

Relationship of COVID-19 and Diabetes Mellitus

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Abstract

When ongoing research established the relationship between Covid-19 infection and diabetes mellitus, the interest of the clinicians and the anxiety of the patients increased. This evidence-based mini-review aims to determine whether or not patients with diabetes are more prone to getting infected with Covid-19 and how this affects their clinical outcomes. Among the reported Covid-19 cases, 6-14% outpatients, 16-25% inpatients, 32-58% ICU patients, and 31-42% cases with a mortal course had diabetes mellitus. The latest meta-analysis did not consider diabetes as a risk factor contributing to the increase in mortality of Covid-19 cases.

Keywords: Covid-19; Diabetes; Adiponectin; Cardiovascular

Introduction

Covid-19 infection, which emerged in December 2019 in China, continues to spread all over the world. Worldwide 3.5 million people have been infected and over 250.000 people have died due to Covid-19. The pathogenesis of Covid-19 infection, the mechanism with which it affects the organ systems, as well as the risk factors which exacerbate the course of the disease are still under research by the medical experts. Scientific papers of many medical journals observed underlying medical conditions such as aging, hypertension, cardiovascular disease, diabetes, obesity, cardiac failure, chronic lung disease, and cancer as severe risk factors. These findings caused a great deal of fear and concern among diabetic patients. Are diabetic patients more likely to get infected with Covid-19 than non-diabetic patients? Is the clinical course of Covid-19 infected patients with diabetes more severe? Is the mortality rate in diabetes patients higher? Is there a necessity to adjust and/or change the treatment guidelines of diabetic patients infected with Covid-19? With the help of the latest literature about Covid-19, this mini-review will try to address all the questions above and give an insight into the issue.

Are diabetic patients more likely to get infected with Covid-19 than non-diabetic patients?

Research so far has not concluded a significant difference between the rate of Covid-19 infection in diabetic and non-diabetic patients. A meta-analysis from China states that in 2108 Covid-19 infected patients, the rate of diabetes (10.3%) [1], is similar to that of the normal population in the same region (10.9%) [2]. In Covid-19 infected patients from Italy, the rate of diabetes was 9%, and in the same region and the same age group, the rate was 11% [3]. Therefore, it would be incorrect to claim that diabetic patients are getting more infected more than the normal population. This correlation is presented in (Figure 1).

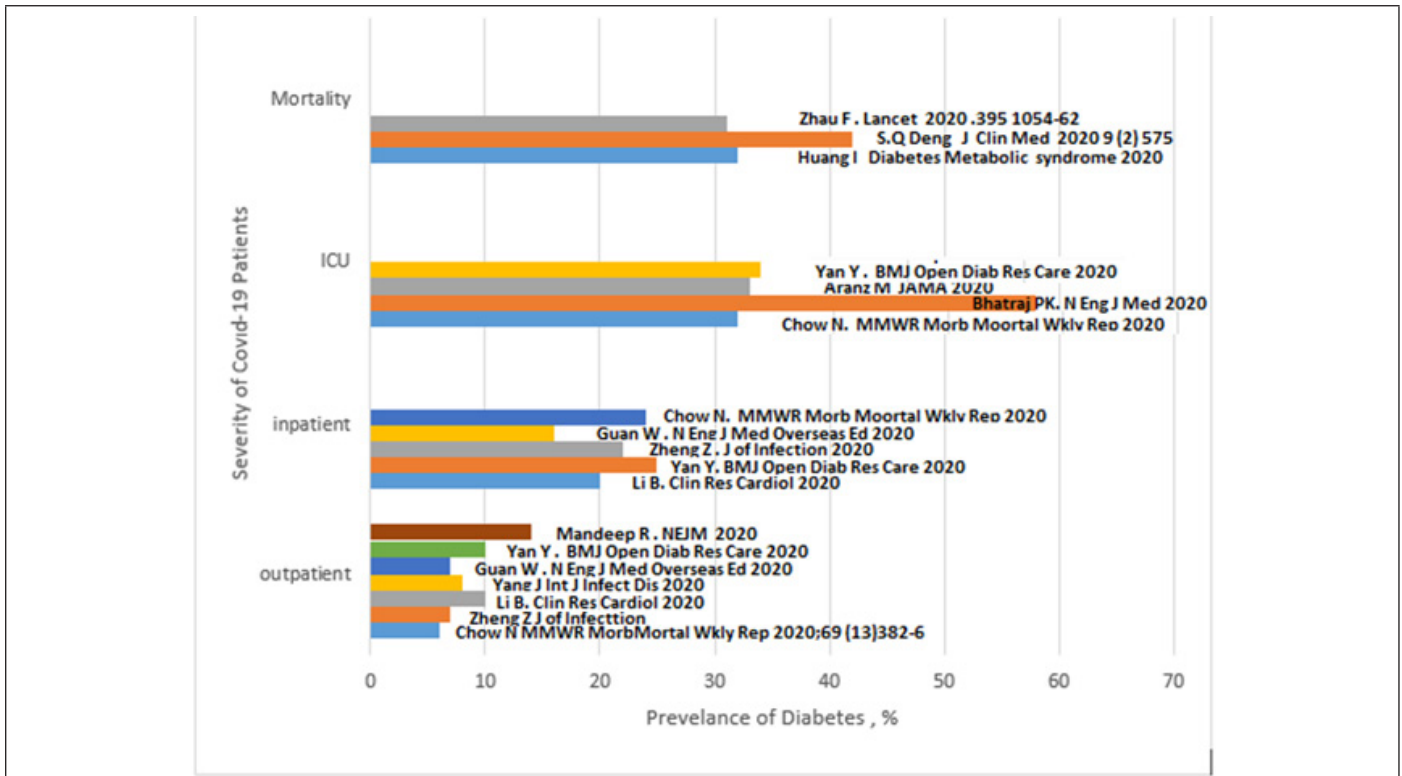


Figure 1: Relation between severity of Covid-19 infection and prevelans of diabetes.

Is the clinical course of Covid-19 infected patients with diabetes more severe?

China Disease Control Center reported that the mortality rate among 72.314 patients was 2.3%, whereas, in the diabetic population it was 7.3% [4]. Moreover, it claimed that in poorly-controlled diabetes, lymphocyte proliferation is inhibited, activation of complement cascade decreases [5,6], the viral replication increases [7], and the forced vital capacity decreases [8]. 29 diabetic inpatients who received Covid-19 treatment in China were evaluated retrospectively, and in 69% of these patients, glucose levels were high according to their 811 measured blood glucose levels [9]. Hypothetically, in diabetes, immune dysfunction forms the basis that increases the severity of the infection. Hyperglycemia leads to chemotaxis inhibition, deterioration of production of cytokines, dysfunction of phagocytosis, T-lymphocytes, and decreased microbial clearance [10]. Furthermore, increased stress levels in Covid-19 patients facilitate an increased release of glucocorticoid and catecholamines [11]. One Chinese research states that among 40 Covid-19 infected patients, 20 cases developed hyperglycemia according to diabetes criteria. This relates to the viral cytopathogenic effect on ACE-2 receptors that are abundant in the pancreas [12]. A Chinese meta-analysis, that included 30 kinds of research, established an association between diabetes, mortality, severe Covid-19 infection, and ARDS [13]. Another Chinese meta-analysis involving 1558 patients displays hypertension, diabetes and chronic obstructive lung disease, cardiovascular and cerebrovascular diseases as independent risk factors [14]. In

Yangli’s research, the critical patients’ data of a hospital were used. 48 (25%) patients of 193 were diabetic and 66% of those diabetic patients were sent to ICU. In the same research, the diabetic patients were old and had decreased lymphocyte count, but had higher D-dimer, CRP, LDH, ferritin, and IL-6 levels than the other infected patients [15]. Type-2 diabetes patients usually have a fatty liver. In these cases, the cytokine storm is more frequent and this may increase the severity of the infection [16]. Also, increasing severity can be related to high levels of proinflammatory leptin and low anti-inflammatory adiponectin in diabetic obese patients [17]. Nonetheless, according to multivariate regression analysis, involving 8910 Asian, American, and European Covid-19 cases, diabetes was not shown as a mortality risk factor among the risk factors of Covid-19 infection [18].

Is there a necessity to adjust and/or change the treatment guidelines of diabetic patients infected with Covid-19?

There is no evidence supporting the necessity for a change in the treatment guidelines of diabetic patients infected with Covid-19. However, sulfonyleureas, pioglitazone, DPP-4 inhibitors, and insulin appear safer than metformin, GLP-1 analogs, and SGLT-2 inhibitors. The anti-inflammatory effect of Metformin causes a decrease in biomarkers [19]. Moreover, if there is a GFR decrease in critical patients, metformin should be used carefully. SGLT-2 inhibitors must not be taken into consideration in severe cases when there are dehydration and risk of ketoacidosis. The administration of GLP-1

analogs is safe in cardiovascular diseases; there is no evidence of its use in severe Covid-19 infected cases. Additionally, DPP-4 molecule levels increase in diabetic patients [20]. Since this molecule is a functional receptor against coronavirus M spike protein [20], it could increase the inflammatory reaction in Covid-19 infected patients and worsen their clinical condition [21]. DPP-4 inhibitors may contribute to decreasing the inflammation. Hypertension and hyperlipidemia often accompany diabetic patients. American and European Cardiology Associations suggest continuing angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and statins in Covid-19 infected patients [22]. In diabetic Covid-19 patients, the development of hypoglycemia should be prevented. In the Wuhan report, among diabetic patients, the rate of hypoglycemia was 10%. In hypoglycemia, proinflammatory monocytes get mobilized, platelets get activated and cardiovascular mortality increases [23].

Conclusion

Diabetic patients are not more disadvantaged than the normal population in terms of getting infected with Covid-19. However, it should be noted that if a diabetic patient is infected, the clinical course is likely to be more severe. The rate of frequency of diabetes in outpatients was 6-14%, in inpatients 16-25%, in ICU patients 32-58% and in mortal cases %31-42. Whether diabetes increases the mortality rate or not, is still a controversial topic. In the diabetes treatment precedence should be given to insulin, DPP-4 inhibitors, sulfonylureas, and pioglitazone.

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