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The impact of COVID-19 infection and vaccine on diabetic peripheral neuropathy in type 2 diabetes: A systematic review

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Abstract

Background and aims: Diabetes is an important comorbidity in patients with COVID-19 infection and who have received the COVID-19 vaccine. We aim to summarize the most recent evidence regarding the impact that COVID-19 infection or vaccination has on diabetes or its complications, including diabetic neuropathy, and the best way to manage COVID-19 patients with diabetes.

Methods: A literature review was conducted within databases of PubMed database and Google Scholar were screened using the key terms 'SARS-CoV-2', 'COVID-19 infection', 'COVID-19 vaccine' 'diabetes', 'diabetic neuropathy' up to December 2, 2022.

Results: We discussed the most recent evidence of diabetes milieus, diabetic neuropathy, and COVID-19 regarding infection, vaccine, management, and complications. There is a possibility that COVID-19 may affect the pathophysiology of diabetes. Controlling blood glucose levels is essential not only for COVID-19 patients but also for those without the disease as well.

Conclusion: As shown in the results of this study, diabetes is a risk factor for COVID-19 as well as contributing to its severity and mortality. This paper also provides recommendations, blood biomarkers, scales, and methods to address the confounding during COVID-19 infection and received doses of the COVID-19 vaccine.

Keywords: Coronavirus disease 2019, diabetes mellitus, diabetic neuropathy.

Introduction

Initial research revealed that people with diabetes mellitus had higher rates of coronavirus disease 2019 (COVID-19), which is caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Additionally, COVID-19 infection may make an individual more susceptible to hyperglycemia. Hyperglycemia may modify immunological and inflammatory responses when combined with other risk factors, predisposing individuals to severe COVID-19 and potentially fatal results. The main entrance receptor for SARS-CoV-2 is angiotensin-converting enzyme 2 (ACE2), a component of the renin-angiotensin-aldosterone system (RAAS); however, dipeptidyl peptidase 4 (DPP4) may potentially function as a binding target. However, preliminary findings do not indicate a significant impact of glucose-lowering DPP4 inhibitors on the susceptibility to SARS-CoV-2. Since sodium-glucose cotransporter 2 (SGLT2) inhibitors may have negative consequences in COVID-19 patients due to their pharmacological makeup, they are not advised. Currently, controlling acute glycemia should primarily involve the use of insulin. The majority of the research, which is related to type 2 diabetes mellitus due to its large prevalence, does not differentiate between the main forms of diabetes mellitus. However, there is now some scant evidence linking type 1 diabetes mellitus to COVID-19. Most of these findings are tentative, therefore further research is needed to determine how best to treat patients with diabetes mellitus (Lim et al., 2021).

Patients with diabetes mellitus (DM) typically have a bad prognosis when they develop a new coronavirus illness (COVID-19). Timely immunization is a key component of primary prevention. In individuals with DM, routine vaccination against pneumococcal pneumonia, influenza, and hepatitis B is advised due to its strong efficacy and acceptable safety profile. The vaccination of people with DM is justified in light of the clinical evidence demonstrating a strong neutralizing antibody response in COVID-19 patients with DM, and COVID-19 immunization should be prioritized in this population. Future research must address numerous outstanding questions about the preferred vaccine type, vaccine efficacy and durability, frequency of administration, vaccination in youngsters (under 18 years), and vaccination in pregnant and breastfeeding women (Pal et al., 2021).

Patients with diabetes experience various related issues such as a weakened immune system, a reduced virus clearance rate, abnormal metabolic activity, and elevated blood glucose levels. This does not make the patients more likely to get COVID-19 infection. However, the co-morbidity of DM can make COVID-19 more severe. Effective treatment options include adequate management, usage of medications that don't promote ACE2 expression, lowering blood sugar levels, reducing the susceptibility of SARS-CoV-2, and keeping a healthy lifestyle (Reshad et al., 2021).

COVID-19 and diabetes mellitus have a complex and bidirectional connection. On the one hand, having diabetes mellitus is regarded as one of the key risk factors for developing COVID-19 with a severe course. This risk is believed to be influenced by several diabetes mellitus risk factors, including advanced age, an

inflammatory and hypercoagulable state, hyperglycemia, and underlying comorbidities (hypertension, cardiovascular disease, chronic kidney disease, and obesity). On the other side, severe COVID-19 infection and associated steroid treatment can have a specific unfavorable influence on diabetes itself, causing hyperglycemia to deteriorate due to increased insulin resistance and decreased b-cell secretory activity. In consequence, worsening hyperglycemia may negatively impact COVID-19's progress. Although more information is rapidly becoming available as the pandemic spreads, there are still difficulties in comprehending how COVID-19 and diabetes are related (Landstra & de Koning, 2021).

Global healthcare systems are facing an unprecedented challenge as a result of the COVID-19 pandemic. For unknown causes, COVID-19 infections and fatalities per 100,000 are higher in nations with a high prevalence of diabetes. According to research, diabetes raises the risk of hospitalization and death in patients with severe COVID-19-related diseases. top priority while thinking of ways to lessen the spread of COVID-19 and its effects. To further understand how COVID-19 interacts with diabetes and how to address the disproportionate burden of COVID-19 in people living with diabetes, more study is required (IDF Diabetes Atlas, 2021).

Since December 2019, illnesses caused by the SARS-CoV-2 coronavirus have created a challenging healthcare environment globally. Coronavirus illness is connected with an increased incidence and severity in people with diabetes mellitus in 2019. High blood sugar was found to lower immunity and promote the replication of SARSCoV-2 while combining with several other risk variables. The

outcome of SARCoV-2 infection in diabetics is worse because oxidative stress and the release of pro-inflammatory cytokines are greater in diabetics than in healthy individuals. In a hyperglycemic milieu, increased expression of furin and the ACE-2 receptor may facilitate the entry of SARS-CoV-2 into the host cell. Infection with COVID-19 predominantly modifies immunological and inflammatory responses and may result in a cytokine storm, which could have fatal consequences in diabetics. pancreatic ACE protein and the SARS-CoV-2 virus generally kill cells that possess ACE-2 receptors, causing diabetes. Additionally, COVID-19 also results in hyperglycemia in diabetics, which may be linked to insulin resistance and degeneration. -cells while infected with SARS-CoV-2. Early findings also point to a connection between the risk of COVID-19 and oral hypoglycemic drugs (Sen et al., 2021).

Extremely contagious SARS-CoV2 is spread through respiratory droplets from infected individuals. People with comorbidities, including CVD, hypertension, and diabetes, have been found to have severe cases of COVID-19. DM is a significant risk factor that influences the severity of numerous other types of infection, according to a growing number of studies. Diabetes patients' dysregulated immune response is a significant factor in the severity being aggravated. One of the comorbidities connected to mortality and morbidity brought on by COVID-19 is DM. Diabetic patients may have a higher risk of COVID-19 infection due to a combination of chronic diseases such as obesity, CVD, and hypertension, altered ACE2 expression, dysregulated immune response, and endothelial dysfunction. The public's perceptions and awareness are likely to affect

the vast majority of prevention measures and ultimately have an impact on the results of clinical research. Therefore, it's crucial to research unique COVID-19 characteristics in diabetics and treat comorbid conditions in addition to the infection, especially in elderly persons who are already dealing with significant and life-threatening diseases (Verma et al., 2021).

Immunization lowers COVID-19-related mortality and morbidity, particularly in high-risk populations like diabetics. Regardless of the vaccine type, studies have shown that persons with diabetes had decreased antibody levels after two vaccination doses. Additionally, controlling blood sugar levels and managing diabetes may be related to antibody responses. Most reports indicate that people with DM have weaker immune responses to the vaccinations than healthy controls Age, diabetes type, BMI, glycemic control, and eGFR are all factors that significantly alter this connection. The best conditions for patients with DM before, during, and after immunization could be provided with the aid of research into these relationships to maximize antibody response. Future research must address several unanswered questions including the types of vaccines, dosage rates, re-vaccination intervals, and hyperglycemia in people with diabetes that may alter vaccine immunogenicity (Amir et al., 2022).

COVID-19: Definition and its mechanism

Respiratory droplets are the principal means by which SARS-CoV-2 is transferred during close face-to-face contact. An infection can spread through asymptomatic, asymptomatic, and symptomatic carriers. Before symptoms start to show up on average 5 days after exposure, and by 11.5 days, symptoms are present

in 97.5% of individuals. The three most frequent symptoms are fever, dry cough, and shortness of breath. Lymphopenia and elevated lactate dehydrogenase are typical but non-specific radiographic and laboratory findings (Wiersinga et al., 2020).

The COVID-19 disease, which poses a serious threat to public health, jumps unexpectedly and spreads swiftly. The mortality rate from COVID-19 infection ranges from 1% to 15% overall but can be as high as 17-38% in older patients with chronic illnesses and patients in intensive care units (ICU). Patients with diabetes, particularly those whose illness is poorly controlled, may be more prone to COVID-19. The underlying pathophysiological processes of new coronavirus in diabetic individuals remain unknown, even though diabetes was present in 5.3%–42.3% of COVID-19 fatalities. Diabetes is the primary medical issue linked to COVID-19, according to the rising global prevalence. Diabetes may be able to predict higher pneumonia severity. Compared to non-diabetic patients, the death rate from a lung infection in those with diabetes is noticeably higher. The therapy of diabetic patients infected with COVID-19 and the mechanisms causing severe pneumonia in diabetic people are both mostly hypothetical (Abbasi et al., 2021).

In fact, severe COVID-19 is likely one of the most complex medical illnesses that medical science is aware of. COVID-19 is a very heterogeneous and complex medical disorder. Although significant progress has been made in understanding the molecular mechanisms at play in patients infected with coronaviruses, a thorough knowledge of the pathogenesis of COVID-19 is still lacking. Making successful prevention and treatment plans need this kind of

expertise. A pulmonary macrophage activation syndrome with uncontrolled inflammation, a complement-mediated endotheliosis combined with a procoagulant state, and thrombotic microangiopathy are three basic pathologic processes that are thought to be connected in severe COVID-19 disease based on clinical, proteomic, and genomic studies as well as autopsy data. Mast cell activation and degranulation also add to the hyper-inflammatory state, as does platelet activity with serotonin production. Numerous hospitalized patients have auto-antibodies, which exacerbate end-organ damage and pro-thrombotic condition (Marik et al., 2021).

Because they aggravate inflammation and alter physiological responses, coronavirus infections are well-documented to have a substantial impact on the management of DM. This makes it more challenging to control blood sugar levels. SARS-CoV-2 infection also increases the risk of occlusion and is more likely to result in metabolic failure in people with diabetes than in people without diabetes. However, it should be noted that while no convincing RCTs are undertaken for anti-inflammatory, Decadron's usefulness in treating COVID-19 has been thoroughly studied in well-designed RCTs like the RECOVERY study. In conclusion, there are significant health hazards associated with the COVID-19 global pandemic, particularly for diabetics. A COVID-19 vaccination or viable treatment has not yet been created. Therefore, preventing infection altogether is the simplest solution. People with diabetes should make a concerted effort to maintain excellent health and minimize potential risk factors in these circumstances. The optimum management strategy for these individuals, including the selection of

glucose-lowering, medication, and lipid-lowering therapies, is an important focus for current and future studies (Memon & Biswas, 2022).

A substantial percentage of people have diabetes, which is the primary cause of a wide range of expensive problems. Diabetes is associated with a multiple-fold rise in mortality, and when compared to non-diabetics, COVID-19 disease severity and prevalence are higher in diabetics. Since its discovery in Wuhan, COVID-19 has expanded quickly and manifested a variety of severity levels. People with COVID-19 disease are known to have a high body temperature, lymphopenia, a non-productive cough, dyspnea, and fatigue. Diabetes and other related comorbidities are important risk factors for illness and mortality in COVID-19 patients. The covid-19 disease virus, SARS-CoV-2, may also cause direct pancreatic damage, which could exacerbate hyperglycemia and possibly result in the development of diabetes in previously non-diabetic people. The burden of COVID-19 and diabetes is a bidirectional relationship that affects healthcare workers globally. Blood glucose levels must be maintained under control, ACE inhibitors should be used sparingly to reduce the frequency of preventable hospitalizations, and nutritional considerations, and some other preventive measures, such as immunization, are strongly advised. The pathophysiology of already-existing diabetes could be made worse by SARS-potential CoV-2's for pleiotropic changes in glucose homeostasis, which could also lead to the emergence of new disease processes (Sharma et al., 2022).

Pathophysiology of COVID-19 infection and vaccine in DM and diabetic neuropathy

Diabetes mellitus patients do not appear to have an elevated primary risk of COVID-19 infection, although a strong conclusion is challenging due to several factors, including differences in social distancing behavior or desire for SARS-CoV-2 testing. Patients who have both type 1 and type 2 diabetes are more likely to die from a severe COVID-19 course. Additionally, the comorbidities and other risk factors that are frequently present in conjunction with diabetes mellitus as well as glycemic management are likely related to this worse prognosis. Diabetes and COVID-19 have a complex and bidirectional relationship; on the one hand, COVID-19 causes hyperglycemia, and on the other, hyperglycemia makes COVID-19 work less effectively. The chance of a severe COVID-19 result is increased by both diabetes and the comorbidities that are frequently linked with it. The fact that some of these risk factors are adjustable must be understood. For instance, better glucose control (better diabetes (self-management) and a healthy BMI directly lower the likelihood of developing a severe course of COVID-19. Diabetes patients and healthcare professionals working in the sector must be aware of the impact they can have on lowering their risk of COVID-19 severity as much as feasible (Landstra & de Koning, 2021).

Peripheral neuropathy, which is characterized by neuropathic symptoms and small and large fiber dysfunction in the feet and face with a loss of smell, may develop in some people with diabetes and severe COVID-19. Using the Nerve-

Check Master integrated into protective gear, quantitative monitor actual seems to be a quick and easy process to objectively quantitate and define the type and spread of these sensory deficiencies. We understand that the absence of a history of diabetic neuropathy and a satisfactory deep tendon reflex does not rule out past diabetic neuropathy. The development and evolution of COVID-19-related neuropathy in people with and without hyperglycemia may be better understood by longitudinal cohort studies using objective measures of neuropathy, such as QST and CCM (Odriozola et al., 2021).

A developing outbreak called COVID-19 has affected millions of individuals and become a major emergency. Major impacts on the pulmonary, cardiac, renal, gastrointestinal, and hepatic systems are caused by this multi-organ-involved disease. Because COVID-19 infection affects multiple organs, it requires a team with a variety of skills to identify and treat the condition. Although there are numerous studies on COVID-19 infection, most of them concentrate on pulmonary involvement, and the effects of the virus on many other organs and systems are still unknown, demonstrating the need for additional research into the condition (Aghdam et al., 2020).

Since its recent advent, the coronavirus disease 2019 (COVID-19), which is brought on by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused significant disruption and fatality. There has been a rush to comprehend the virus and its pathogenesis concurrently. The respiratory tract is only one of many clinical symptoms of COVID-19. There have been numerous reports of extrapulmonary symptoms affecting the gastrointestinal tract,

hepatobiliary system, cardiovascular system, and renal system. The etiology of many of these manifestations is debatable, with dubious evidence supporting the direct viral invasion and a plethora of competing hypotheses, including severe illness and pre-existing medical disorders. It didn't take long to determine that the angiotensin-converting enzyme 2 (ACE2) receptor is the primary cell surface receptor for SARS-CoV-2. For estimating the degree to which different tissue types are susceptible to SARS-CoV-2 infection, the distribution of ACE2 has been employed as a starting point. Extrapulmonary tissues' infectivity has been demonstrated in vitro using sophisticated organoid and animal models, but the therapeutic applicability of these discoveries is yet unknown. Clinical autopsy investigations are often modest in size and invariably favor patients who have severe COVID-19 and need a lot of time in the hospital (Siddharth & John, 2021).

Patients with COVID-19 frequently develop peripheral neuropathy, which is primarily brought on by immune processes or neurotoxic side effects of medications used to treat COVID-19 symptoms. Peripheral nerve compression brought on by protracted bed rest in the intensive care unit (ICU) and pre-existing risk factors like diabetes also play a small role. Viral neuropathy is not a side effect of SARS-CoV-2. To prevent SARS-CoV-2-associated neuropathy, patients should be appropriately bedded in the ICU and neurotoxic medications such as daptomycin, linezolid, lopinavir, ritonavir, hydro-chloroquine, cisatracurium, and glucocorticoids should be administered with caution. steroids, plasma exchange, and immunoglobulin therapy are helpful for GBS patients. Conclusions: Patients with COVID-19 frequently develop peripheral neuropathies, which are mostly

brought on by immunological processes or neurotoxic side effects of medications used to treat COVID-19 symptoms. Peripheral nerve compression brought on by protracted bed rest in the ICU also plays a minor role (Finsterer et al., 2021).

The COVID-19 epidemic is the greatest public health emergency that people have ever experienced. The beta coronaviruses, which include SARS-CoV-2, are remarkably similar to the bat coronavirus. The respiratory, cardiovascular, gastrointestinal, and neurological systems experience pathophysiologic changes as a result of the virus, which enters cells via the ACE2 receptor. With a reproduction number ranging from 2.24 to 3.58, which indicates increased transmission, human-to-human transfer is present. As well as temperature, coughing, and shortness of breath are clinical signs. gastrointestinal, cardiac, and neurological system symptoms. The elderly, people with comorbid conditions, and people with impaired immune systems are patients who are more likely to contract an infection (Azer, S. A., 2020).

Health communication materials should underline that the COVID-19 vaccine is safe for all people with diabetes and that the majority only experience minor side effects. Positive testimonies provided by COVID-19 vaccine recipients with diabetes may allay their fears and increase immunization coverage. Future initiatives ought to include DM patients' families. They might act as role models and persuade others with DM to get the COVID-19 vaccine. People with DM reported having a low uptake of the COVID-19 vaccine. Those with chronic DM had the lowest uptake rates. complications. In DM patients with and without chronic problems, various tactics might be used to encourage vaccination against

COVID-19. While stressing the advantages of COVID-19 immunization may be more effective among those without such difficulties, using the fear appeal strategy and doctors' recommendations is more likely to be successful with those who already have chronic complications. Some tactics, such as allaying worries about safety and side effects and leveraging the influence of family and friends, are helpful to boost the coverage of COVID-19 vaccination (Xu et al., 2022).

In coronaviruses that contain glycoprotein S can offer a sufficient defense. Cross-protection amongst viruses in this family makes it likely that a vaccination containing this protein will be successful. The HBV vaccine and attenuated vaccinations like the influenza vaccine, according to earlier sections, are helpful in diabetics and have demonstrated a similar immune response to healthy people. It might be a tactic for the development of the proper COVID-19 vaccination in diabetics. However, the first stage of clinical trials for each of the proposed vaccines in phase 1 clinical trials for safety and immunogenicity, followed by phase 2 and phase 3 trials for both safety and efficacy, in order to reach the commercially available and testing stages and be able to begin clinical progress. Finally, reducing morbidity and death in COVID-19 patients depends on the effectiveness of the SARS-CoV-2 vaccine. Several SARS-CoV-2 vaccines are now through various stages of clinical development. Different vaccination strategies have various benefits and restrictions. An ideal vaccine must be accessible to large populations, effective, safe, and long-lasting (Soltani et al., 2022)

The current main worldwide health concern is the COVID-19 pandemic. Evidence suggests that people with diabetes are more likely than people without

diabetes to have a serious illness or pass away as a result of COVID-19. The underlying mechanism for his differing effects on people with and without diabetes, however, is unclear. the pathophysiological processes that could make it easier for a virus to enter or make it more infectious to host cells in a diabetic environment. Patients with poorly controlled diabetes have a higher risk of infection and a higher incidence of tissue damage and death, which are caused by underlying pathogenic pathways. It is now understood that the state of the host cell significantly affects the infectiousness and pathogenicity of viruses like SARS-CoV2. Potential molecular processes may increase patients' chance of developing severe COVID-19 compared to infected people without DM. Preexisting pathophysiological pathways either directly or indirectly promote the pathogenicity of SARS-CoV2 in patients with poorly managed diabetes (Yaribeygi et al., 2020).

A severe impact on the individual, society, and economy could result from COVID-19, which has superimposed on the pre-existing diabetes pandemic. Because diabetes and COVID-19 share several pathologies, outcomes for patients with COVID-19 are poorer, especially for those who have microvascular and macrovascular problems. A growing amount of evidence points to a link between diabetic microvascular problems and unfavorable outcomes in patients with acute COVID-19. Diabetes patients, particularly those with microvascular problems, may also be more susceptible to developing post-COVID-19 syndrome (PCS). Diabetes may raise the likelihood of severe COVID-19 infection and hospitalization, making people more likely to develop PCS. Theoretically, the same pathophysiological overlap that is evident in patients with COVID-19 and

diabetes may also be responsible for the higher risk of PCS and the onset and progression of microvascular damage (Zaghloul & Malik, 2022).

SARS-CoV2 vaccines have been developed and produced as a result of the severity of the disease and its effects on global health. Vaccination against the virus has been created as of April 2020. In order to defend against high-risk respiratory infections, vaccines should be developed since conditions like diabetes, hypertension, and cardiovascular disease make people more susceptible to viruses and increase their risk of infection. A secure immune response is offered by SARS, MERS influenza, and the SARS-CoV-2 virus. A safe and optimal vaccination must be developed to prevent COVID-19 in healthy individuals, especially in high-risk populations like diabetes patients. The development of a SARS-CoV-2 vaccine is essential for reducing COVID-19 morbidity and death in diabetes individuals (Soltani et al., 2022).

According to the idea of the health belief model (HBM), the safety of the COVID-19 vaccine and the adverse effects of vaccination are the key factors influencing the vaccination behavior of diabetic patients. To increase vaccination practices among persons with diabetes, healthcare professionals should spread the word and educate the public more about the safety and preventive effects of vaccine delivery. Additionally, for vaccination efforts to be successful among the diabetic community, the general public needs to be fully informed about the safety of vaccination. Examining the variables influencing vaccination behavior involved using the health belief model (HBM). Multivariable logistic regression was performed to identify determinants of COVID-19 immunization uptake after

controlling for factors with substantial differences in social background characteristics. Based on the safety and protective effects premise of HBM, healthcare professionals should offer targeted educational interventions to promote vaccination habits in diabetic patients (Duan et al., 2022).

Infected persons with COVID-19 may also be more susceptible to hyperglycemia. Hyperglycemia may modify immunological and inflammatory responses when combined with other risk factors, predisposing individuals to severe COVID-19 and potentially fatal results. The main entrance receptor for SARS-CoV-2 is angiotensin-converting enzyme 2 (ACE2), a component of the renin-angiotensin-aldosterone system (RAAS); however, dipeptidyl peptidase 4 (DPP4) may potentially function as a binding target. However, preliminary findings do not indicate a significant impact of glucose-lowering DPP4 inhibitors on the susceptibility to SARS-CoV-2. Since sodium-glucose cotransporter 2 (SGLT2) inhibitors may have negative consequences in COVID-19 patients due to their pharmacological makeup, they are not advised. Currently, controlling acute glycemia should primarily involve the use of insulin. The majority of the research, which is related to type 2 diabetes mellitus due to its large prevalence, does not differentiate between the main forms of diabetes mellitus. However, there is now some scant evidence linking type 1 diabetes mellitus to COVID-19. Most of these findings are tentative, therefore further research is needed to determine how best to treat patients with diabetes mellitus (Lim, et al., 2021).

Blood Biomarkers and scales during COVID-19 infection and received of doses vaccine (mechanism of change and implications for patient outcomes)

Rapid diagnosis and early care of COVID-19 variations are essential for controlling the disease and halting its progression. In people with COVID-19, diabetes-related complications are significant risk factors for morbidity and mortality. Understanding the potential genetic and demographic differences in SARS-CoV-2 quickly will reveal the pathophysiological mechanisms at play. Despite the availability of vaccinations, specific treatments, particularly drugs to maintain insulin levels and control hyperglycemia during COVID-19 infection, are essential to regulate glycemia and reduce inflammation in diabetic patients (Aluganti & Singla, 2022).

Acute Respiratory Syndrome with Severity The SARS-CoV-2 coronavirus vaccination has been linked to adverse immunological reactions. A small number of cases of type 1 diabetes caused by an autoimmune/inflammatory syndrome brought on by adjuvants have been linked to immunizations. After receiving the SARS-CoV-2 vaccine, a few incidences of type 1 diabetes have been documented. Several weeks after receiving the BNT162b2 vaccine, type 1 diabetes manifested. All patients required significantly less insulin after being diagnosed with type 1 diabetes, and three patients no longer required insulin therapy. An acute decrease in a patient's ability to control their blood sugar after receiving BNT162b2

treatment could be the result of autoimmune diabetes brought on by vaccination. The BNT162b2 vaccine may cause type 1 diabetes **(**Aydoğan et al., 2022)**.**

Patients with diabetes mellitus should follow the clinical guidelines for the management of diabetes mellitus more closely, as stated below, during the COVID-19 pandemic since COVID-19 can raise blood glucose levels. Patients should be extremely careful to take their prescribed medications as directed, including insulin injections, and to monitor their blood sugar levels more frequently than usual. Patients should consult their doctor if their blood glucose levels are consistently elevated above the normal range. More focus needs to be given by healthcare providers on appropriate food intake and physical activity in people with diabetes mellitus in light of current worldwide quarantine regulations. Patients should be recommended to see their doctor right away if they have symptoms such as a dry cough, increased sputum production, fever, or a fast rise in blood sugar. Additionally, it is strongly advised that patients rigorously follow their doctor's prescriptions and avoid statements spread through other media, including the internet, as they frequently do not hold up to scientific scrutiny. Most importantly, to lower the risk of infection in people with diabetes mellitus, standard measures including social seclusion, wearing a mask, washing hands, and using disinfectants should closely adhere to both health care professionals and their patients. Remote consultations or telehealth may be able to lessen the danger associated with direct physical interaction between patients and medical workers **(**Lim et al., 2021).

The global pandemic COVID-19 is spreading quickly, placing a greater load on healthcare. There is little evidence from observational research linking several biomarkers to adverse outcomes. Laboratory biomarkers are the preferred method for monitoring and predicting outcomes and disease prognosis since they are less expensive, quicker, easier to collect, and less time-consuming. It is hypothesized that heightened laboratory biomarkers for poor outcomes in COVID-19 patients include lymphopenia, thrombocytopenia, high CRP, PCT, D-dimer, CK, LDH, AST, ALT, and creatinine. Additionally, the development of prevention strategies and countermeasures to critical adverse COVID-19 outcomes may benefit from the use of these biomarkers (Malik et al., 2021).

Methods to address the confounding during COVID-19 infection and received doses of vaccine.

Patients should be extremely careful to take their prescribed medications as directed, including insulin injections, and to monitor their blood sugar levels more frequently than usual. Patients should see their doctor if their blood glucose levels are consistently higher than normal. More focus needs to be given by healthcare professionals on appropriate food intake and physical activity in people with diabetes mellitus in light of current worldwide quarantine regulations. Patients should be recommended to see their doctor right away if they have symptoms such as a dry cough, increased sputum production, fever, or a fast rise in blood sugar. Additionally, it is vitally advised that patients closely follow their doctor's

recommendations and be cautious of statements presented by various media (including the internet) (Lim et al., 2021).

A higher perception of the risk and severity of COVID-19 infection, a belief that doctors would advise them to get vaccinated against it, and a belief that relatives' vaccination status would influence their own would all be associated with higher COVID-19 vaccination uptake for people with chronic DM complications. A perception of more serious consequences of COVID-19 infection, a belief that receiving a COVID-19 vaccination could lower the risk of infection, and a belief that relatives' vaccination uptake would influence their own decision to receive a COVID-19 vaccination were all linked to higher COVID-19 vaccination uptake for their counterparts without chronic complications. The adoption of COVID-19 immunization was adversely correlated with worries about vaccination safety and side effects in both groups of DM patients (Xu et al., 2022).

Patients with diabetes need to be made aware that the COVID-19 pandemic will raise their blood aldohexose levels. They must therefore strictly adhere to the clinical guidelines for the management of diabetes. Patients should be more cautious when taking their prescribed drugs, particularly hypoglycemic agent injections, and should have their blood levels of aldohexose monitored more regularly than they previously did. Patients should see their doctor if their aldohexose blood concentrations are consistently above normal. Given the current global quarantine restrictions, healthcare professionals must focus heavily on DM patients' good dietary consumption and physical exercise. Patients should be instructed to see their doctor right away if they experience symptoms like a chronic

cough, excessive liquid bodily material production, fever, or a sharp increase in aldohexose levels. Furthermore, it is strongly urged that patients strictly adhere to their doctor's recommendations and stay away from statements made in the media, even online, as they usually fall apart under scientific investigation. Most importantly, all healthcare professionals and their patients should strictly abide by conventional precautions including social seclusion, wearing a mask, washing their hands, and improperly using disinfectants in order to reduce the chance of infection in patients with DM. Virtual consultations or telehealth services may be able to assist lower the risk associated with in-person contact between patients and medical providers. These additional precautions could reduce the danger of SARS-CoV-2 transmission while ensuring the public's safety (Memon & Biswas, 2022).

In many cases, neurological symptoms are unrelated to vaccination, and their association with vaccination is coincidental. As well, peripheral neuropathy has been reported in only a few cases despite billions of individuals receiving the COVID-19 vaccine, which indicates that this complication is very rare. However, based on the available information, it is not possible to determine the frequency of peripheral neuropathy following COVID-19 vaccination.

Our study has some limitations despite our efforts to maintain a comprehensive search strategy in our search for articles that assess both diabetes and COVID-19.

In many cases, neurological symptoms are unrelated to vaccination, and their association with vaccination is coincidental. As well, peripheral neuropathy has been reported in only a few cases despite billions of individuals receiving the COVID-19 vaccine, which indicates that this complication is very rare. However,

based on the available information, it is not possible to determine the frequency of peripheral neuropathy following COVID-19 vaccination.

Conclusion

In this review, diabetes is a chronic disease that is linked with poor outcomes in patients with COVID-19 as well as contributing to its severity and mortality. It is particularly important to address the needs of underserved patients, due to their disproportionate impact. It is important to link the symptoms and signs of diabetes and diabetic neuropathy to a history of COVID-19 vaccination to ensure a timely diagnosis and early management. Lastly, this review provides recommendations, blood biomarkers, scales, and methods to address the confounding during COVID-19 infection and received doses of the COVID-19 vaccine and was not intended to be comprehensive, as gaps in the literature still exist, and future investigations will help to fill in those gaps.

Ethics approval

In this study, no ethical approval was required.

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Consent

No consent was required for this study.

Availability of data

The data that support the findings of this review are available from the Corresponding author.

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