabolism research and reviews, e3319.

[6] Jang, J. G., Hur, J., Choi, E. Y., Hong, K. S., Lee, W., & Ahn, J. H. (2020). Prognostic Factors for Severe Coronavirus Disease 2019 in Daegu, Korea. Journal of Korean Medical Science, 35(23).

[7] Ortiz-Brizuela, E., Villanueva-Reza, M., González-Lara, M. F., Tamez-Torres, K. M., Román-Montes, C. M., Díaz-Mejía, B. A., ... & de-León-Cividanes, N. A. (2020). CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF PATIENTS DIAGNOSED WITH COVID-19 IN A TERTIARY CARE CENTER IN MEXICO CITY: A

PROSPECTIVE COHORT STUDY. Revista de investigacion clinica; organo del Hospital de Enfermedades de la Nutricion, 72(3), 165-177.

[8] Shang, J., Wang, Q., Zhang, H., Wang, X., Wan, J., Yan, Y., ... & Lin, J. (2020). The Relationship between Diabetes Mellitus and COVID-19 Prognosis: A Retrospective Cohort Study in Wuhan, China. The American journal of medicine.

[9] Shi, Q., Zhang, X., Jiang, F., Zhang, X., Hu, N., Bimu, C., ... & He, G. (2020). Clinical characteristics and risk factors for mortality of COVID-19 patients with diabetes in Wuhan, China: a two-center, retrospective study. Diabetes Care.

[10] Suleyman, G., Fadel, R. A., Malette, K. M., Hammond, C., Abdulla, H., Entz, A., ... & Chaudhry, Z. (2020). Clinical characteristics and morbidity associated with coronavirus disease 2019 in a series of patients in metropolitan detroit. JAMA network open, 3(6), e2012270-e2012270.

[11] Wang, F., Yang, Y., Dong, K., Yan, Y., Zhang, S., Ren, H., ... & Shi, X. (2020). CLINICAL CHARACTERISTICS OF 28 PATIENTS WITH DIABETES AND COVID-19 IN WUHAN, CHINA. Endocrine Practice.

[12] Yan, Y., Yang, Y., Wang, F., Ren, H., Zhang, S., Shi, X., ... & Dong, K. (2020). Clinical characteristics and outcomes of patients with severe covid-19 with diabetes. BMJ Open Diabetes Research and Care, 8(1), e001343.

[13] Yu, C., Lei, Q., Li, W., Wang, X., Liu, W., Fan, X., & Li, W. (2020). Clinical Characteristics, Associated Factors, and Predicting COVID-19 Mortality Risk: A Retrospective Study in Wuhan, China. American journal of preventive medicine, 59(2), 168–175. https://doi.org/10.1016/j.amepre.2020.05.002

[14] Zhang, Y., Cui, Y., Shen, M., Zhang, J., Liu, B., Dai, M., Chen, L., Han, D., Fan, Y., Zeng, Y., Li, W., Lin, F., Li, S., Chen, X., Pan, P., & medical team from Xiangya Hospital to support Hubei, China (2020). Association of diabetes mellitus with disease severity and prognosis in COVID-19: A retrospective cohort study. Diabetes research and clinical practice, 165, 108227. https://doi.org/10.1016/j.diabres.2020.108227

[15] Zhang, Y., Li, H., Zhang, J., Cao, Y., Zhao, X., Yu, N., ... & Guo, X. (2020). The clinical characteristics and outcomes of patients with diabetes and secondary hyperglycaemia with coronavirus disease 2019: A single-centre, retrospective, observational study in Wuhan. Diabetes, obesity & metabolism, 22(8), 1443-1454.

[16] Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., ... & Guan, L. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet.