Managing Diabetic Patients duringthe Coronavirus Disease (COVID-19) Pandemic

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Abstract

On March 11, 2020, the outbreak caused bySARS-CoV-2 that is identified as the coronavirus disease 2019 (covid-19) was considered as global pandemic. Covid-19pandemic has wide spread worldwide. The risks, morbidity and case fatality of covid-19 are associated with chronic diseases such as cardiac, renal diseases and diabetes mellitus. Recent studies reported that individuals with type1 and those with type2 diabetes are at risk of sever covid-19. The reasons for poor outcome in diabetic patients may be due to multiple factors as longstanding diabetes, old age, obesity and comorbidities such as cardiac disorders. Anti-hyperglycemic drugs can increase the risk. Sever covid-19 can be worsening factor for individuals with diabetes. Covid-19 may lead to dysregulation of blood glucose in individuals with diabetes above that caused by stress hyperglycemia. It may cause acute metabolic complications such as diabetic ketoacidosis. This review discussed the interactions between novel coronavirus infection and diabetes mellitus.The comprehension of this association can help face covid-19 pandemic and future challenges.

Conclusion: Diabetes mellitus is related with high risk for occurrence and prognosis of covid-19 infection. There is several studies proved that diabetes increases viral entry into the cell and inflammatory reaction to the infection. This is necessary to regulate the glucose level in diabetic patients with SARS-CoV-2. Patient with mild covid-19 must be under medical advice. Diabetic patients with severe covid-19 must be hospitalized.

Keywords: COVID-19, diabetes, comorbidity, mortality.

Introduction

In December, 2019, a condition ofatypicalinterstitial pneumonia caused bynovel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was diagnosed in Wuhan, China. On March 11, 2020, WHO considered covid-19 as a global pandemic due to its rapid spread. Covid-19 caused more than 54million cases and more than one million deaths worldwide. Among individuals with concomitant disorders such as chronic obstructive pulmonary disease, diabetes, hypertension, obesity and cardiovascular disease there is high prevalence of sever covid-19 and high mortality rate**(Singhet al., 2020).**

Diabetes is considered as high risk for infection. Diabetes suppresses innate and humoral immunity. Diabetic patients had shown bad outcome in previous outbreak as outbreak of SARS-CoV-1(Severe Acute Respiratory Syndrome) in 2002-2003

(Yang et al., 2006)and H1N1 outbreak in 2009(Allardet al., 2010). In these outbreaks, diabetes caused bad outcome. Diabetic patients had high riskfor sever disease. Diabetic patients needed hospitalization and intensive care unit (ICU) admission more than non-diabetic patients(Wu et al., 2020).

Studies revealed that diabetic patients with covid-19 are associated with severe or critical illness(Fig.1).A study on 138 covid-19 patients revealed   that 72%

ofdiabetic patients required admission inICU, compared to 37% of non-diabetic patients (Wang et al., 2020).Studies proved that diabetic patients with covid-19 had high risk for acute respiratory disease(Yanget al., 2020).

Disease Control and Prevention Center in China revealed a case fatality rate of 2.3% in Covid patients. Case fatality rate was as high as 7.3% with comorbidity of diabetes and 6.0% in hypertension(Wu and McGoogan, 2020).
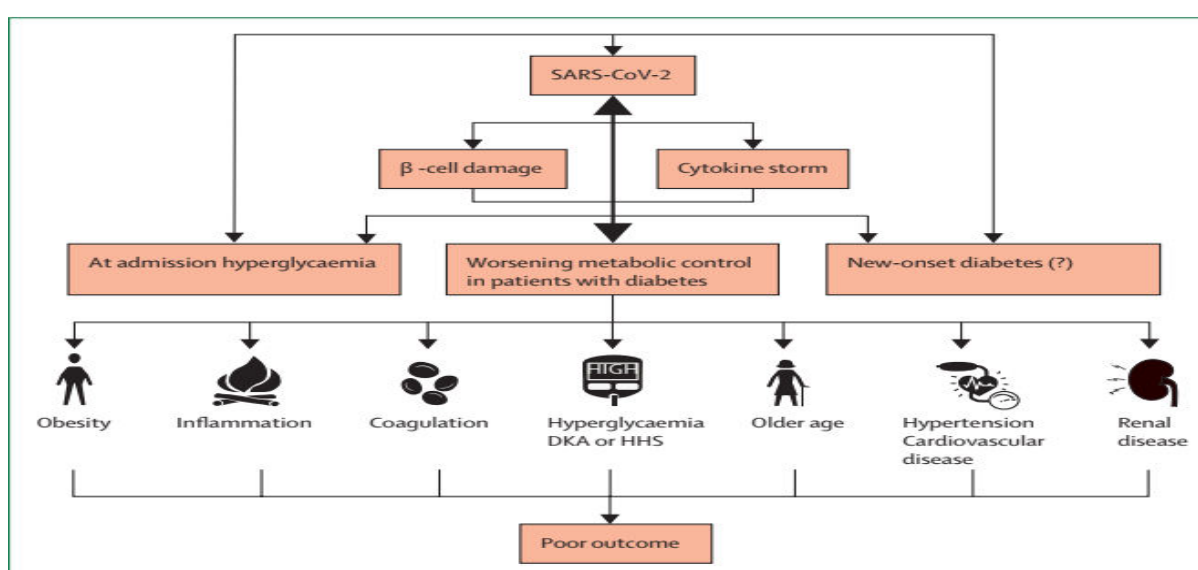

Figure 1. The association between diabetes and novel corona virus infection . Diabetic patients have bad outcome due to many associated conditions increasing the risk. Covid-19 might cause acute metabolic complications for diabetic patients. It also may causes sustain hyperglycaemia or new-onset diabetes at hospital admission. DKA=diabetic ketoacidosis. HHS=hyperglycaemic hyperosmolar syndrome(Apicella et al., 2020).

Corona virus infection may cause insulin resistance, B-cell damage, and drugs used in the management of coronavirus

infection ascorticosteroids or interferon can cause dysglycemia in diabetic patients (Table.1)(Pal and Bhadada, 2020).

Table 1.The effects of drugs used in the treatment of covid-19 on blood glucose(Pal and Bhadada, 2020).

Drugs	Mechanism of action	Effect on glucose level
Corticosteroids	Anti-inflammatory, blocks cytokine storm	Hyperglycemia

Ritonavir /Lopinavir	Inhibit protease, prevents viral cellular entrance	Increased blood glucose
Remdesivir	Adenosine analogue, prevents viral replication	Hyperglycemia
Interferon	Increases immunity	May cause autoimmune B-cell damage
Chloroquine/Hydroxychloroquine	Blocks viral entrance	Improves blood glucose level and HbA1c in diabetic patients
Azithromycin	Decreases severity of respiratory tract infection in patients with viral disease	May cause dysglycemia in diabetic patients
Tocilizumab	Monoclonal antibody against interleukin-6, prevents cytokine storm	Improves blood glucose level and reduces HbA1c in diabetic patients
Convalescent plasma	Provides antibodies for SARS-CoV-2 virus	unknown

Pathophysiology of Diabetes and covid-19:

It was reported that coronavirus uses angiotensin converting enzyme 2(ACE2)receptor for entrance into the cell. This receptor presents in epithelial cells of the lung (type I and II alveolar cells), endothelial cells of blood vessels,heart, tubular cells of kidney, epithelial cells of intestine and pancreas.S-glycoprotein on the surface of coronavirus binds to angiotensin receptor and leads to changes in the conformation of S-glycoprotein. that causes proteolytic digestion by proteases of host cell leading to entrance of the virus. The virus causes recruitment of inflammatory cells as T helper cells that produce interferon γ and other mediators this cause inflammatory response that leads to tissue injury. The inflammatory mediators lead to recruitment of other inflammatory cells. This causes a 'cytokine storm'. That leads to organ damage and can cause multi-organ failure that presents in severe covid-19**(Fig.2)(Vaduganathanet al., 2020).**
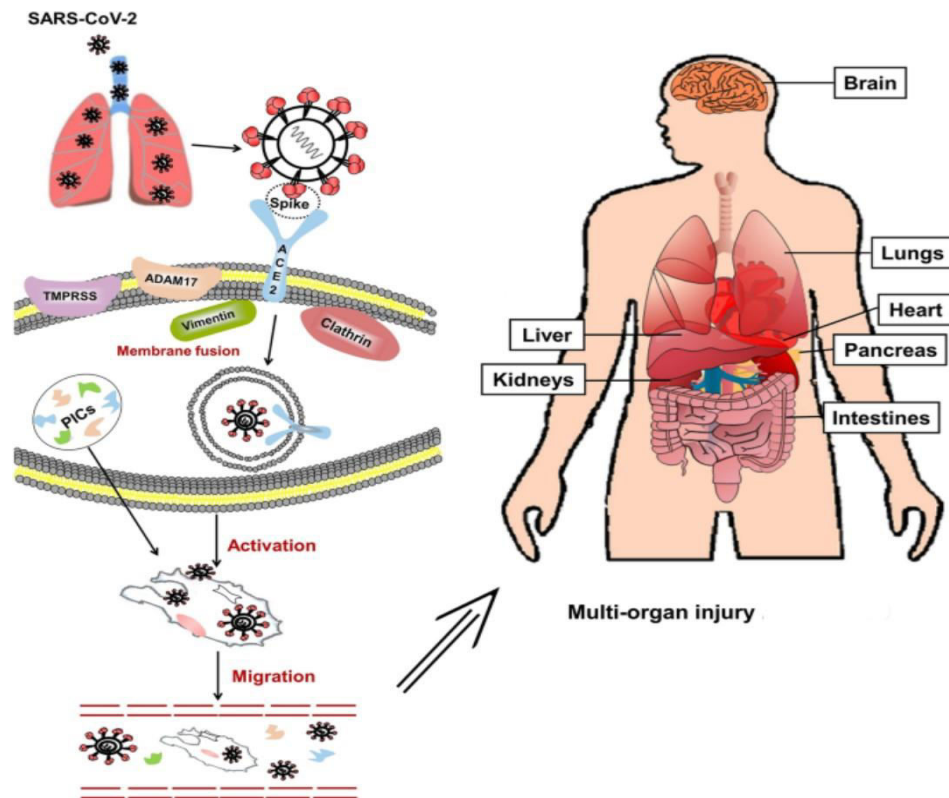
Fig (2): Diagram shows viral entry into the cell by binding to ACE2 receptor. This cause releases of pro-inflammatory cytokines (PICs) that may cause cytokine storm that causes multi-organ failure(**Ni,et al., 2020).**

Diabetic patients with covid-19 have bad prognosis. Diabetes in general predisposes to infections.It affects innate and humoral immunity by several mechanisms as impaired phagocytosis and neutrophil chemotaxis (**Pearson-Stuttard et al., 2016**). There are several factors cause poor outcome in covid-19 with diabetes:

1-Increased ACE-2 expression: Studies reported that diabetes leads to increased angiotensin expression in liver, renal cortex and pancreas (**Raoet al., 2020**).

2-Increased Furin: Diabetes leads to increase in furin. It works as membrane bound protease. It is associated with the entrance of the virus into the cell. The increase of Furin in diabetes can lead to viral replication (**Fernandez et al., 2018).**

3-Impaired T-Cell function: Covid-19 causes lymphocytopenia inpatients and associates with prognosis. Diabetes impairs T-cell function (**Guan et al., 2020).**

4-Increased IL-6 (Interleukin-6): Many inflammatory mediators are increased in covid-19. Diabetes increases cytokines as IL-6 that may play a role in the prognosis of covid-19 infection (**Maddaloni and Buzzetti, 2020).**

Management of diabetic patients with covid-19:

Glycemic control

Studies on other infections as SARS and H1N1 influenza reported that individuals with poor glucose regulation were at high risk of sever disease and complications. Diabetic patients with mild covid-19 infection can continue anti-hyperglycemic medications. It is advisable to stop metformin if there is low oral intake or vomiting. Doses of hypoglycemic drugs must be changed depending upon the blood glucose levels. Diabetic patients with severe coronavirus infection with

respiratory distress must be hospitalized. They mostly would require insulin. Patients need respiratory help as mechanical ventilation would require intravenous insulin infusion (**Tran, et al., 2019**).

Blood glucose measurements

Frequent blood glucose monitoring must be performed for all diabetic patients with corona virus infection. Covid-19 patients that are critically ill or receiving intravenous insulin require more follow up all over the day (**Singh et al. 2020**).

Role of ACE inhibitor

The use of ACE inhibitors can be helpful in treatment of covid-19(**Basu et al., 2017**). Studies on mice infected with covid-19 with lung injury reported improvement of the changes with an angiotensin receptor blocker, losartan.

American Heart Association and European Society of Hypertension recommended to continue using angiotensin receptor inhibitors in hypertensive patients (**Nainet al., 2020**).

Benefit of Statins, Calcium Channel Blockers

Studies reported the benefit of the use of statins in pneumonia. Statins reported to inhibit activation of Nuclear factor kappa B (NFκB) that may help cytokine storm (**Fedson et al., 2020**).

Calcium channel blockers reported to decrease severity of disease and improve outcome in patients with pneumonia that might be caused by preventing calcium influx into the cell (**Zheng et al., 2017**).

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