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Short Review

Diabetes Complications during COVID-19

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ABSTRACT

Coronavirus Disease 2019 (COVID-19) is a global epidemic that is affected by a coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was reported in Wuhan, China. Subsequently, the World Health Organization (WHO) announced an outbreak of pneumonia on January 10, 2020. Outbreaks spread due to human transmission of the virus infection led to the isolation of patients and controlled by a variety of treatments. Corona viruses are large envelope positive single-stranded RNA viruses that infect humans as well as a variety of animals. It spread rapidly to more than 216 countries claimed and 30,295,744 people affected as of September 2020 and 947,933 people had lost their lives. Data from studies explore the details of the mortality rate among people suffering from diabetes mellitus. Information regarding symptoms, pathogenesis, epidemiology, clinical presentation, diagnosis, and treatment of the virus. Risk of infectious diseases in people with diabetes while highlighting the mechanisms of immune dysregulation. Disease caused by the SARS-CoV-2 can lead to adverse diabetes effects, including stress, changes in diet and low physical activities, slow healing and nerve impairment. We studied the clinical considerations, treatment, and management of the diabetic individuals with COVID-19 in this review.

INTRODUCTION

At the end of 2019, COVID-19 (Coronavirus disease-2019), a disease caused by SARS-CoV-2 (Severe acute respiratory syndrome - Coronavirus-2)resulted an outbreak in Wuhan, China, has now become a rapidly spreading communicable disease, with over 100countries worldwide [1]. A decade later, another pathogenic coronavirus with a clinical picture similar to SARS, the Middle East respiratory syndrome coronavirus (MERS-CoV) was isolated from patients with pneumonia in the counties of the Middle East. The World Health Organization (WHO) has stated by September 2020 that 30,295,744 confirmed Covid-19 cases and 947,933 deaths were determined all over the world [2]. The disease is mainly transmitted by large respiratory droplets, although the possibility of other transmission routes cannot be ruled out, as the virus has been found in the urine and feces of infected people. The severity of the disease ranges from a mild, self-limiting flu-like illness to pneumonia, respiratory distress, and death. Symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days. COVID-19 symptoms to death range from 6 days to 41 days from the onset of symptoms to 14 days. This period depends on the patient's age and the status of the patient's immune system. The effect of COVID-19 is considered as an increase the mortality rate among older people (>70

years of age). Common symptoms of COVID-19 are fever, fatigue, and cough, while other symptoms include headache, diarrhea, hemoptysis, shortness of breath, and lymphopenia. Major risk factors of COVID-19 are associated with diabetes, hypertension, and cardiovascular disease [3].

Coronavirus (CoV-2) is a single-stranded, positively enveloped virus contains the RNA genome that belongs to the family Coronaviridae which causes respiratory infections in humans (Figure 1). The coronavirus spikes are glycoproteins that mediate entry into the cells that express Angiotensin-Converting Enzyme-2 (ACE2) receptor with high affinity for a successful cell invasion. The person to person transmission of COVID-19 has led to the isolation of patients who have been prescribed various treatments. There is currently no specific antiviral drug or vaccine for COVID-19 infection for potential treatment in humans [4]. Diabetes mellitus affects approximately 463 million people worldwide population. Patients with diabetes are the third most prevalent risk factor behind cardio-cerebrovascular disease and hypertension. This review focused on Diabetes complications during COVID-19 infection [5].

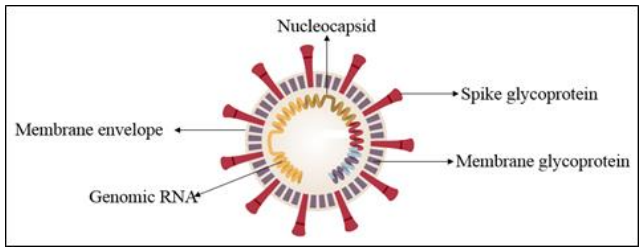

Figure 1: Structure of coronavirus.

CORONAVIRUS DISEASE (COVID-19)

Coronavirus disease (COVID-19) is caused by SARS-COV-2 and represents the leading cause of fatal public health diseases worldwide. Coronavirus is one of the major pathogens that primarily targets the human respiratory system. Symptoms of COVID- 19 infection appear 6 days after the period of incubation. This period depends on the age and the immune system of the patient [6]. Fever, dry cough, tiredness are the most common symptoms, While sore throat, aches, and pains, diarrhea, conjunctivitis, headache, rash on the skin, or discoloration of fingers or toes are the less common symptoms due to COVID -19. Stroke, encephalopathy, neuropathy, neurological disorders, myalgia, intra-cerebral haemorrhage, dysfunction of taste and smell are also found associated with COVID-19. The clinical features revealed by a chest CT scan presented as pneumonia [7].

Abnormal respiratory symptoms, high white blood cell counts, and increased levels of plasma pro-inflammatory cytokines were observed in patients infected with COVID-19.Morbidities due to acute heart damage, pneumonia, cancer, chronic kidney disease, type 2 diabetes are the major consequences of COVID-19 infection (Figure 2). Several reports suggest that person to person transmission is the route to spread COVID-19 transmission. The transmission occurs primarily by direct contact or by droplets spread by sneezing or coughing from an infected person [8].

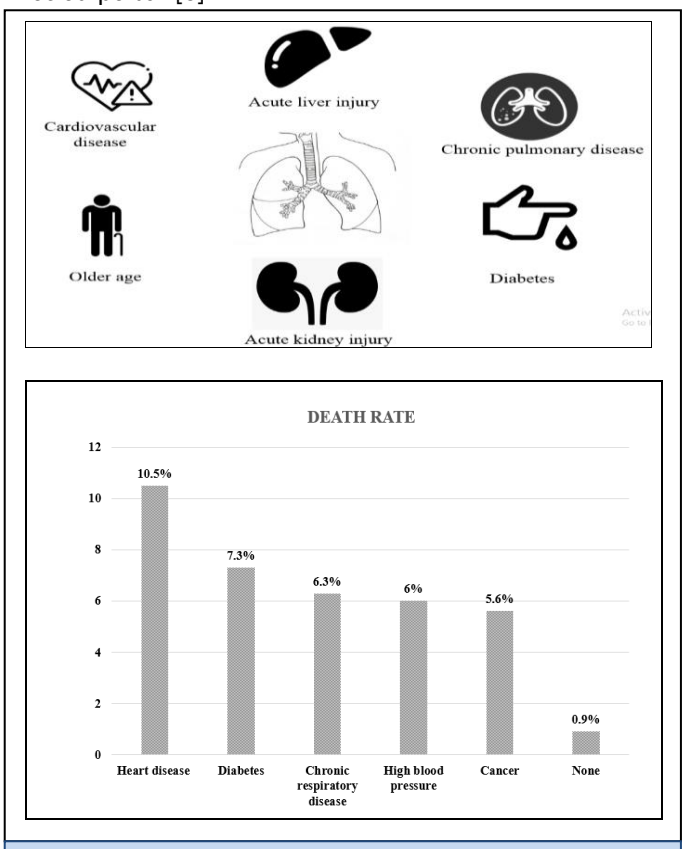

Figure 2: (a) Complication during COVID-19 and (b) COVID- 19 related death rates in people with pre-existing health conditions.

Individual transmission from person to person in COVID-19 infection has been controlled by the isolation of patients. Currently, there are no specific antiviral vaccines or drugs for possible treatment of COVID -19 in humans. There is no specific antiviral treatment approved for COVID-19, and no vaccine is currently available. However, further research is immediately required to develop a novel drug for the treatment of COVID-

19. Comprehensive measures are needed to reduce the person to person transmission of COVID-19 to control the current epidemic [9]. The early death cases caused by the COVID-19 are mostly found in older aged people due to physiological changes associated with ageing and comorbidities (Figure 4). Special attention and effort to protect or reduce transmission should be applied to susceptible populations including aged people, children, and health care providers. Guidelines for health professionals, health service providers, and public health professionals and researchers have been published. Epidemiological changes in COVID-19 should be monitored considering possible routes of transmission and subclinical infections [10].

DIABETICS AND COVID -19

Diabetes is one of the prominent causes of morbidity and mortality worldwide. This chronic disease is related with abnormal accumulation of glucose in blood and increased liver gluconeogenesis. Type 1 diabetes is characterized by the destruction of insulin-producing pancreatic beta cells and type2 diabetes results from a combination of insulin resistance and deficiency and depletion of insulin-producing beta cells. High blood sugar can damage small and large blood vessels, increasing the risk of microvascular and macrovascular complications [11]. People with diabetes have much higher complications and death rate than people without diabetes. SARS-CoV-2 infected people with diabetes can precipitate acute metabolic complications through direct negative effects on β-cell function. The effects on β-cell function might also cause diabetic ketoacidosis in diabetic people (Figure 3). As the overall number of deaths associated with heart disease in people with diabetes is declining while pneumonia is the leading cause of death in diabetes with infections of a variety of pathogens [12].

Diabetes and uncontrolled glycemia have been critically predicted as leading to the deaths of patients infected with various viruses, including the 2009 epidemic influenza A (H1N1) [13], MERS-CoV [14], and SARS-CoV-2 [15]. In the current pandemic, reports have shown that elderly patients with chronic diseases, including diabetes, remain at higher risk of severe COVID-19 and death. Diabetes is a chronic inflammatory disease characterized by multiple metabolic and vascular abnormalities that can affect response to pathogens.

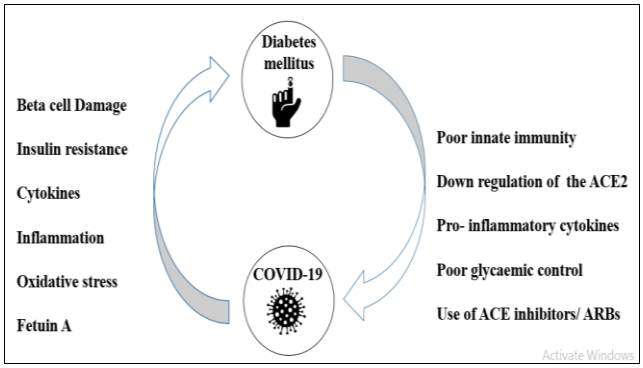

Figure 3: Relationship between coronavirus infection (COVID-19) and diabetes.

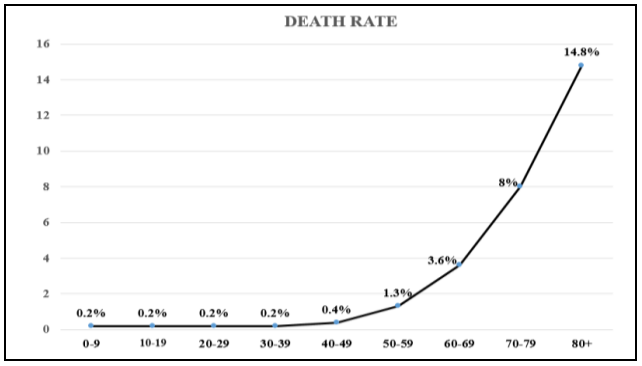

Figure 4: Death rate by age group in the general population diagnosed with COVID-19 in worldwide.

Hyperglycaemic state in diabetes mellitus, glucose forms covalent adducts with the plasma proteins through glycation. Protein glycation and formation of Advanced Glycation End products (AGEs) play a significant role in the pathogenesis. Glycation of proteins obstruct the normal functions, altering enzymatic activity, and impeding with receptor functioning [16]. Hypoglycemia has been shown to mobilize pro-inflammatory monocytes and improve platelet response contributing to increased cardiac mortality in patients with diabetes [17]. Infection with SARS-CoV-2 in diabetics increases the release of hyperglycaemic hormones such as glucocorticoids and catecholamine causing hyper stress, leading to elevated blood glucose levels and abnormal glucose circulation [18]. Although various immune deficiencies are associated with hyperglycemia. The clinical relevance of some of the in vitro disturbances is still not fully understood. Poorly controlled diabetes has been associated with proliferative lymphocyte

responses to a variety of stimuli as well as impaired macrophage and neutrophil functions [19]. In animal models, pulmonary structural changes are associated with diabetes, such as an increase in vascular permeability and alveolar epithelial collapse [20].

IMMUNE DYSFUNCTION IN INDIVIDUALS WITH DIABETES

The immune system is divided into innate and adaptive immune systems. Innate immunity refers to a non-specific initial defence mechanism caused by the recognition of pathogens. Adaptive immunity states to an antigen-specific response designed to eliminate and recollect certain non-pathogenic microorganisms. Based on epidemiological evidence, diabetic patients are more susceptible to infections and more prone to complications when infected with pathogens [21]. The regulation of the immune system is disrupted in diabetic people. Humoral immunity is relatively unaffected in people with diabetes. Cells of innate immunity of common myeloid progenitor are impaired and show impaired phagocytosis and bactericidal activity. Defects in adaptive immunity are associated with poor production of interferon. Also, increased production of AGEs could prevent the production of interferon-gamma by T lymphocytes. These could reduce antiviral activity and increase the intensity of the infection. Low T lymphocyte count in patients with diabetes can weaken antiviral reactions to interferon [22].

Based on reports the reduced intestinal absorption with hyperglycemia increased the systemic spread of pathogens and increases the risk of systemic infection. In people with hyperglycemia, bacteria can invade the system easily. Although there are individual specific mechanisms for increasing the prevalence of infectious diseases in individuals with diabetes and the common pathogenic mechanisms are associated with immunodeficiency [23]. A decrease in phagocytic activity, which is important to kill pathogens and process them for antigen presentation may partly explain the increased severity of infection in people with diabetes [24]. Significantly lower degrees of chemotaxis was found in Polymorphonuclear Leukocytes (PMNs) in people with diabetics compared to controls [25].

People with diabetes, high blood pressure, or other chronic diseases are more affected by COVID-19, but one possible clarification contains Angiotensin-Converting Enzyme 2 (ACE2). The surface of SARS CoV-2 has glycoprotein spikes that bind to the Angiotensin-Converting Enzyme 2 (ACE2) receptor in target cells. Binding to ACE2, the virus is processed by proteases such as Transmembrane Serine Protease 2 (TMPRSS2) and furin resulting in internalization of the virion complex. Increased expression of ACE2 and furin in diabetic individuals, which can promote virus invasion and replication [26].

MANAGEMENT OF THE DIABETIC PATIENT WITH COVID-19

In the current epidemic, comprehensive action is needed to reduce human to human transmission of COVID-19. Special attention and efforts to protect or reduce transmission must be given to sensitive populations including children, people with cardiovascular disease, diabetes, kidney disease, obesity and hypertension, health care providers, and elderly people. Overall knowledge of the prevalence of COVID-19 and disease in people with diabetes continues to evolve as more detailed studies are conducted [27]. At present, it is reasonable that diabetic individuals are at increased risk of developing SARS- CoV-2 infection. Blood glucose control is important for all patients. The diabetes was seen as a risk factor for mortality in patients infected with epidemic influenza A 2009 (H1N1), Middle East Respiratory Syndrome-related coronavirus (MERS-CoV), and Severe Acute Respiratory Syndrome (SARS) coronavirus. Based on knowledge with SARS-CoV and present data on COVID-19 have shown that diabetes and hyperglycemia are significant risk factors for complications and mortality. Diabetic patients become serious when infected with a respiratory virus [28].

Management of diabetic individuals with COVID-19 includes several aspects. Diabetics need to maintain glycaemic control as it helps reduce the risk and severity of infections. Management of diabetes in COVID-19 patients with a regimen of good glycemic control is probable and may help in reducing complications [29]. Blood sugar levels require regular monitoring. Good glycaemic control may reduce the risks of bacterial pneumonia. Patients with heart or kidney disease which may coexist with diabetes need special care and should try to stabilize the heart and kidney conditions. It is important to pay attention to nutrition and adequate protein intake, aware of mineral and vitamin deficiencies and regular Exercise has been shown to improve immunity. It is significant to vaccinate against influenza and pneumonia which may reduce the risk of bacterial pneumonia after respiratory viral infections

[30]. In general preventive measures are used to manage infection of COVID-19. When coughing or sneezing, proper breathing hygiene should be practiced by covering the mouth and nose. Washing hands thoroughly with soap and water can kill the virus. Alcohol-based hand massages are also beneficial. Contact with the affected person should be minimized. The use of masks is recommended when in contact with those with respiratory symptoms. Minimal travel to large affected areas should be avoided to limit the spread of infection [31].

CONCLUSION

COVID-19 has spread rapidly since it was first identified in Wuhan and has shown widespread severity. Early isolation, early diagnosis, and early treatment might work together to improve control of the disease. Diabetes and COVID-19 have significant clinical implications and impact on mortality in patients. Dysregulated immune cell populations and visible activity in people with diabetes play a key role in exacerbating the severity. A combination of dominant chronic conditions such as heart disease, hypertension, and obesity as well as altered ACE2 receptor expression, may expose immune dysfunction, alveolar and endothelial dysregulation and increased systemic clotting among people with diabetes are at increased risk for COVID-19.The clinical course and how hypoglycaemic drugs affect the severity of SARS-CoV-2 infection is of critical significance for the management of the disease.

CONFLICTS OF INTEREST

The authors do not have any conflict of interest

REFERENCES

1. De Oliveira NS, Abreu FP, de Ávila S. (2020). Sars-COV-2 (severe acute respiratory syndrome-related coronavirus): A biological perspective. In COVID-19: environment and technology (pp. 302-315). Univali.
2. Rockx B, Kuiken T, Herfst S, Bestebroer T, Lamers MM, et al. (2020). Comparative pathogenesis of COVID-19, MERS, and SARS in a nonhuman primate model. Science. 368: 1012-1015.
3. Gupta R, Ghosh A, Singh AK, Misra A. (2020). Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diabetes & Metabolic Syndrome. 14: 211-212.
4. Chen Y, Liu, Q, Guo D. (2020). Emerging coronaviruses: genome structure, replication, and pathogenesis. Journal of Medical Virology. 92: 418-423.
5. Hussain A, Bhowmik B, do Vale Moreira NC. (2020). COVID-19 and diabetes: Knowledge in progress. Diabetes Research and Clinical Practice. 162: 108142.
6. Rothan HA, Byrareddy SN. (2020). The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. Journal of Autoimmunity. 109: 102433.
7. Bernheim A, Mei X, Huang M, Yang Y, Fayad ZA, et al. (2020). Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. Radiology. 295: 200463.
8. Cao M, Zhang D, Wang Y, Lu Y, Zhu X, et al. (2020). Clinical features of patients infected with the 2019 novel coronavirus (COVID-19) in Shanghai, China. Med Rxiv.
9. Li P, Fu JB, Li KF, Liu JN, Wang HL, et al. (2020). Transmission of COVID-19 in the terminal stages of the incubation period: A familial cluster. International Journal of Infectious Diseases. 96: 452-453.
10. Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, et al. (2020). Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infectious Diseases of Poverty. 9: 1-12.
11. Fang L, Karakiulakis G, Roth M. (2020). Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?. The Lancet. Respiratory Medicine. 8: e21.
12. Ma RCW, Holt RIG. (2020). COVID-19 and diabetes. Diabetic Medicine.
13. Schoen K, Horvat N, Guerreiro NF, de Castro I, de Giassi KS. (2019). Spectrum of clinical and radiographic findings in patients with diagnosis of H1N1 and correlation with clinical severity. BMC Infectious Diseases. 19: 1-8.
14. Banik GR, Alqahtani AS, Booy R, Rashid H. (2016). Risk factors for severity and mortality in patients with MERS-CoV: Analysis of publicly available data from Saudi Arabia. Virologica Sinica. 31: 81-84.
15. Yang JK, Feng Y, Yuan MY, Yuan SY, Fu HJ, et al. (2006). Plasma glucose levels and diabetes are independent

predictors for mortality and morbidity in patients with SARS. Diabetic Medicine. 23: 623-628.

16. Knapp S. (2013). Diabetes and infection: Is there a link?-A mini-review. Gerontology. 59: 99-104.
17. Iqbal A, Prince LR, Novodvorsky P, Bernjak A, Thomas MR, et al. (2019). Effect of hypoglycemia on inflammatory responses and the response to low-dose endotoxemia in humans. The Journal of Clinical Endocrinology & Metabolism. 104: 1187-1199.
18. Wang A, Zhao W, Xu Z, Gu J. (2020). Timely blood glucose management for the outbreak of 2019 novel coronavirus disease (COVID-19) is urgently needed. Diabetes Research and Clinical Practice. 162: 108118.
19. Hodgson K, Morris J, Bridson T, Govan B, Rush C, et al. (2015). Immunological mechanisms contributing to the double burden of diabetes and intracellular bacterial infections. Immunology. 144: 171-185.
20. Popov, D. and Simionescu, M., 1997. Alterations of lung structure in experimental diabetes, and diabetes associated with hyperlipidaemia in hamsters. European Respiratory Journal. 10: 1850-1858.
21. Erener S. (2020). Diabetes, infection risk and COVID-19. Molecular Metabolism. 39: 101044.
22. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, et al. (2020). Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metabolism. 31: 1068-1077.
23. Casqueiro J, Casqueiro J, Alves C. (2012). Infections in patients with diabetes mellitus: A review of pathogenesis. Indian journal of endocrinology and metabolism. 16: S27-S36.
24. Drucker DJ. (2020). Coronavirus infections and type 2 diabetes-shared pathways with therapeutic implications. Endocrine Reviews. 41: bnaa011.
25. Rao S. (2008). Comparison of Neutrophil Function in Diabetic and Healthy Subjects with Chronic Generalized Periodontitis. 12: 41-44.
26. Bourgonje AR, Abdulle AE, Timens W, Hillebrands JL, Navis GJ, et al. (2020). Angiotensin-converting enzyme-2 (ACE2), SARS-CoV-2 and pathophysiology of coronavirus disease 2019 (COVID-19). The Journal of Pathology. 251: 228-248.
27. Singh AK, Singh A, Shaikh A, Singh R, Misra A. (2020). Chloroquine and hydroxychloroquine in the treatment of COVID-19 with or without diabetes: A systematic search and a narrative review with a special reference to India and other developing countries. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 14: 241-246.
28. Bornstein SR, Rubino F, Khunti K, Mingrone G, Hopkins D, et al. (2020). Practical recommendations for the management of diabetes in patients with COVID-19. The Lancet Diabetes & Endocrinology. 8: 546-550.
29. Hamdy O, Gabbay RA. (2020). Early observation and mitigation of challenges in diabetes management of COVID-19 patients in critical care units. Diabetes Care. 43.
30. Wu J, Li W, Shi X, Chen Z, Jiang B, et al. (2020). Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19). Journal of Internal Medicine. 288: 128-138.
31. Hartmann-Boyce J, Morris E, Goyder C, Kinton J, Perring J, et al. (2020). Diabetes and COVID-19: risks, management, and learnings from other national disasters. Diabetes Care. 43: 1695-1703.