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A Review Study of the effect of COVID-19 on Diabetic patients

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Abstract

Coronavirus disease 2019 (CoVID-19), which has spread widely around the world, has had a major impact on the health of individuals, especially those suffering from chronic diseases. One of these diseases is diabetes, which is considered one of the common diseases, main entry receptor for SARS-CoV-2 virus is Angiotensin-converting enzyme 2 (ACE2). Many patients with diabetes suffered from high blood sugar after their infected with Covid-19, in addition to the effect of insulin and its relationship to mortality. Studies have also indicated that chronic inflammation leads to the development of the disease and insulin resistance. Inflammation activating plasmin has an effect on D-dimer, leading to its increase ،this increase also leads to mortality. Patients older than 50 years old were more likely to be affected by CoVID-19.

The aim behind this study is to explore this link to be managed appropriately, as people with diabetes need to control their sugar levels because imbalances in these ratios may lead to an increase in the effects of covid-19 infection.

Keywords: Coronavirus disease, Diabetes patients, Chronic inflammatory, Angiotensin-converting enzyme 2, Defect in glucose metabolism

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Introduction

Diabetes considered a disease that is widespread in the world; adults from 20 to 79 are diagnosed with diabetes1. Diabetes type 1 has occurred because of destroying b-cells by T cell (CD4 and CD8); it is considering a genetic autoimmune disease 2, While Diabetes type 2 was due to resistance of insulin that come from losing of insulin secretion from beta cells 3. More prevalent type is diabetes mellitus type 2 (T2D) about 90-92% case, body mass index (BMI) ≥25 kg/m2 , old ages and physical activity that is limited all are considered a risk factors for T2D 4. Special care is important to control and reduce from complications that diabetes patients maybe suffering from 5. Coronavirus disease 2019 (CoVID-19) is a lung disease that leads to acute respiratory syndrome. It has spread worldwide recently, and the infected people showed mild to moderate symptoms. In contrast, at a rate of 5%, others have caused acute respiratory distress and failure in multiple organs, while 15% developed into acute pneumonia 6,7. According to gender type male where more susceptible than female to CoVID-19, this was mentioned in some studies 6. The World Health Organization (WHO) called it a coronavirus outbreak on March 11, 2020. The nuclear material of this virus is ribonucleic acid RNA 8. Surrounded by lipid bilayer that is decorate with protein, this virus led to intense acute respiratory syndrome (SARS) 9. Angiotensin-converting enzyme 2 (ACE2) is the primary entry receptor for the virus into human cells 10. It is expressed in cardiac myocytes, lung alveolar cells, and vascular endothelium 11. Through the ACE2, the pancreas will be infected by the virus and expressed more than other organs, and this infection affects the pancreas, and thus the secretion of insulin, which will decline and thus raise the level of sugar in the blood of patients, whether they have diabetes or not 12. This expression of the pancreatic receptor ACE2 will lead to pancreatic injury 13. There is also a second receptor called dipeptidyl peptidase-4 (DPP-4) enzyme, this receptor in type 2 diabetes patients is targeted pharmacologically, this considers a Second mechanism for diabetes patients to be infected with CoVID-19 14. Those patients required high amount of insulin and previous studies mentioned

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that there was an elevated level of ketoacidosis in them 15. It is essential to mention that this virus's main transmission route is through virus-carrying droplets secreted from the respiratory tract 6.

Symptoms in DM patients

The patient infected with this virus is identified by the symptoms of cough, fever, shortness of breath, and headache16. People who are at greater risk of complications due to this virus are those who have cardiovascular disease, cancer, kidney disease, and diabetes. 17,18. People with diabetes may be more likely to get CoVID-19 for a long time, as preliminary studies indicated fatigue, inability to focus, shortness of breath, and muscle and joint pain ("long CoVID-19") 19. Diabetic patients suffer from a low-grade chronic inflammatory condition with lipid metabolism and glucose changes. Thus, complications associated with diabetes are developed, represented by cardiovascular disease, neuropathy and retinopathy 20. As for the damage to the immune system, it results from high blood sugar, which leads to metabolic inflammation, and therefore, the body's ability to deal with the infection will decrease, which weakens the healing process and prolongs the recovery period 21.

Treatment and recovery

The clinical treatment for CoVID-19 is represented by symptom control and oxygen therapy. For people who suffer from damage to the respiratory system, the treatment is with mechanical ventilation, and no treatment has been available so far to treat CoVID-19 patients despite the testing of many antiviruses such as nucleotide analog Remdesivir, it was also directed to develop vaccines that target the virus and prevent its entry 22. The treatment for patients whose blood sugar level before eating is more significant than 180 mg/dL is intensive Antidiabetic therapy. 23. Therefore, people with diabetes are more likely to be hospitalized 24,25. They are also more susceptible to infection, and symptoms are worse than people without diabetes 26, where CoVID-19 can also cause death to Diabetic patients 27,2. Previous studies

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mentioned that there was a significantly improve in the level of HbA1c in patients with good glycemic control this lead to develop macro- and microvascular and decrease in complication that occurs due to this disease 29. However, there was a change in the management of diabetes because of lockdown overall the world to prevent spread of CoVID-19 30.

Effect of diabetes on covid-19 patients

Diabetic patients have increased risk to mortality by CoVID-19 infection as function of innate and humeral immunity has been suppressed, during the infection severity of pneumonia have been linked to glycated hemoglobin HbA1c 31. CoVID-19 Patients with new onset diabetes or pre-existing are suffering from metabolic decompensation such as hyperglycemic hyperosmolar state (HHS) 32. There was an elevation in the expression of ACE2 because of using the Angiotensin 2 receptor blocker, this elevation contributes to the entry of virus 33. Injury in the lung alveoli is the most finding among diabetes patients also infiltration of inflammatory cell within hyaline membranes 34. High glucose levels in the blood help the infection progress, as the percentage of the virus that needs glucose for its reproduction increases 35. The risk of death is lower in diabetics who can maintain a low blood glucose level 36,37. Another evidence of the effect of the virus is the defect in glucose metabolism in patients with diabetes. This increases their need for insulin doses and thus aggravates the disease and its effect on the severity of pneumonia. What also proves the seriousness of the virus is the increase in death rate in people who suffer from complications of diabetes 38.

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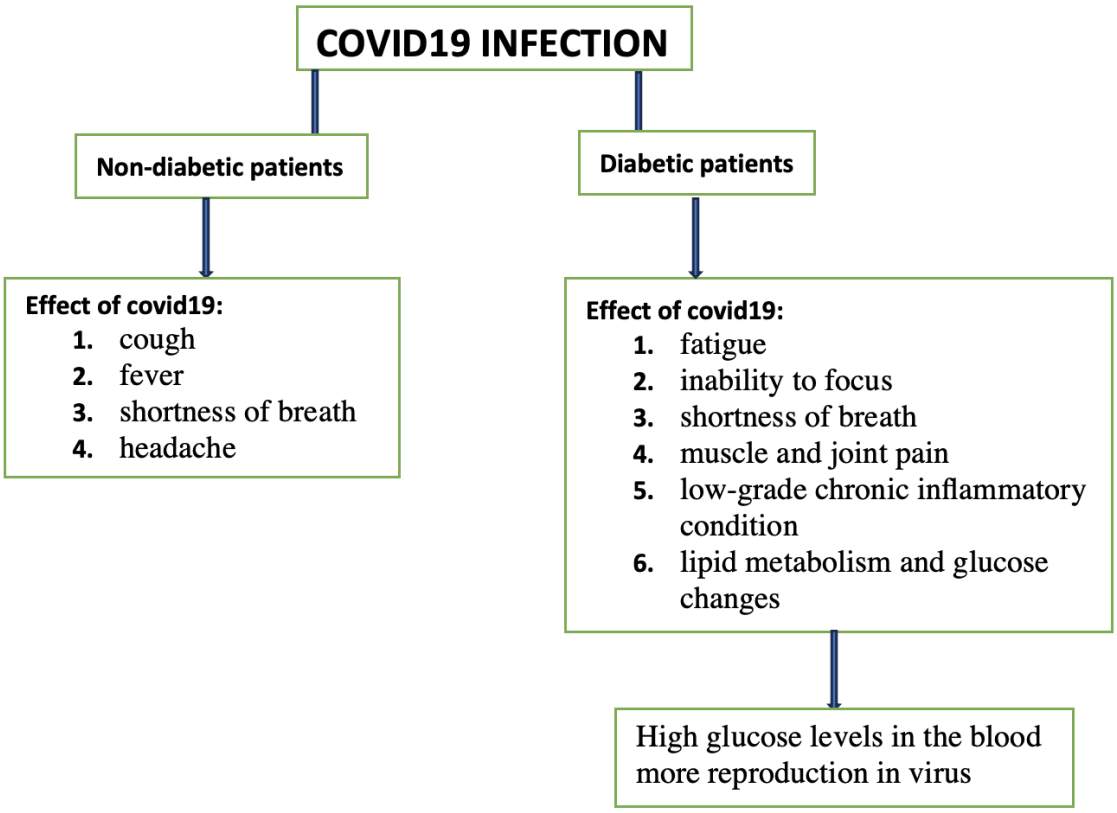

Fig. 1 Risk of CoVID-19 in diabetic patients

Examinations and Diagnosis

The most critical test for symptomatic people that helps in the diagnosis is real-time Reverse Transcription Polymerase Chain Reaction (RT-PCR) that is used to examine a nasal swab from them. As another auxiliary examination, antibody-based tests are offered 39. People whose result is negative mean that they are not infected with the SARS-CoV-2 virus 40. Other routine examinations that must be taken are complete blood cell count CBC, renal function testing creatine kinase, lactic dehydrogenase (LDH), and liver examinations of alanine aminotransferase (ALT) and c-reactive protein (CRP) and aspartate

aminotransferase (AST) 41. Studies also indicated that the increase in inflammatory parameters in patients is associated with the severity of infection 39,42.

For early diagnosis, a Computed tomography (CT) of the chest is done, where interstitial lung abnormalities will appear, and the result of the patients is the presence of bilateral ground-glass opacity without subsegmental areas of consolidation or mass shadows 43

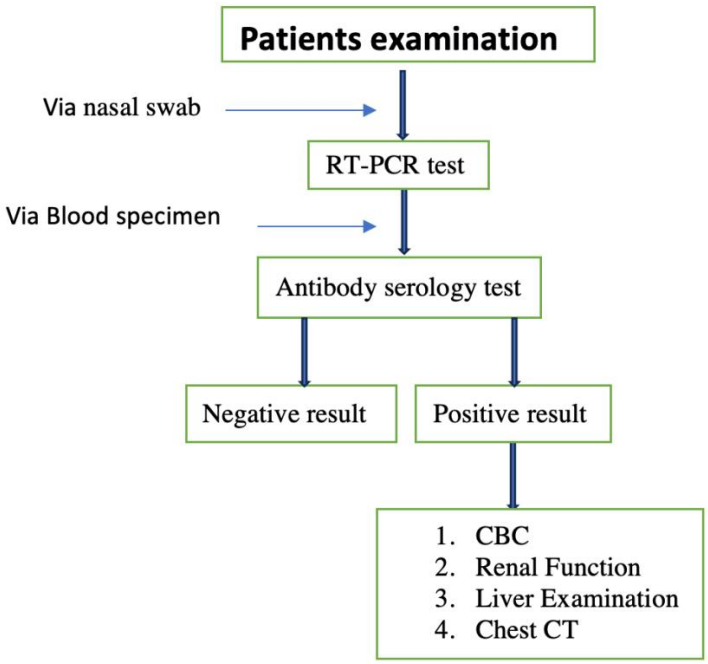

Fig. 2 Examination of CoVID-19 in diabetic patients

Effect of CoVID-19 on immunity

Inflammatory responses are triggered by infected cells that undergo to apoptosis leading to inflammatory cells recruitment 44. Innate immune system gets rid of cells that infected with virus by natural killer cell without prior sensitization and. With no effect on normal cells, evidence of previous studies noticed low level of NK cell in diabetic patients with a high level of blood glucose 45. The immune system is activated to induce insulin resistance and elevated blood glucose levels, with an outpouring of immune parameters

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such as pro-inflammatory cytokines such as Interleukin 6 (IL-6) and Tumor Necrosis Factor (TNF) alpha, and counter-regulatory hormones 46. The chronic inflammatory process in diabetic patients leads to the development of infection, insulin-resistant states, and hyperglycemic conditions that induce the pro-inflammatory cytokines and increased production of glycosylation end products 47,48. In addition, what indicates a high viral load in the blood is a decrease in IFNα activity in the blood and a severe weakness in the response to interferon type I 49. When infected people try to improve their immune system by food intake, this will disrupt regular food schedules and lead to an imbalance in blood sugar levels 50. Inflammation activating plasmin will lead to an increase in D-dimer. Also, thrombin will be activated by hypoxia-induced molecules and the secretion of tissue factors by the activated monocyte macrophages with the activation of the exogenous coagulation pathway. It will cause a hypercoagulable state or even disseminated intravascular coagulation 38, the levels of D-Dimer associated with mortality rates in CoVID-19 51. Autoimmune damage causes Type 1 diabetes. This damage is due to the limited destruction of beta cells, with the release of antigens from the islet cells and the activation of autoreactive T-cells. The production of these markers is likely triggered by a viral infection, leading to the subsequent activation of CD8+ T-cells mediated by high levels of antigen. 2.

Conclusion:

Diabetes is a significant risk factor that affects the intensity of a wide range of infections, according to more and more studies. People with diabetes have immune cell numbers and activities that are out of whack, which makes the condition much worse. When someone has CoVID-19, it is essential to keep his blood sugar under control. During the CoVID-19 pandemic, patients with diabetes required special care and a comprehensive understanding of how CoVID-19 could impact diabetes management.

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