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Review Article

## The Impact of SARS-CoV-2 on Type 2 Diabetic Individuals: A Review of Current Evidence

Ahmed M. Ashour<sup>1</sup>

Department of Pharmacology and Toxicology, College of Pharmacy, Umm Al-Qura University, Makkah-21955, Saudi Arabia

### CORRESPONDING AUTHOR

**Ahmed M. Ashour**

Department of  
Pharmacology and  
Toxicology, College of  
Pharmacy, Umm Al-Qura  
University, P.O. Box 13578,  
Makkah-21955, Saudi  
Arabia

Email: .

amashour@uqu.edu.sa



<https://orcid.org/0000-0002-2118-0499>

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### ABSTRACT

As the SARS-CoV-2 pandemic continues to cause havoc globally, many people have expressed the hope that things will become easier as more people are vaccinated against the virus. The pandemic has disproportionately affected certain sections of the global population, such as those living with type 2 diabetes, however, and this study thus aims to evaluate the effects of infection on individuals with type 2 diabetes, particularly those who are also smokers. The relevant review was thus done in two sections, one focusing on individuals with type 2 diabetes in general and the other examining people with diabetes who are also smokers. Twenty studies published between 2020 to 2021 were examined with respect to the impacts of SARS-CoV-2 on people with diabetes, including those who are also smokers. In general, people with diabetes were found to be more likely to be hospitalised when infected with SARS-CoV-2, as well as three times more likely than non-diabetics to have extreme outcomes such as requiring intensive care or even dying. The situation is a further 4.5 times worse for people with diabetes who are also smokers, creating profound economic implications faced for society.

**Conclusion:** SARS-CoV-2 severely affects individuals with diabetes in terms of both health and logistics. A combination of SARS-CoV-2 infection and diabetes makes such individuals more susceptible to severe health outcomes, and these are further exacerbated by comorbidities such as smoking, underlying health conditions, ethnic and racial disparities, and a lack of access to high-quality health care.

**Keywords:** SARS-CoV-2, Diabetes, Vaccine, Comorbidities, Smoking

### INTRODUCTION

The SARS-CoV-2 pandemic continues to disproportionately affect certain individuals and communities across the globe, especially those with underlying medical conditions, such as the immunocompromised and those with hypertension, cardiovascular diseases, and diabetes. So far, the pandemic has claimed the lives of over 6 million people globally out of over 509 million cases as of the end of April 2022.<sup>[1]</sup> As with many chronic conditions, SARS-CoV-2 also has more severe prognoses and therapeutic implications for diabetic individuals.<sup>[2]</sup> Just a few months into the pandemic, several studies showed that more than a quarter of people entering hospitals with severe SARS-CoV-2 infections were diabetic, and this trend has not changed significantly.

High blood glucose levels weaken the immune system, and the resulting problems become even more complicated for those with heart or lung disease or those who smoke.<sup>[3]</sup> When people with diabetes contract SARS-CoV-2, their risks for complications such as diabetic ketoacidosis or sepsis significantly increase, and SARS-CoV-2 has thus significantly affected hospitalisations, mortality rates, and the social and personal economic burdens related to diabetes, especially in low-income communities. This increased risk occurs primarily because of individuals with diabetes' increased risk of developing complications when they contract the SARS-CoV-2 virus<sup>[4]</sup>, though the available data suggest that even those with diabetes who have not contracted the virus personally have still been affected negatively by the associated lockdowns, with many having difficulties obtaining their required medication as well as multiple reports of varying levels of anxiety and depression.<sup>[5]</sup>

This paper presents a focused review of current evidence regarding the impact of SARS-CoV-2 on individuals with type 2 diabetes in Saudi Arabia and the Middle East. Although various vaccines for SARS-CoV-2 are now available in different parts of the world, new variants that are more resistant to these vaccines have begun to emerge, making it more difficult to protect people from the virus, and the risks of the disease remain high for both diabetics and other individuals with underlying medical conditions.<sup>[6]</sup>

The review is presented in two parts. The first part evaluates the available evidence from studies on the impact of the SARS-CoV-2 pandemic on diabetic individuals, while the second part examines the effects of SARS-CoV-2 on people with diabetes who smoke more specifically. An extensive online search on various databases for work published up to 20 July 2021 was conducted. The databases used included Scopus, PubMed, Science Direct, Web of Science, and Medline. Independent screening by all researchers involved was then applied, and all identified relevant studies were included, examined, and analysed.

To perform the search, keywords were selected using expert input to address the necessary combination of the impacts of SARS-CoV-2, type 2 diabetes, and smoking. The searches were performed initially on global databases, and then these were narrowed down to focus on Saudi Arabia and the Middle East. Numerous articles on the impact of SARS-CoV-2 on people with diabetes emerged during this process, while very few studies on the effects of SARS-CoV-2 on diabetic smokers appeared at any stage.

This review includes all available studies published in 2020 and 2021 that examine or describe the effects of the SARS-CoV-2 pandemic on diabetic individuals, particularly diabetic individuals who smoke, with a special focus on Saudi Arabia and the Middle East. Full-text articles for the selected studies were thus collected and scrutinised, and their findings summarised and analysed to develop the results section.

After carefully examining and eliminating all articles and removing those that did not qualify, 17 studies were found to fit the inclusion criteria. Different studies took different approaches to address their primary questions with respect to the impact of SARS-CoV-2 on people with diabetes, though most were retrospective studies that collected clinical information about patients such as symptoms, demographics, serological tests, and anthropometrics alongside data on diagnosis, admissions, intensive care, intubation, and outcome (whether patients recovered and were discharged or died). One study found that the rate of type 2 diabetes patients hospitalised with SARS-CoV-2 was more than twice that of individuals hospitalised for SARS-CoV-2 who were not diabetic.<sup>[7]</sup> Death rates were also significantly higher in the group with diabetes mellitus than in the group without diabetes. Generally, SARS-CoV-2 patients with type 2 diabetes demonstrated worse clinical symptoms than those without type 2 diabetes, a finding consistent across the majority of studies.<sup>[8]</sup> Moreover, these findings agree with previous pooled analysis results that suggested that type 2 diabetes is associated with severe outcomes of SARS-CoV-2. Interestingly, however, one study suggested that type 2 diabetes is not associated with mortality after adjustments are made for sex, age, and body mass index (BMI)<sup>[7]</sup>, implying that type 2 diabetes

contributes to severe outcomes among SARS-CoV-2 patients when combined with other factors such as age and BMI, but is not impactful on its own. Contrary to many others' findings, Giorgino et al.<sup>[6]</sup> found that individuals with type 2 diabetes were no more likely to contract SARS-CoV-2 than others: however, they were found to have a three-times higher risk (4.5 times if they are also obese) of hospitalisation from any resulting complications after they contract the virus.

The media and the internet have been sources of information and misinformation for many communities worldwide during the pandemic, and people with diabetes and people living with other underlying health conditions seem to have become wary of going to hospitals, based on being told that they are at a higher risk. This trend has in some cases thwarted efforts by care providers to convince people with diabetes to seek much-needed care. Furthermore, this situation has also resulted in delays in some individuals receiving functional treatment for their diseases and those complications inherent to their health conditions. In many cases, this has resulted in people with diabetes reporting to the emergency rooms of care facilities when it is too late for effective early treatment, at which point they must be hospitalised or even placed in intensive care.<sup>[4]</sup>

With regard to other health issues that would generally require a doctor's attention, individuals with type 2 diabetes have been found to be resorting to alternative means of care, such as sending others to obtain over-the-counter medications, including painkillers, due to fears of contracting the SARS-CoV-2 virus on visiting healthcare facilities among those who are aware that they have an increased risk of complications on becoming infected. This has been seen across various parts of the world: for instance, a study in Serbia found that even after the easing of lockdowns, less than half of the diabetic population participating in the study were willing to go to the hospital, even to address issues difficult to diagnose through telemedicine.<sup>[9]</sup>

The prevalence of type 2 diabetes is particularly high among hospitalised SARS-CoV-2 patients in Riyadh, Saudi Arabia, yet although type 2 diabetes patients have higher mortality rates than non-diabetic patients, other co-existent factors seem to play a more significant role in this phenomenon. These factors include old age, smoking, congestive heart failure,  $\beta$ -blocker use, elevated creatinine, the presence of bilateral lung infiltrates, and severe vitamin D deficiency, which all appear to be more significant predictors of mortality.<sup>[2]</sup> Having two or more of these factors in one patient significantly increases their chances of mortality and poor outcomes, though SARS-CoV-2 patients with hyperglycaemia are also more likely to require intensive care.<sup>[10]</sup>

Type 2 diabetes inherently places a strain on healthcare services and the economy, primarily through decreases in work productivity, increased mortality risk, and the likelihood of early retirement in affected individuals. All these factors place a burden on the national economy<sup>[8]</sup>, but the situation has become even more complicated in the era of SARS-CoV-2, especially as diabetic individuals have an increased risk of negative outcomes from the virus. When they become infected, they are thus more likely to require additional time and resources to be spent on care and medication, and the increased rates of severe outcomes, such as requiring intensive care or oxygen support, or even dying, also have an impact.<sup>[9]</sup> The combination of type 2 diabetes and SARS-CoV-2 has thus generated unprecedented social, economic, and health burdens for individuals, families, economies, and healthcare systems globally. The effects on individuals' employment and careers should, in particular, not be understated, especially in light of lockdowns and partial lockdowns, travel restrictions, and other measures aimed at curbing the spread of the disease, which have had huge impacts on economies across the globe, further damaging many people's careers and mental health.<sup>[12]</sup>

An increase in severe hypoglycaemia among type 2 diabetes patients has been observed in the Middle East and Africa as well as South and East Europe throughout the pandemic<sup>[6]</sup>, a finding notable across

multiple reports. Based on the impact of various lockdowns and distancing mandates, it has been suggested that irregularity of glucose monitoring and a lack of contact with doctors might be the main cause of this trend. Ongoing and effective hypoglycaemia management is critical to the successful treatment of patients with diabetes, and blood glucose levels must be carefully monitored, particularly as patients get older.<sup>[13]</sup> Ultra-long-acting basal insulin offers a new way to address this, and many guidelines now recommend the provision of this to ensure better glycaemic control with lower hypoglycaemic risk in patients with both type 1 and type 2 diabetes. This is relevant in the pandemic context, as several studies offer data showing that patients with SARS-CoV-2 both with and without diabetes tend to demonstrate hyperglycaemia after hospital admission, attributable to both a direct virus-induced decrease in insulin secretion and a simultaneous increase in insulin resistance triggered by the SARS-CoV-2 virus.<sup>[6]</sup>

As those with type 2 diabetes are more susceptible to SARS-CoV-2 and have a higher risk of severe outcomes, they have been advised to take extra precautions to preserve their health, which has caused many of them to experience additional issues, commonly reducing exercise levels, increasing weight gain, multiplying mental stress, reducing the quality of sleep, and undermining glycaemic control. This was compounded by the World Health Organization (WHO) recommendations<sup>[11]</sup> that governments and healthcare authorities contain the spread of the SARS-CoV-2 virus by implementing draconian social distancing restrictions and closing all public spaces<sup>[3]</sup>, including recreational areas such as parks and places to exercise such as gyms. People were also made to stay inside their homes where they had no immediate reason to travel, reducing incidental movement levels significantly. Exercise is an integral part of diabetes prevention and management plans, however, with studies suggesting that lifestyle interventions such as physical activity and diet-induced weight loss reduce the risk of progression from impaired glucose tolerance to type 2 diabetes by 58%.<sup>[8]</sup> While the WHO ostensibly recognised this, encouraging people with diabetes to stay physically active within their homes via its *'Stay Physically Active During Quarantine'* initiative, such activity was not practical for most people in their limited home spaces.<sup>[12]</sup>

Al-Husseini and Alqahtani<sup>[14]</sup> examined the effects of the pandemic on eating habits across a population from Saudi Arabia. Their results indicated that a slightly greater proportion of respondents bought groceries three or more times each week during the SARS-CoV-2 period (38.9%) as compared to before the pandemic (35.9%), while concerns about external food hygiene increased significantly, from 17.3% before the pandemic to 72.9% during the study. Their examination of food intake quality during this period also showed that, among their sample, carbohydrate consumption increased by 21%, fat intake increased by 13%, and fruit consumption increased by 7%.

The pandemic, and government reactions to it, raised significant concerns about potential food shortages, resulting in people purchasing additional packaged and long-life foods rather than focusing on fresh foods. This had an almost immediate effect on the quality of the food consumed during the pandemic period, generating both weight gain and increased oxidant intake. Thus, while some eating habits improved with the spread of SARS-CoV-2 and related responses such as workplace shut-downs, such as the creation of more home-cooked meals, the quality and the quantity of food generally consumed during the pandemic fell notably.<sup>[14]</sup>

Various full and partial lockdowns further limited access to key foods such as vegetables and fresh fruit for many people, resulting in many people with type 2 diabetes consuming additional quantities of processed foods based on their longer shelf lives. These foods typically contain high levels of carbohydrates and fats, thus being very calorie-dense and not recommended, particularly for people with diabetes, as unintentionally increased calorie intake may increase the risk of weight gain and

associated cardiovascular, respiratory, and thrombotic complications.<sup>[15]</sup> Those with type 2 diabetes must be particularly wary of such complications, as they are compounding factors in other co-morbidities of the disease.<sup>[16]</sup>

Both obesity and diabetes can affect the forced expiratory and vital volume capacities of the lungs, having detrimental effects on their functional capability.<sup>[12]</sup> Some studies have also produced evidence that the pulmonary lipo-fibroblasts that emerge in the presence of adipocytes play a role in SARS-CoV-2 pathogenic responses while increasing expression of angiotensin-converting enzyme-two receptors can cause such adipocytes to become 'reservoirs' for viruses, including SARS-CoV-2. Lipo-fibroblast trans differentiation into myofibroblasts may also lead to pulmonary fibrosis, and based on these multiple negative outcomes, fibrosis can create severe complications in cases of SARS-CoV-2 infection among the diabetic population, which is prone to obesity.<sup>[12]</sup>

The SARS-CoV-2 pandemic has also caused a recurrent issue of increased mental stress and negative changes in sleeping habits among people with diabetes. The increases in anxiety arose from feeling at increased risk of contracting the virus, being locked down in a single location without freedom of movement and being prevented from accessing family or loved ones due to such restrictions. These conditions were reported to cause mental stress in 80% of participants in one 2020 study<sup>[3]</sup>, with 12.5% of participants reporting that they were worried about the implications of SARS-CoV-2 for their lives to the extent that they could not sleep. These findings were also consistent with other studies across the world: a study conducted in China found that SARS-CoV-2 had moderate to severe effects on mental health among 53.8% of participants, for example, particularly exacerbating the stress and sleep disturbance that diabetics and individuals living with other chronic and lifestyle diseases commonly experience in any case.<sup>[16]</sup>

Previous studies have found that erratic sleeping patterns and shorter sleep durations are linked to being overweight or obese and to cardiovascular problems, and a significant number of people with diabetes have at least one of these conditions. Individuals with type 2 diabetes also report higher rates of insomnia, use of sleep medication, and sleeping during the day, all of which disrupt beneficial sleeping patterns.<sup>[12]</sup>

In some cases, the lockdown restrictions also resulted in diabetic individuals developing inadequate vitamin D levels due to spending most of the time indoors, with minimal exposure to sunlight. Vitamin D deficiency has been suggested to increase the risk of mortality and morbidity in cases of SARS-CoV-2 infection<sup>[4]</sup>, and supplementing vitamin D is thought to decrease the risk of severe disease, having thus been suggested as support for infected patients. Vitamin D has numerous mechanisms which may reduce the risks of microbial infections and death: these can be thought of as physical barriers, adaptive mechanisms, and increased natural immunity.<sup>[12]</sup>

### **Diabetic Smokers**

Few studies to date have looked at the impact of SARS-CoV-2 on diabetic individuals who smoke; all available data are thus from cross-sectional observational studies. Mohamed Abbas et al.<sup>[17]</sup> found that populations of patients with more than one comorbidity, especially those with both diabetes and a history of smoking, showed higher rates of severe-critical cases than those populations of those with diabetes who did not smoke or of healthy patients. They thus sought to compare the adverse risks of smoking versus more general diabetes comorbidities to examine outcomes in SARS-CoV-2 patients. The study examined 284 patients admitted to a Bagdad hospital between 7 June and 26 July 2020 who had confirmed cases of SARS-CoV-2, grouped with respect to standard cases (72 "healthy" patients), smokers (n=71), diabetes (n=71), and those who both smoked and had diabetes (n=70).

As expected, standard SARS-CoV-2 patients showed minimal levels of symptoms as compared to smokers, diabetics, and diabetic smokers. This study found that the presence of two or more comorbidities was more prevalent in older age groups, while smokers were found to have a tendency to higher temperatures and blood cell counts. Diabetic patients showed a wider range of symptoms, including sore throats, headaches, and lymphocytopenia, and it took longer for their health to improve generally.<sup>[17]</sup>

The impact of smoking and diabetes on SARS-CoV-2 patients can thus be seen to be the generation of a significantly higher rate of symptoms and complications than in patients without comorbidities. Patients with more than one comorbidity primarily present in critical situations and require respiratory care units, while patients without comorbidity more commonly present at a mild stage. The duration of the disease is also significantly longer for patients with diabetes who also smoke.<sup>[16]</sup> Body temperature, respiratory rates, diastolic blood pressure, pulse rates, and other concerning metrics are also higher in diabetic smokers, while increased mortality rates are higher among both SARS-CoV-2 patients who are smokers (4.2%) and those who are diabetic (7.04%), being highest (10%) among diabetic smokers, with all rates given in comparison to patients without comorbidities.<sup>[10]</sup>

It has proved difficult to obtain data on SARS-COV-2 hospitalisations in the Middle East and the Gulf Cooperation Council (GCC) countries. However, a few studies have managed to collect comprehensive data on the clinical characteristics and outcomes of SARS-COV-2 patients with type 2 diabetes admitted caring facilities across the Kingdom of Saudi Arabia (KSA). Understanding the impact of type 2 diabetes at population and community levels is essential in assessing its influence on the community, and the effect of this disease during the SARS-COV-2 pandemic may best be quantified in terms of premature mortality, decreased quality of life, economic impact, morbidity, and the various impacts on healthcare.<sup>[10]</sup>

Type 2 diabetes has been a burden for healthcare communities across the globe for decades, but it has become an even more significant burden since the onset of the SARS-COV-2 pandemic. At both the local and global levels, healthcare systems and the diabetic population have been significantly impacted by this pandemic<sup>[15]</sup> directly, while mitigation restrictions aimed at curbing the spread of the disease have commonly negatively influenced the diabetic population. Examining the difficulties faced by this vulnerable population should, however, enable healthcare professionals, healthcare providers, and policymakers to create better-targeted action plans that may be practically implemented to address this.<sup>[13]</sup>

The SARS-CoV-2 pandemic has caused undeniable and dramatic challenges for global healthcare, particularly across certain sections of the population, which have emerged in disproportionate ways in some cases. However, although individuals with diabetes and obesity clearly require optimal care when they contract the virus, they often actually receive sub-optimal care, a situation likely to persist where movement restrictions and lockdowns continue.<sup>[13]</sup> While the availability of vaccines is good news for these vulnerable populations in general, and is certainly a step in the right direction, the advent of new variants of the SARS-CoV-2 virus across the globe nevertheless means that progress in combatting this disease may remain slow for a while. The need to share relevant clinical experiences across different countries among specialists and healthcare professionals globally has thus been emphasised.<sup>[10]</sup>

Such information sharing has proven to be particularly critical during the SARS-CoV-2 period, helping to prevent increases in severe hypoglycaemia episodes. Vitality, it can also help identify those risk factors associated with unfavourable infection outcomes even where patients have no obvious symptoms, Medical responses continue to adapt rapidly to an ever-shifting SARS-CoV-2 landscape, as new variants have emerged and governmental and international restrictions have changed; the need for timely

distribution of advice and sharing of best practice is thus acute, while the implementation of critical learning must be swift as medical institutions globally seek to both improve disease control and prevent acute and chronic complications in patients.<sup>[18]</sup>

Multiple cardiometabolic risk factors accompany or are associated with type 2 diabetes and obesity, creating demand for a more holistic approach to caring for patients with these conditions during SARS-CoV-2 outbreaks in order to reduce the overall cardio-metabolic risk.<sup>[18]</sup> Several studies have thus called for greater congruence between treatment approaches and the significant cardio-metabolic threat posed by SARS-CoV-2. One study also noted that BMI is positively associated with combined outcomes of tracheal intubation and/or death within seven days of admission among patients with diabetes diagnosed with SARS-CoV-2<sup>[6]</sup>, leading to a need to target patients with both diabetes and obesity in terms of increased monitoring, testing priority, and comorbidity control.<sup>[18]</sup> Further, this phenomenon supports previous calls for individuals with diabetes and obesity to be prioritised during SARS-CoV-2 vaccination programmes.<sup>[6]</sup>

SARS-CoV-2 has created additional issues with respect to encouraging those with chronic conditions such as diabetes, hypertension, and cardiovascular disease to visit clinics and hospitals regularly, based on media-driven fears of contracting the SARS-CoV-2 infection. Nevertheless, patients who are not infected should continue with their ongoing treatment based on standard global and local guidelines, including regular blood glucose monitoring and support for healthy eating, increased exercise, and appropriate nutritional supplementation [8] among those with diabetes and/or obesity. A decision to give vitamin D was made by Israel early in the pandemic, even before any strong evidence was available to support its use in the management of SARS-CoV-2 infections; however, there are various potential mechanisms by which vitamin D might reduce the risks from SARS-CoV-2, including a lowering of viral replication rates, the induction of antimicrobial peptides, and the regulation of inflammatory responses<sup>[13]</sup>, highlighting the importance of nutritional considerations.

Due to the additional risks for patients with hyperglycaemia in cases of SARS-CoV-2, the control of hyperglycaemic tendencies during the initial stages of SARS-CoV-2 infection is vital, particularly among the immunocompromised, the malnourished, those with terminal illnesses, and those with gestational diabetes. Patients with type 1 diabetes must also be made aware of the risk of diabetic ketoacidosis that accompanies excessive hyperglycaemia, though one study conducted in Italy suggested that patients with type 1 diabetes who utilised flash glucose monitoring during the various lockdowns there experienced significantly fewer hypoglycaemic events or periods where their blood glucose levels were below the intended level, with no changes noted with respect to time in range or time above range. Such improved glycaemic control was, however, most closely associated with increased access to food, including sweet items, due to being at home during the lockdowns.<sup>[6]</sup>

## CONCLUSION

Experiencing both type 2 diabetes and SARS-CoV-2 has caused a significant section of the population to become more susceptible to severe health outcomes, a situation further exacerbated by a lack of access to proper high-quality care during the early stages of the pandemic due to governmental restrictions. This study has thus established that SARS-CoV-2 disproportionately affected individuals with type 2 diabetes. People with diabetes have an increased risk of severe infection and poor prognosis when they become infected, and they are more than twice as likely to develop severe symptoms requiring intensive care as compared to non-diabetics. This situation is made even worse if the diabetic person is also a smoker, at which point they become about 4.5 times more likely to need intensive care.

On contracting the disease, the mortality rate for diabetics is also significantly higher than that for non-diabetics. There is an increased risk of developing severe symptoms and complications among SARS-CoV-2 patients with diabetes or other comorbidities such as smoking, obesity, hypertension, cancer, and chronic respiratory infections or underlying cardiovascular conditions. Additionally, people with diabetes who have managed to not contract the SARS-CoV-2 virus have still experienced adverse effects with respect to various logistical aspects. Lockdowns and movement restrictions have affected them negatively in numerous ways, limiting access to fresh vegetables and fruits and limiting access to medication and technology to manage their diabetes, as well as keeping them away from their loved ones, all of which have increased the rates of mental stress, anxiety, and depression among many people with diabetes.

### Conflict of Interest

The author declares that there are no conflicts of interest relevant to this article.

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