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RISKS, COMPLICATIONS, AND MORTALITY IN COVID-19 PATIENTS WITH PRE-EXISTING DIABETES – A REVIEW

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ABSTRACT

SARS-CoV-2 has shown detrimental effects on Diabetes patients and has become a major cause of mortality since its outbreak in Wuhan, China. The novel Coronavirus-2019 spreads via respiratory droplets from an infected person causing symptoms that range from fever, cough, muscle pain, sore throat to complicated eye and respiratory problems. Various published studies suggested that Diabetes patients were more prone to mortality risk once they were infected by COVID-19 as compared to a non-diabetic. This review article was accomplished with an objective to study the risks, complications and mortality associated with the COVID-19 in diabetic patients by analysing and evaluating reports and data from various scientifically published observational studies. Thus, this narrative review infers that Diabetes is a prime comorbidity linked to the severity of COVID-19 in terms of risks, complications, and mortality.

KEYWORDS: COVID-19; Diabetes; Mortality; Complications; Risks.

INTRODUCTION

The SARS-CoV-2 which was originated in Wuhan, China, has created a havoc on the planet earth. Not only the health and lives of people are at stake, but the economy has also been devasted since the existence of COVID-19. The SARS-CoV-2, a single stranded, RNA virus which transmits from infected patients to a healthy person via respiratory droplets oral-faecal routes. The virus spreads in the body by binding the ACE2 by its S Spike protein (Azer 2020). Thus, the active replication and release of the virus in the in-lung cells leads to the occurrence of symptoms. The Covid-19 patients may be symptomatic or asymptomatic (Azer

2020). The symptoms associated due to corona disease 2019 illness are fever, dry cough, shortness of breath. WHO has also mentioned the less common symptoms including nasal congestion, loss of taste and smell, sore throat, headache, joint pain, conjunctivitis (WHO 2020) whereas some other symptoms have been also reported such as Nausea, vomiting, diarrheal, and abdominal pain. In addition to these complications, Anosmia, hyposmia, dysgeusia have also been reported (Azer 2020).

Diabetes is a chronic disease which is characterised as hyperglycaemia. There are various types of diabetes, but the two prominent types are Type1 and Type 2. T1D occurred due to inadequate or insufficient production of Insulin by the Pancreases in the body (WHO). The causes of T1D is still unknown. In T2D the body become resistance to the insulin action because of autoimmune destruction of beta cells of pancreases. T2D occurred due to the obesity or weight gain and physical inactivity. Diabetes occurred due to the obesity or weight gain and physical inactivity. The risk associated with the diabetes are Ketoacidosis, skin complications (skin infection or problem), eye complications (cataract, glaucoma, etc), neuropathy, foot problems, kidney diseases, high blood pressure, and stroke (American Diabetes Association). Diabetes patients have typical symptoms but sometimes, so mild that become unnoticed. Some of the symptoms associated with diabetes are, Extreme fatigue, thirst, starvation, blurry vision, cuts and bruises pain, numbness, loss of weight, etc. (American Diabetes Association).

In 2019 only 463 million adults of age group 20-79 years have developed Diabetes and this number will raise to 400 million by 2045 (International Diabetes Federation). 1 in 5 above 65 years old is having Diabetes and 1 in 2 is still undiagnosed (International Diabetes Federation).

As of 9 November 2020, 5,02,66033 positive cases of Covid-19 were confirmed and 12,54,567 death cases due to COVID-19 have been reported (WHO).

Thus, the numbers are significantly growing, and all the eyes are waiting for the launch of the effective vaccines against the virus. Until then, the risk of Covid-19 in patients with pre-existing Diabetes is a serious concern, as there has been critical reports and guidelines issued by various competent authority for the and risk associated to the Diabetic patients infected to Corona virus-2019. Thus, this study was carried out to evaluate and outline various clinical

report cases and studies related to the covid-19 infected patients who had pre-existing diabetes.

METHODS

Various scientific papers were explored and searched on Google scholar and PubMed for collection of case reports that are published by venerated scientists and researchers since January 2020.

Inclusion criteria: Only clinical and Scientific papers and letters with cohort, case control and case report were used for studying and concluding this paper. Studies that focused on diabetes patients infected by corona virus- 2019 were included.

Exclusion criteria: letter to the editor, literature review, review report letter, case study, new articles, etc. were not included in this review. Also, data and reports from unauthentic sources were not studied and included in this study.

Data: Table 1.0- Scientific papers used for narrative review after screening"

Name	Type of study	Diabetes patients infected by COVID-19
A scientific study on Clinical Characteristics and Risk Factors for Mortality of COVID-19 Patients with Diabetes in Wuhan, China: A Two-Centre, Retrospective Study (Shi et al. 2020).	Retrospective Study	153
Risk and predictors of in-hospital mortality from COVID-19 in patients with diabetes and cardiovascular disease (Rastad el at. 2020).	Retrospective cohort Study	267
Diabetes is a risk factor for the progression and prognosis of COVID-19 (Weina et al. 2020).	Retrospective Study	37
Patients with diabetes are at higher risk for severe illness from COVID-19 (Targher et al. 2020).	Retrospective cohort Study	59
Preadmission Diabetes-Specific Risk Factors for Mortality in Hospitalized Patients with Diabetes and Coronavirus Disease 2019 (Agarwal et al. 2020)	Retrospective cohort Study	1226
The impact of type 2 diabetes and its management on the prognosis of patients with severe COVID-19 (Xu et al. 2020).	Cohort Study	62
Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes (Zhu et al. 2020).	Cohort Study	952
A retrospective study, Independent Impact of Diabetes on the Severity of Coronavirus Disease 2019 (Moon et al. 2020).	Retrospective Study	770

Risk factors of COVID-19 mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study (Holman at al. 2020).	Cohort Study	10989
Total	9	14515

RESULTS

RISKS, COMPLICATIONS AND MORTALITY IN COVID-19 PATIENTS WITH PRE-EXISTING TO DIABETIC

A scientific study on "Clinical Characteristics and Risk Factors for Mortality of COVID-19 Patients with Diabetes in Wuhan, China: A Two-Centre, Retrospective Study", analysed the risk factors for in-hospital mortality of Covid-19 patients with Diabetes (Shi et al. 2020). In their retrospective study on 1561 patients, 153 (9.8%) found with Diabetes with the age range of 56-72 years old (Shi et al. 2020). Through multivariable regression model, Diabetic patients were found to had a high prevalence of hypertension, cardiovascular diseases, and cerebrovascular diseases at 56.9%, 20% 7.8%, respectively as compared to others and had higher possibilities of ADRs (Shi et al. 2020). Patients with diabetes had more chances of Intensive care Unit. Also, the Covid-19 patients with diabetes had lower cholesterol level (3.8 vs. 4.1 mmol/L) and CD4+ cells (164.0 vs. 242.0/μL) but high blood glucose level 9.4 vs. 5.7 mmol/L and procalcitonin 0.06 vs. 0.05 ng/mL. It was found that diabetes was not an independent factor associated with the death of Covid-19 patients (Shi et al. 2020).

"Risk and predictors of in-hospital mortality from COVID-19 in patients with diabetes and cardiovascular disease", another retrospective and cohort study on 2957 patients out of which patients with Diabetes were 9% (267) (Rastad et al. 2020). Researchers in this study investigated that DM increased the risk of death significantly in all the patients (Rastad et al. 2020). The lymphocyte counts, Creatinine, and CRP were ranged to 0.58 (0.51–0.66), 1.46 (1.23–1.78), and 1.09 (1.07–1.11) with P-value- <0.05(Rastad et al. 2020). Thus, the prevalence of DM was the most reported, 19% in hospitalized patient and 31% in non-survivors (Rastad el at. 2020).

Weina Guo et al. in their research on Diabetes is a risk factor for the progression and prognosis of COVID-19", found that Patients with Diabetes had higher risk chances of Pneumonia, the release of tissue injury related enzymes, hypercoagulation and uncontrolled inflammation responses (Weina et al. 2020). In their retrospective study on 174 COVID-19 infected patients, 37 were diabetic and had 0.86 (0.5-1.3) range of lymphocytes cell count and

a higher level of CRF (Weina et al. 2020). The older patients with diabetes had more nausea and vomiting and higher morbidity whereas three patients were more likely to die due to complications (Weina et al. 2020).

A research reported that patients with diabetes were at higher risk for severe illness from COVID-19 (Targher et al 2020). It reported that 59 patients out of 339 laboratory-confirmed cases were diabetics (Targher et al. 2020). In that study, it was reported that the COVID-19 infected diabetics patients were older, obese, hypertensive but had lower number of lymphocytes counts, and albumins (Targher et al. 2020). The diabetics patients were notably had greater severity of COVID-19 illness as compared to non-diabetics as the researchers measured through the binary logistic regression analysis (Targher et al. 2020). Through the analysis, the researchers found that diabetic patients were at greater risk with approximately four-folds of COVID-19 illness (Targher et al. 2020).

Agarwal S. et al. in their research on "Preadmission Diabetes-Specific Risk Factors for Mortality in Hospitalized Patients with Diabetes and Coronavirus Disease 2019" studied the relationship of various factors such age, Hba1, sex, clinical characteristics, etc. in respect to the mortality due to COVID-19 risk for Diabetic patients (Agarwal et al. 2020) . In their research, 1226 patients with COVID-19 and Diabetes were involved and the mortality rate was 33.1% (Agarwal et al. 2020). Most of the patients had diabetes type-2 with mean Hba1 level at 7.5% (Agarwal et al. 2020). Although in their sensitivity analysis finding, there was no association between Hb1Ac and motility in poorly controlled diabetes (Agarwal et al. 2020).

In a research, "The impact of type 2 diabetes and its management on the prognosis of patients with severe COVID-19", out of 1584 diagnosed COVID-19 patients, 114 patients (31.3%) with T2DM history were involved in their study (Xu et al. 2020). In their study, 62 DM patients were male and a total of 27 Diabetes patients (23.7%) died due to COVID-19 as compared to 32 (12.7%) NON-DM patients who are 250 in total (Xu et al. 2020). The study suggested that patients with DM were at severity of inflammation, coagulation activation, myocardial injury, hepatic injury, and kidney injury as the NEWS score was IQR 5(4-8 vs 5 (3-6) than the patients with no DM (Xu et al. 2020). Thus, the diabetes patients were severely ill compared against the non-diabetic patients on admission in hospital (Xu et al. 2020).

Zhu L. et al. in their research, "Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes" involved 7337 patients inclusive of 952 subjects with pre-existing Type 2 Diabetes (Zhu et al. 2020). In their clinical study, the researcher found that patients with T2D reported significantly higher cases of fatigue (38.0 vs 31.4%) dyspnoea (20.5% vs 15.4%) as compared to the non-T2D patients (Zhu et al. 2020). Also, the T2D patients had higher frequencies of pre-existing coronary heart diseases (13.7 vs .37), hypertension (53.4% versus 19.7%), CVD (5.6% vs 1.5%) and chronic kidney disease (4.9% vs 1.3) as compared to the group of non-T2D patients (Zhu et al. 2020). The study also suggested that DM patients had a lower level of lymphocytes cell count but a higher incidence of lymphopenia (44.5% vs 32.6%), and elevation of leukocyte and neutrophils at 11.3% and 17% vs 6.6% and 9.9% respectively, as compared to the patients with non-DM cases (Zhu et al. 2020).

A retrospective study, "Independent Impact of Diabetes on the Severity of Coronavirus Disease 2019 in 5,307 Patients in South Korea: A Nationwide Cohort Study", involved 5307 patients out which 770 diabetic patients with confirmed Covid-19 cases (Moon et al. 2020). In this study 49.3% were male.95.2%, patients underwent hospitalisation, 32.2% needed oxygen support 6.5% supported by ventilator 12.2% diseases as compared to the non-DM patients at 93.7% 14% 1.6%, and 2.6% respectively (Moon et al. 2020).

A cohort study, "Risk factors of COVID-19 mortality in people with type 1 and type 2 diabetes in England: a population based cohort study", in which they analysed that out of 37895 total death of diabetes patients in 2020, 10989 deaths of diabetes patients (464 in T2D and 10525 in T2D) were reported due to COVID-19 infection (Holman at al. 2020). In the survival model analysis, they observed that older age and male sex were the prime factors associated with mortality in diabetes patients due to coronavirus 2019 (Holman et al. 2020). It was also concluded in their study that hbA1c higher than 59mmom/mol (7.6) had higher mortality due to the virus (Holman et al. 2020).

CONCLUSION

T2D patients were severely affected by the virus as compared to the T1D patients. Older diabetes patients, particularly 60 year and above were more at risk of mortality as compared to the younger diabetic patients. Some studies also showed that male-diabetics were at higher risk of complications and mortality as compared to the female diabetic patients. The above studies suggested that Diabetic patients suffered from high prevalence of hypertension,

cardiovascular diseases, and cerebrovascular diseases, inflammation, coagulation activation, myocardial injury, hepatic injury, and kidney injury, etc than the non-Diabetic and Covid-19 patients. The Diabetic patients required more intensive care or instant hospitalisation. In addition to that, laboratory findings in above studies also suggested that Diabetic patients had lower level of CD4+ cell count, lymphocyte counts, Creatinine, and CRP level but, high blood glucose, and procalcitonin level.

After gauging scientifically published 9 observational studies on total 14,515 diabetic patients infected by Covid-19, it can be easily interpreted that Diabetic patients are more prone to the risks and complications associated with COVID-19 illness in respect to the non-Diabetic patients. Thus, it can be concluded through this review paper that COVID-19 patients with pre-existing Diabetics suffer more than COVID-19 patients with no history of Diabetes in terms of mortality, complications, and risks.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

ETHICAL APPROVAL AND INFORMED CONSENT

Not applicable.

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