



COVID-19 AND DIABETES-A FOCUSED REVIEW

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ABSTRACT

In Wuhan, China pneumonia of an unidentified source was reported in December, 2019. The World health organization (WHO) later termed this pneumonia as Corona Virus Infectious Disease 2019 (COVID-19) and declared this epidemic as pandemic after it hit most countries worldwide. There is an increase in the prevalence of diseases like cardiovascular disease (CVD), diabetes mellitus (DM), obesity and hypertension in critically ill COVID patients. Diabetes mellitus has been predicted as a significant risk aspect for mortality in covid-19 patients admitted to hospitals. However, the data about COVID-19 in patients with diabetes and associated comorbidities is inadequate yet. This review aims to figure out the clinical characteristics of severe COVID-19 patients with diabetes and evaluate the comorbidities and inferior outcomes of patients with COVID-19. The literature on COVID-19 related to diabetes mellitus (DM) and its worse effects was critically reviewed. A detailed literature search was carried out using a combination of different keywords; including of SARS-CoV-2/COVID19, diabetes and hyperglycemia/diabetes in various databases and nine studies were selected to exhibit the outcomes related to COVID-19 in diabetic patients. Older age and male sex are greatly related to the inferior effects in COVID-19 patients. As far as the population of minorities like ethnic minorities are concerned, the risk factors associated with cardiovascular problems like obesity, hypersensitivity and diabetes are responsible for severe outcomes. Furthermore, it was concluded that diabetes is a major risk factor for mortality in patients with severe COVID-19. Intensive care management should be applied to managing COVID-19 patients with diabetes mellitus (DM).

1. INTRODUCTION

Diabetes Mellitus (DM) is a debilitating condition, the prevalence of which has been rising since the start of the new century, 2000. The figure has increased to 285 million in 2010 from 30 million in 1985.^[1] According to the International Diabetes Federation's current worldwide assessment, the ratio of affected patients has increased to 483M in 2019 and is expected to reach around 700M by 2045.^[2] Diabetic patients are at greater risk of infection and reveal inferior diagnosis with numerous agitations of metabolic disorders and innate immunity. These days pneumonia due to diverse causative pathogens has

become the main cause of mortality and morbidity in diabetic patients.^[3]

In Wuhan, China pneumonia of an unidentified source was spotted in December 2019. The World Health Organization later termed this pneumonia as Corona Virus Infectious Disease, 2019. (COVID-19). The novel virus that instigated the pandemic was called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of December 2020, a total number of 2.24 million deaths have been reported out of 103 million cases.^[4] As a result, communal control precautions have been implemented globally, and health-care organizations are

restructured to handle the rising number of intensely affected patients. There is an upsurge incidence of associated diseases like cardiovascular disease (CVD), diabetes mellitus (DM), obesity, hypertension and former chronic disruptive pulmonary disease.^[5]

Reports from China, the U.S., and worldwide with an increasing number of studies have concentrated on physiognomies and inferences of hospitalized COVID-19 patients. Diabetes mellitus has been recognized as a significant risk factor for development to ARDS (acute respiratory distress syndrome), and mortality in covid-19 patients admitted to hospitals. According to Wuhan's initial reports, a greater DM dominance was observed among severe cases of covid-19.^[6] A greater incidence was also investigated in reports from hospitalized covid-19 patients in Italy.^[7] To date, numerous studies have investigated the incidence of diabetes mellitus (DM) in patients with slight COVID-19, and it varies from 5.8% to 6.2% while the incidence of DM type 2 patients with austere COVID-19 has perceived a severe upsurge from 24.1% to 28.6 %.^[8] These epidemiological confirmations signpost a precarious part of diabetes in patients with mild and severe COVID-19. Hyperglycemia and diabetes are investigated to aggravate inflammation by increasing the proclamation of TNF α (tumor necrosis factor) and IL (interleukin).^[9] Also, diabetes may lead to dysfunction of lungs by decreasing forced expiratory capacity and forced vital volume.^[10]

As there's an immense need to develop strategies for improvement in diabetes care through this pandemic, it is vital to ponder the clinical knowledge generated about COVID-19 among diabetes mellitus (DM) patients worldwide. Wu and McGoogan from china studied the clinical physiognomies of COVID-19 patients and reported a mortality rate of 2.3% while it was significantly higher among COVID-19 patients with DM (7.3%).^[11] Zhou investigated that 31% of deaths due to COVID-19 were former diabetes mellitus (DM) patients.^[12] However, reports related to clinical characteristics of COVID-19 patients with diabetes mellitus (DM) or clinical experiences evaluating risk aspects among diabetic COVID-19 patients are inadequate. Also, attention should be made towards the direct effect of CoV-2 on function β -cells and persistence, instigating deteriorating, and severe decline of the metabolic regulator in diabetic patients. This concise review summarized the published data from the literature on the range of outcomes from COVID-19 in diabetic patients and associated comorbidities. Also, the status of diabetic patients in COVID-19 pandemic and associated factors were narrowed in our review.

2. MATERIAL AND METHODOLOGY

The literature on COVID-19 related to diabetes mellitus (DM) and its worse effects was critically reviewed. A detailed literature search was carried out using a combination of different keywords including Corona,

SARS-CoV-2/COVID19, diabetes and hyperglycemia/diabetes in various databases like Cochrane library, PubMed, EMBASE and Web of science up to January, 2021. In Inclusion criteria, data after 2019 were included as first COVID-19 was verified in 2019. Hypothetically worthy manuscripts were selected. At this phase, the chosen manuscripts were curtailed to pinpoint the relevant articles to diabetes and COVID-19, and the duplicated articles were eradicated. Our study comprises adult COVID-19 patients. Randomized studies, retrospective studies, cohort studies non-randomized trials, case series, case reports and observational studies published previously were included in our study. While Editorials, commentaries, letters to editors and abstract conference remained in exclusion criteria. For appropriate analysis, all the information regarding the main author, inclusion/exclusion norms, age, sex, sample size and location of the study were documented.

3. LITERATURE REVIEW

3.1 Potential Analysis facets like age, sex and ethnicity

Certain other factors are responsible for severe outcomes in COVID19 patients, but the maximum prevalence and severe clinical progression of COVID-19 are mainly associated with male sex and older age. In the initial phases of this pandemic, the greater incidence of COVID-19 happened in older age people in utmost countries worldwide. The incidence of diabetes mellitus (DM) upsurges with age in both the general and COVID-19 patients. Shi et al. investigated the worse consequences of COVID-19 patients with diabetes compared to sex and age relating to patients with no diabetes. Comorbid hypertension and older age are independent risk factors associated with diabetes mortality rate.^[13] The different effects of COVID-19 have been reported in different ethnic groups. The greater prevalence and worse effects of COVID-19 stated in ethnic minority society are dubious about revealing biological reasons and are mostly due to their regime and socioeconomic issues.

Table 1: Characteristics of DM Patients from various studies infected with CoV. (2020-2021).

Sr. No	Study	Study Type	Total Patients (N)	Prevalence of DM	Consequences	Total deaths	Deaths in the DM group	Odd ration
1	Shi et al. ^[13]	Retrospective	1561	153 9.8 %	Mortality	317 (20.3 %)	64 (20 %)	1.58 (0.84–2.99)
2	Chen et al. ^[14]	Retrospective	904	136 15.04 %	Mortality	92 (10.18 %)	NA	1.09 (1.04-1.15)
3	Sardu et al. ^[15]	Retrospective	187	25 42.45 %	Survival	NA	NA	0.172 (0.051–0.576)
4	Yan et al. ^[16]	Retrospective	193	48 (24 %)	Mortality	108 (55 %)	39	1.53 (95% CI 1.02 to 2.30)
5	Wang et al. ^[17]	Retrospective	138	14 (10.1%)	Survival	6 (4.3%)	NA	1.97 (7.0-14.0)
6	Holman et al. ^[18]	Cohort	NA	264390	Mortality	464 (23%)	289 (62.2%)	2.45 (95% CI 1.60–3.75)
7	Zhang et al. ^[19]	Retrospective	74	74	Survival	10 (13.5%)	10 (13.5%)	1.029, (95% CI 1.002–1.058)
8	Gregory et al. ^[20]	Prospective	6451	313 (4.8%)	Survival	30 (0.5%)	NA	3.90 (95% CI 1.75–8.69)
9	McGurnaghan et al. ^[21]	Cohort	546300	319349 (5.8%)	Mortality	NA	963 (0.3%)	1.395 (95% CI 1.304–1.494)

3.2 Patient comorbidities

In a retrospective analysis, Shi et al. reported incidence of diabetes as 9.8% (153) with a median age of 64 years in total of 1,561 COVID-19 patients among which 56.9%, 20.9% and 7.8% hypertension, cardiovascular disease and cerebrovascular diseases were prevalent respectively. They reported that in patients with high Random Blood Glucose (RBG) levels, SARS-CoV-2 was detectable until death while in patients with low RBG levels, PCR results came negative.^[13]

Chen et al. investigated through their retrospective study that among the total 904 cases of COVID-19, diabetes was the second common comorbidity (15.04%) after hypertension (30.20%). They also reported that the median age of confirmed COVID-19 diabetic patients was 66 years, hypertension was the most common comorbidity (61.22%) and the patients required longer stay at the hospital as compared to non-diabetic COVID-19 patients.^[14]

It was reported that among the total 59 COVID-19 patients, 8 out of 34 normoglycemic patients while 18 out of 25 hyperglycemic patients were diagnosed with diabetes. They also noted that the median time of discharge or death was more (18 days) in hyperglycemic patients while it was low in patients with normoglycemia.^[15]

Reported that among the total 193 COVID-19 hospitalized patients, 94 patients had comorbidities among which hypertension was the most common (37.8%) followed by cardiovascular disease (16.1%) while chronic pulmonary disease (7.3%), cerebrovascular disease (4.1%), chronic kidney disease (2.1%) and chronic liver disease (0.5%) were least common.^[16]

Wang et al. reported the Median age for the 138 studied NCIP (Novel Coronavirus Infected Pneumonia) patients was 56 years, with 31.2% had hypertension, 10.1% had diabetes, 14.5% had cardiovascular disease, and 7.2% had malignancy as comorbidity. Mean age was recorded 46.6 years for type 1 diabetes patients while 67.5 years for type 2 diabetes patients. Increased mortality of COVID-19 was associated with older age and male gender. After adjustment of other risk factors, prior hyperglycemia was strongly related to augmented COVID-19 deaths.^[17]

Zhang et al., in a retrospective study, reported the Median age for the 74 confirmed COVID-19 type 2 diabetic patients was 62 years, among which males were 48.6% while females were 51.4%. 74.3% of the total patients had comorbidities with 47.3% were hypertensive, 17.6% had coronary heart disease, and 16.2% had secondary pulmonary tuberculosis.^[19]

Table 2: Comorbidities of DM patients infected with CoV.

Sr. No	Study	Prior Coronary heart disease		Prior Cerebrovascular disease		Prior Heart failure/hypertension	
		Yes	No	Yes	No	Yes	No
1	Shi et al. ^[13]	32 (20.9%)	121 (79.1%)	12 (7.8%)	141 (92.2%)	88 (56.9%)	66 (43.2%)
2	Chen et al. ^[14]	91 (10.07%)	813 (89.93%)	52 (5.75%)	852 (94.25%)	273 (30.2%)	631 (69.8%)
3	Sardu et al. ^[15]	5 (20%)	20 (80%)	NA	NA	18 (72%)	7 (28%)
4	Yan et al. ^[16]	13 (27.1%)	35 (72.9%)	2 (4.1%)	46 (95.9%)	18 (37.8%)	30 (62.5%)
5	Wang et al. ^[17]	20 (14.5%)	118 (85.6%)	7 (5.1)	131 (94%)	43 (31.2%)	95 (68%)
6	Holman et al. ^[18]	51,435 (1.63%)	3,086,975 (98.27%)	60,255 (1.9%)	3,078,155 (98.1%)	144,870 (4.6%)	2,993,540 (95.4%)
7	Zhang et al. ^[19]	13(17.6%)	61 (82.43%)	2 (2.7%)	72 (97.2%)	35 (47.3%)	39 (52.70)
8	Gregory et al. ^[20]	NA	NA	30 (9.6%)	283 (90.415)	207 (66%)	106 (33.8%)
9	McGurnaghan et al. ^[21]	101178 (31.7%)	218171 (68.31%)	NA	NA	166709 (52.2%)	147862 (47.8%)

4. DISCUSSION

Data about COVID-19 in patients with diabetes and associated comorbidities is limited yet. The purpose of this review is to figure out the clinical features of severe COVID-19 patients with diabetes and also to evaluate the comorbidities and inferior outcomes of patients with COVID-19. Diabetes was reported 42.3 % in 26 mortalities due to COVID-19. In Wuhan, China, a study on 140 patients with COVID-19 was conducted, and diabetes was revealed as an important risk factor for disease severity. Some other comorbidities also play a significant role in the upsurge mortality rate.^[22] Different studies have reported the comorbidities and worse outcomes of the disease like hypertension, cardiovascular diseases and cerebrovascular diseases. Age and male sex with ethnicity also show a vital part in the prevalence of COVID-19 in diabetic patients.

In summary, accessible data recommend that the patient's age is related to inferior effects in COVID-19 patients. This also happens in the case of diabetes. The prevalence of diabetes upsurges in older age people above 65 years. Also, diabetes mellitus (DM) and older age frequently associate with comorbidities like hypertension, cardiovascular disease and obesity.

CONCLUSION

When it comes to COVID19 patients, diabetes accounts for severe outcomes and a poorer prognosis. As far as the populations of minorities like ethnic minorities are concerned, the risk factors associated with cardiovascular problems like obesity, hypersensitivity and diabetes are responsible for severe outcomes. This scenario is somewhat different in white populations. Certain other factors are also responsible for severe outcomes in COVID19 patients, and age is one of them. When it comes to antiviral therapy, it should be subjected to caution, care and clinical efficacy because there are

bright chances of adverse effects due to its interface with the antidiabetic agents. Furthermore, it was concluded that diabetes is a significant threat to improvement in mortality in patients with severe COVID-19. Intensive care management should be applied to managing COVID-19 patients with diabetes mellitus (DM).

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