



Research Article

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Diabetes, Heart Disease, Fatty Liver, Blood Groups And COVID-19 Disease: A Brief Review of Evidence

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Abstract

SARS-CoV-2 infection can have a severe evolution and complications in people who present comorbidities. Indeed, people with diabetes, especially those with type 1, and COVID19 are exposed to and an increased risk of diabetic ketoacidosis. Also, cardiac complications due to coronary heart disease or other cardiovascular one, such as hypertension, are possible. These complications may be caused by the virus entering cardiomyocytes or even other surrounding cells. In people with fatty liver/hepatic impairment and COVID-19, there is an increased expression of ACE2 receptors through the HEK293 cell line, which allows SARS-CoV-2 to enter the cells through the TMPRSS2 interface with the help of the regulatory protein PIKIFYE, by therefore increasing the severity of the disease. Moreover SARS-CoV-2 after entry causes T-cell CD8 + reaction, which leads to liver cell damage. The incidence of COVID-19 seems to be high in people with blood group A and low in those with blood group O. For this reason, the aim of this review is to summarize evidence of main metabolic comorbidities (diabetes, cardiovascular diseases, and liver diseases) and blood groups and COVID-19.

Keywords: SARS-Cov-2; Diabetes; Cardiovascular Diseases; Liver Diseases; Metabolic; Corona Virus2; Respiratory; Blood Group; Pneumonia; Hypoxia Occurs; Patients

Abbreviations: ICNARC: Intensive Care National Audit and Research Centre; BMI: Body mass index; NAFLD: Non-Alcoholic Fatty Liver Disease; MAFLD: Metabolic-Associated Fatty Liver Disease; RT-PCR: Reverse transcription polymerase chain reaction; LDH: Lactate Dehydrogenase; DPP4: Dipeptidyl-peptidase 4; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ACE: angiotensin-converting enzyme; VTE: venous thromboembolism; VWF: von Willebrand factor; ICAM: intracellular adhesion molecule.

Introduction

It has been over a year since the Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) originated into China and rapidly spread around the world, causing a terrible pandemic. The incidence and severity of Coronavirus Disease 19 (COVID-19) depends on a variety of factors [REF]. It has been shown how elderly, diabetic people, those with cardiovascular and liver diseases are more likely to develop a severe form of COVID-19. Also, some a relationship between blood group and severity of COVID-19 has been established. Quite often, people present multimorbidity that further increases risk of COVID-19-related complications [1-3]. During pandemic, clinical studies have shown that obese patients become infected by SARS-CoV-2 earlier than the general population and experience severe illnesses more frequently requiring intubation [4,5]. The ICNARC in the United Kingdom reported that 38% of patients with COVID-19 admitted to the Intensive Care Units (ICU) were obese [6]. BMI > 35 were 3.6 times more likely to be admitted to the ICU than patients with a BMI <30 [7]. It should be noted that obesity itself is the cause of cardiovascular disease [8], which is itself a risk factor for severe coronary heart disease [9,10]. People with coronavirus may develop some cardiovascular disease.

If people with coronavirus develop pneumonia, hypoxia occurs, which in turn causes anaerobic fermentation and increased intracellular acidity, and ultimately radical Free radicals damage cell membranes, heart cells, and the secretion of catecholamine's in these patients due to stress causes hypertension, which can cause serious problems for the heart tissue. However, a history of hypertension before contracting the virus can predispose to Cause more problems in these patients [11,12]. Non-Alcoholic Fatty Liver Disease (NAFLD) is another important risk factor in increasing the severity of COVID-19 because cytokines are high in these people and in case of COVID-19 the effects of the disease are doubled. Also due to the active inflammatory pathways in these patients the coronavirus can cause Hepatic fibrosis therefore has a direct relationship between NAFLD and Covid-19 and the effects of Covid-19 are more severe in these individuals [13,14]. It should be noted that the severity of Covid-19 virus disease is related to people with MAFLD, so that people with MAFLD spend more time in the hospital [15]. It should also be noted the incidence of symptoms of COVID-19 disease is related to the patient's blood type [16]. The function and effects of this virus may not be clear yet, but according to the studies that have been done, in this article we tried to review the relationship between diabetes, cardiovascular disease, fatty liver and blood groups with COVID-19.

Recent Findings on Diabetes as A Comorbidity for Covid-19

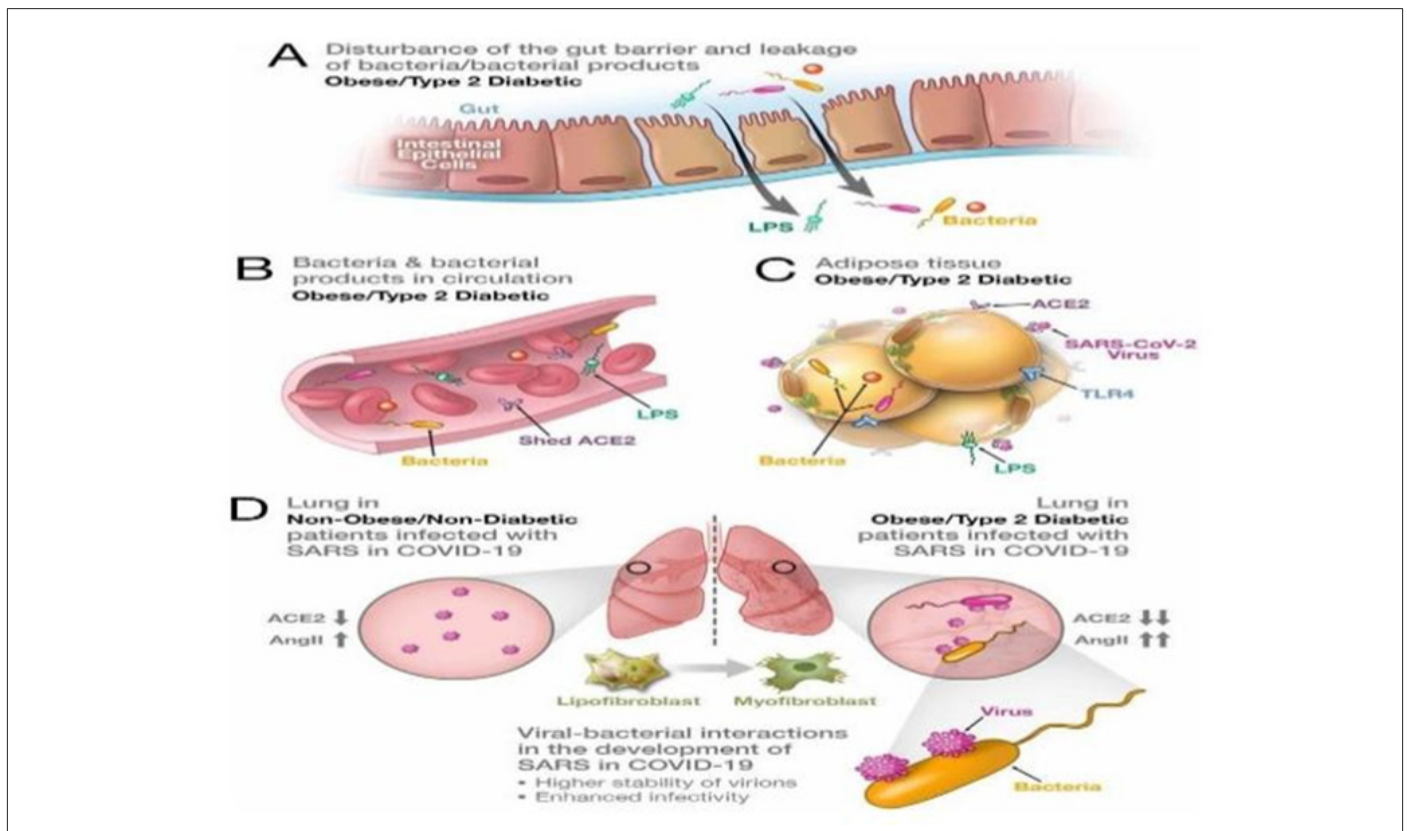


Figure 1: Diabetes and obesity are two comorbidities in Covid-19.

COVID-19 virus from the coronavirus family can be transmitted through aerosol, direct contact, and respiratory droplets of cough and sneezing [17]. Transmission of people with asymptomatic virus during incubation is high [18]. Risk factors such as age (older age), sex (males) and ethnicity (black and Hispanic) are involved in disease severity and mortality [19,20]. All people with underlying diseases such as diabetes, hypertension, chronic kidney disease, cancers, people with immunodeficiency and people with cardiovascular disease who have symptoms (high fever and respiratory symptoms) Such as cough and shortness of breath are a priority in RT-PCR and should be evaluated for SARS-COV-2 [21] (Figure1). Diabetes mellitus, which is a systemic disease, affects the response of the human immune system to infectious agents. During diabetic syndrome, hyperglycemia and insulin resistance cause the release of pro-inflammatory cytokines and stimulate the production of adhesion molecules [22]. High plasma glucose during uncontrolled diabetes in patients with COVID-19, along with severe reductions in FEV1 and FVC, cause respiratory distress and damage to pulmonary epithelial cells [23]. Diabetes alone cannot increase a person's risk of get SARS-CoV-2 infection but it can exacerbate the COVID-19 and increase the severity of symptoms [24]. Previous study findings indicated that the incidence of COVID-19 disease in diabetic patients is the same as the non-diabetic population [23].

In a Chinese study conducted on 3 groups of patients (80 patients without coronary artery disease, 76 non-diabetic patients with coronary artery disease, 55 diabetic patients with coronary artery disease), authors found that there was no difference in the level of white blood cells and liver enzymes, but the number of lymphocytes and albumin in patients with coronary artery disease was significantly higher than the other two groups. LDH levels increase in most respiratory diseases, including Covid-19. And is one of the aggravating factors of respiratory diseases [25,26]. Diabetics are always at risk for various infections and impaired immune responses [27]. Storms of cytokines and lymphopenia are effective in exacerbating Covid disease and given that inflammatory mediators are active in patients with coronary artery by inhibiting their dominant pathways such as DPP4, they can prevent T lymphocytes from proliferating and producing inflammatory cytokines [28]. The NF-KAPPA-BETA pathway plays an important role in the attack of cytokines, and in the case of COVID 19, inflammation is seen through this pathway. By suppressing this pathway through SITAGLIPTIN, which is a DPP4 inhibitor, Controlled inflammation caused by the virus [29]. Following the COVID-19 pandemic, in most parts of the world we saw quarantine of all individuals seeking relative improvement.

According to a cross-sectional study of patients with type 1 diabetes, they found that control of blood sugar in diabetic patients decreased during this period. It was severe and was measured

irregularly, which can be attributed to patients' lack of access to insulin and needed medications, poor diet, and less physical activity [30]. In another study, the effect of quarantine and psychological factors of this period on patients with diabetes was investigated. According to available information, COVID-19 disease causes overeating in diabetics and consequently reduces blood sugar control in these people Slowly [31]. Meanwhile, many diabetic patients who do not have coronary artery disease are concerned with managing the disease and controlling it if it occurs [32]. One of the effective factors that increase anxiety and consequently decrease the immune system of a diabetic person against various infections such as COVID-19, can be loneliness and lack of social communication during this period, worry about reduced access to insulin. The need in case of quarantine and lack of support from care and medical teams [33]. Possible interventions for monitoring diabetic patients during quarantine include proper screening, referral of patients for psychological problems to relevant clinics and centers, proper diets, and regular blood sugar control [34].

D-dimer is a small protein that appears in the blood following the destruction of a blood clot (thrombus) by fibrinolysis, and its presence in the blood in COVID-19 disease indicates a worsening of the disease and an increase in coagulation. In a group of patients with COVID-19, the concentration of D-dimer in the blood of diabetics was 1509 mg/ml +_1509 and in non-diabetics was 624 +_515 mg/ml, which was found to be diabetic in COVID-19, level D- had higher dimers than non-diabetics and D-dimer levels above 2000ng/ml resulted in increased mortality [35]. As a result, the association of COVID-19 with diabetes due to glycosylation of hemoglobin leads to excessive coagulation [36]. To diagnose Gestational Diabetes Mellitus (GDM), we use the Oral Glucose Tolerance Test (OGTT) [37]. Due to the increased risk of COVID-19 by attending health centers, this test is performed less than before and a suitable alternative for this test is measuring HbA1c 41mmol/mol (5.9%) in 24 to 28 weeks of pregnancy Is [38].

According to a study conducted by an article at Ican School of Medicine in Mount Sinai, New York, they found that the mortality rate of diabetic patients with COVID-19 is higher than that of cardiovascular patients and cancer patients with COVID disease. MERS and SARS viruses can also be generalized [39]. Diabetes along with obesity is a very important risk factor among patients with COVID-19 [40]. A study of 450 eligible patients admitted to the Massachusetts General Hospital (MGH) between March 11 and April 30, 2020, found that the number of patients with COVID-19 diabetes in the ICU, as well as mortality Most non-diabetic patients had COVID-19. High BMI with diabetes also increased the severity of the disease [41].

ACE2 is an anti-inflammatory receptor suitable for the invasion of SARS-COV-2 and CORONAVIRUS in human cells, which due to

decreased glycosylation in diabetics, its expression is reduced and provides the basis for ARDS [42]. SARS-COV-2 is also able to destroy pancreatic islet cells, which further reduces insulin and worsens the condition for diabetics, especially type 1 diabetics [43]. The results of a study conducted in South Korea on 211 patients with COVID-19 showed that the severity and severity of COVID-19 symptoms in diabetic patients was approximately 60 times higher than in non-diabetic patients due to reduced immune cell function. And the increase in blood glucose was progressive [44].

Hyperglycemia, which means an abnormal rise in blood sugar, increases the risk of death from pneumonia, heart attack, injury and similar injuries seen in patients with COVID-19 due to an increase in TNF-ALPHA, a major cause of increased ICU hospitalization and Mortality from hyperglycemic patients has been higher than diabetes mellitus [45]. Also, SARS-COV-2 infection, following the destruction of pancreatic islets and beta cells, reduces insulin secretion and causes uncontrolled and excessive increase in blood sugar [46]. In other articles, high levels of dimer, which causes microscopic venous clots in various parts of the body, especially the brain, following diabetes, high blood pressure, and stroke, are among the reasons for the increased mortality of diabetic patients following COVID-19 Was [47,48]. Despite the large number of articles and reviews, there are still doubts about increasing the mortality rate of diabetic patients with COVID-19. According to this study, although anti-diabetic drugs such as metformin improve the condition of patients with SARS-COV- 2. They are effective but their mortality rate has been measured more than the non-diabetic population [49].

Diabetic blood sugar levels may rise during periods of stress or with COVID-19 and manifest as Diabetic Ketoacidosis (DKA); in this case, the body does not have enough insulin to manage this high blood sugar level. Decomposes fats and acidifies the blood [50]. In the case of COVID-19, if the respiratory problems are so severe that the person needs the help of a device to breathe, in such cases, diabetics should not be prescribed oral diabetes medications and intravenous insulin should be started under the supervision of a physician [51]. However, some studies show the progression and recurrence of coronary heart disease following the use of insulin and the need for mechanical ventilation and hospitalization in the intensive care unit following the use or injection of insulin [52]. Obese diabetics with a BMI of more than 30 experience dangerous complications and severe symptoms of COVID-19 disease following an increase in IL-6, which is a response to excess fat mass [53]. During coronary quarantine, diabetic patients suffered severe wounds due to lack of DFU care and foot hygiene, and unfortunately, we have seen a significant increase in the rate of lower limb amputations in diabetic patients [54].

Side Effects of Coronavirus on Cardiovascular System

An evaluation was conducted in the Netherlands among 3011 patients with hospitalized COVID-19 in the age range of 67 years with most men (62.8%) that heart diseases such as atrial fibrillation and heart failure were very common [55]. Different cardiac complications have been observed among coronary heart disease patients. Some studies show that the lack of control of heart rhythm by the main sinus node has the highest incidence [56]. In addition, sinus bradycardia [57,58] and sinus tachycardia [59,60] have been observed among patients. The mechanism of association of this complication with COVID- 19 is not yet fully understood but is likely due to various factors including: decreased ACE2 receptor [61], interaction between sialic acid protein and CD147, hypoxia, direct endocardial damage, fear, and disorder. In the amount of electrolyte and acidity [62-66]. Other causes of cardiac arrhythmia in patients with COVID -19 include side effects of drugs used [67]. In fact, it can be said that cardiac arrhythmias are not simply due to the entry of the virus into the cell and the development of infection [68]. Right ventricular failure was another complication observed in patients with COVID-19. The causes of right ventricular failure include the release of various cytokines and disorders of the renin-angiotensin system [69,70]. Acute coronary syndrome or impaired blood supply to the heart itself was one of the cardiac complications, but in other studies in countries such as the United States, we saw a significant reduction (half of all) in the admission of patients with this syndrome, which is mostly statistical and its cause. it is not specified yet.

Risk factors for atherosclerosis increase the risk of developing this syndrome [71-73]. This syndrome in turn can cause myocardial infarction [70]. In general, the prevalence of fatal cardiovascular complications in these patients is relatively low, although the background of the heart problem increases the risk [74,75]. Hypersensitive C-reactive protein (hs-CRP) and serum creatinine were observed in more than one study in China The severity and mortality of these patients are directly related [76-78]. A research team in Germany evaluated a group of 40 patients. In this evaluation, a myocardial infarction was observed that could affect left ventricular systole. They can be caused by troponin T software. Other research in China also confirms this [79-81] (Figure2). Fatty liver is said to be one of the risk factors for COVID-19 [82]. There are several types of fatty liver. Among NASH fatty liver types, NAFLD is strongly associated with increased severity of COVID-19 disease [83]. Studies show that people with MAFLD who develop COVID-19 become more acute due to increased expression of ACE2 receptors [84,85] through the HEK293 cell line [86-89]. TMPRSS2 is also a linker for the binding of SARS-COV-2 to the ACE2 receptor, and

PIKFYE is a regulatory protein used to deliver SARS-COV-2 into cells [86]. We conclude that SARS-COV-2 infection prefers to enter the cell through the ACE2 receptor and become pathogenic [90,91]. Another type of fatty liver, NAFLD, which is known as simple non-

alcoholic fatty liver, also increases the severity of the disease in patients with COVID-19 through macrophages M1 and M2 and by increasing the activity of cells [93,94].

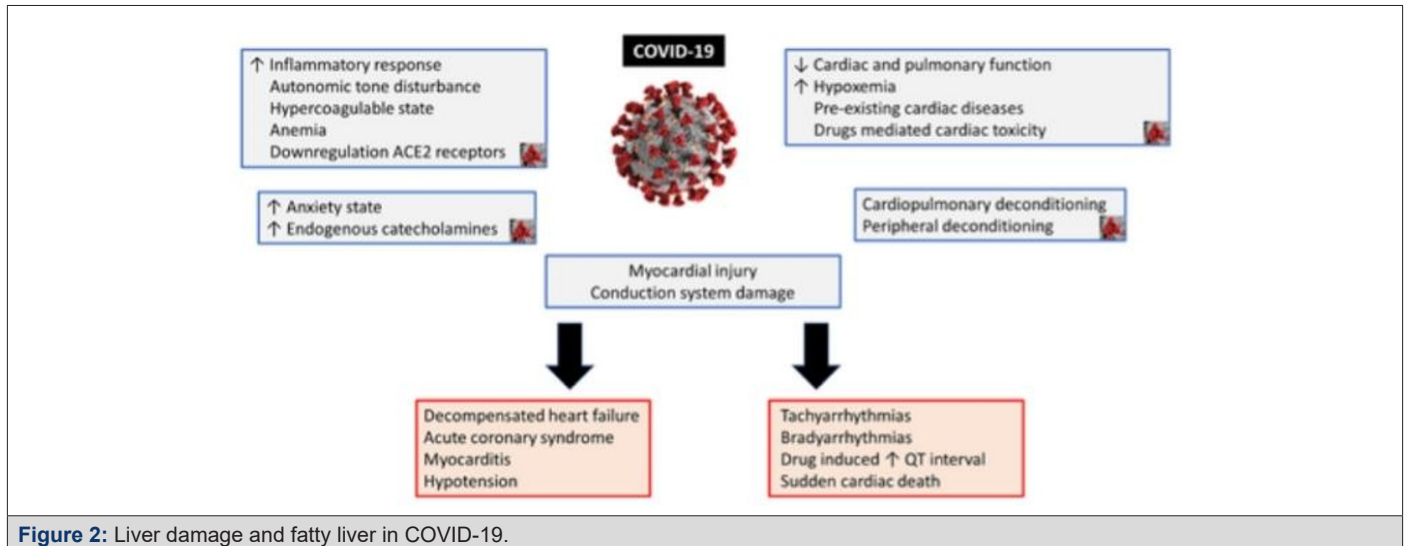


Figure 2: Liver damage and fatty liver in COVID-19.

Risk factors such as high BMI [95], obesity [96], blood pressure and especially smoking in NAFLD, MAFLD people are significantly more admitted to the ICU and use mechanical ventilation than healthy people who take COVID-19 [97]. A study of humans with different skin colors showed that people with NASH, NAFLD who develop COVID-19 have a higher incidence of COVID-19 than black people, and that life expectancy increases every year in proportion to the symptoms of COVID-19 becomes more severe [98]. COVID-19 in the acute stages of the disease because SARS-COV-2 infection triggers a CD8 + reaction that attacks and kills virus-infected cells [99]. As a result, they can cause liver disorders [100]. Following the development of liver disorders, such as those with NAFLD, MAFLD, factors such as AST, ALT [101] CRP, Ferritin [99], GGT [102], WBC and neutrophils [103] and ALP [104,105] increase. Some studies show that among the above factors, the higher the levels of TBIL [106] and AST enzymes, the much higher the mortality rate is compared to other enzymes [107]. However, in the field of liver enzymes, there is a difference in research results. Few studies show that ALT and AST levels do not change much [108]. Albumin levels also increase [109]. While many studies have shown that COVID-19 causes significant changes in ALT and AST levels and decreases albumin levels [110], according to studies, it seems that because Numerous studies confirm the change in ALT and AST levels. ALT and AST levels affect the course of COVID-19 disease.

For Various Reasons, Blood Type O Has the Lowest and Blood Type a Has the Highest Incidence of Covid- 19

The question of which blood group is most susceptible to COVID

-19 depends on factors such as geography and the frequency of blood groups in that area [111]. According to studies, most people with this virus have a positive blood type A [112-114]. The lowest incidence is related to O-negative [115-118]. This difference must be found in the blood composition of these people [119]. Blood type A has antigen A and antigen A has galactose called saccharide but blood group O does not have it [120,121]. The coronary factor is SARS-COV-2, which has a strong tendency to bind to carbohydrates, which can be the cause of high blood group A infection with COVID -19 [122]. The SARS-COV-2 receptor in the body is a protein called ACE2 [123,124]. Blood group O has more IL_6 than other groups. IL_6 activates ACE inhibitors [125]. One of the causes of death due to coronary heart disease is heart attack and blood clotting [126]. Blood type O has a slight tendency to form blood clots [127-129]. This may be due to lower VWF in this blood group [130]. increases during inflammation and causes platelets to bind together [131]. As a result, the mortality of this group is lower than other groups [132-134]. Blood type A is more severely affected by COVID-19. This can be due to a decrease in the breakdown of P_SELECTIN and ICAM_1, which will increase inflammation and decrease blood flow [125]. People with anti-A antibodies have been observed to be less likely to develop COVID -19, but this natural antibody is only resistant to the entry of viruses, not their replication.

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Conflicts of interest

No conflicts of interest.

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