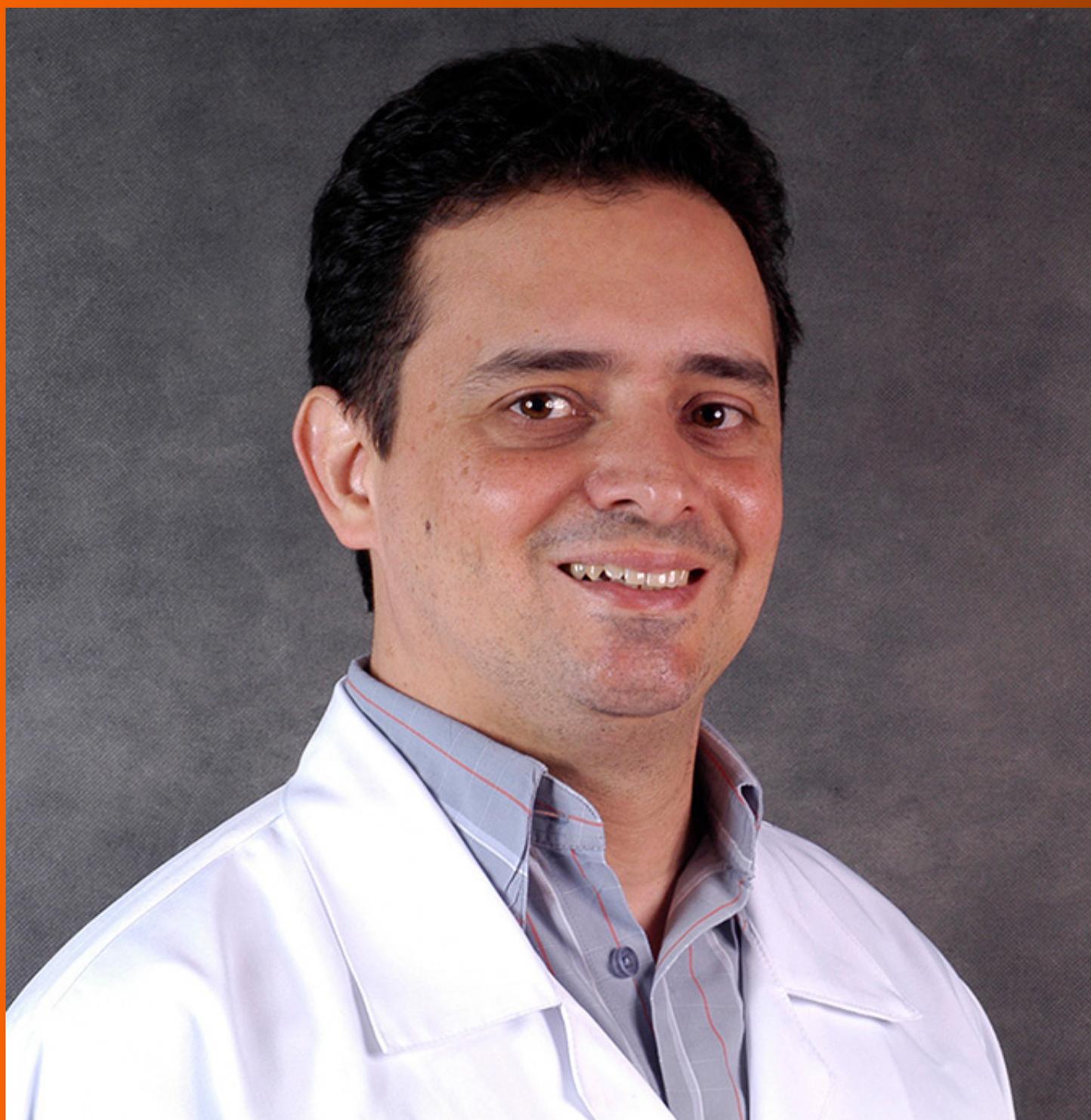


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WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

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COVID-19 vaccination and diabetic ketoacidosis

Beuy Joob, Viroj Wiwanitkit

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Abstract

An efficient coronavirus disease 2019 (COVID-19) vaccine is urgently required to fight the pandemic due to its high transmission rate and quick dissemination. There have been numerous reports on the side effects of the COVID-19 immunization, with a focus on its negative effects. Clinical endocrinology is extremely interested in the endocrine issue that arises after receiving the COVID-19 vaccine. As was already mentioned, after receiving the COVID-19 vaccine, many clinical problems could occur. Additionally, there are some compelling reports on diabetes. After receiving the COVID-19 vaccine, a patient experienced hyperosmolar hyperglycemia state, a case of newly-onset type 2 diabetes. There has also been information on a potential connection between the COVID-19 vaccine and diabetic ketoacidosis. Common symptoms include thirst, polydipsia, polyuria, palpitations, a lack of appetite, and weariness. In extremely rare clinical circumstances, a COVID-19 vaccine recipient may develop diabetes complications such as hyperglycemia and ketoacidosis. In these circumstances, routine clinical care has a successful track record. It is advised to give vaccine recipients who are vulnerable to problems, such as those with type 1 diabetes as an underlying illness, extra attention.

Key Words: Diabetes; COVID-19; Vaccine; Ketoacidosis; Effect

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Core Tip: There has also been information on a potential connection between the coronavirus disease 2019 (COVID-19) vaccine and diabetic ketoacidosis. Common symptoms include thirst, polydipsia, polyuria, palpitations, a lack of appetite, and weariness. In extremely rare clinical circumstances, a COVID-19 vaccine recipient may develop diabetes complications such as hyperglycemia and ketoacidosis.

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INTRODUCTION

Because of the pandemic's high transmission rate, an effective coronavirus disease 2019 (COVID-19) vaccine is urgently needed[1]. The available literature indicates that both vaccines help prevent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. However, given that the vaccination is new, any potential side effects are of greater concern[2-3]. When a handful of novel vaccines created in response to the COVID-19 pandemic got emergency approval and were widely distributed in late 2020[2], pharmacovigilance was unwittingly thrust into the spotlight. An effective global post marketing safety surveillance system was emphasized due to the employment of cutting-edge technologies and the anticipated rapid and widespread deployment of the vaccinations. The vaccinations went through extensive clinical evaluation and regulatory authority review. Many reports on the adverse effects of the COVID-19 vaccination have focused on how diverse they are. Clinical endocrinology is quite concerned about the endocrine issue that manifests after receiving the COVID-19 vaccination. The main concern expressed by the authors of this paper is that diabetes can become a medical problem after receiving the COVID-19 vaccine. After getting the COVID-19 vaccination, numerous clinical issues could arise, as was already mentioned. There are also some interesting reports regarding diabetes. The key words are provided here with a brief explanation.

Diabetes and COVID-19 have a well-established association. There is a bidirectional causal relationship between COVID-19 and type 2 diabetes. Diabetes may exacerbate COVID-19 severity, and COVID-19 vulnerability may increase diabetes risk[4]. Diabetes patients should receive the COVID-19 vaccine, just like everyone else, to protect themselves from the disease. It is critical to discuss the risks of vaccination for those who currently have diabetes mellitus. Piccini *et al*[5] evaluate the likelihood of glycemic control modification, insulin dose adjustment, and adverse effects following COVID-19 vaccination in young people with type 1 diabetes who use varying degrees of technology[5]. Piccini *et al* [5] came to the conclusion that receiving the COVID-19 immunization did not significantly increase the risk of glycemic control disturbance in type 1 diabetes adolescents and young adults[5]. This information may be helpful clinically[6] when counseling families about the SARS-CoV-2 vaccine for young people with type 1 diabetes. In a study by D'Addio *et al*[6] that investigated the immunogenicity and security of SARS-CoV-2 mRNA vaccines, a cohort of individuals with type 1 diabetes took part[5]. The vaccination demonstrated both dependability and security, according to D'Addio *et al*[6].

Several reports claim that COVID-19 vaccine recipients have problems with their diabetes. The exacerbation of hyperglycemia in people with type 2 diabetes after receiving the COVID-19 vaccination is the first problem that needs to be addressed[7]. Mishra *et al*[7] claim that an early inflammatory reaction to the vaccine and a subsequent immunological response are likely to be the causes of a minor and transient rise in blood sugar levels[7]. Mishra *et al*[7] published a case series that substantiated the etiology of transient immuno-inflammation because all episodes of hyperglycemia were self-limited and did not require significant treatment modifications[7]. A rapid jump in blood sugar levels appears to be caused by a vaccine. The possibility of a mild to moderate rise in blood sugar levels following vaccination has been theorized[7]. One patient experienced new-onset type 2 diabetes after receiving the COVID-19 vaccine, which is known as hyperosmolar hyperglycemia state[8].

COVID-19 VACCINATION AND DIABETIC KETOACIDOSIS

Clinical diabetology has an intriguing discussion regarding the COVID-19 vaccine and diabetic ketoacidosis. As was already indicated, the immunization may cause hyperviscosity and have unintended side effects. Additionally, reports of a connection between the COVID-19 immunization and diabetic ketoacidosis have been made. Three days after the first dose of COVID-19 RNA-based vaccines, the patient typically experiences thirst, polydipsia, polyuria, palpitations, a lack of appetite, and exhaustion without a prior history of diabetes[9]. Hyperglycemia, anion gap metabolic acidosis, and ketonuria are the three main signs of classic diabetic ketoacidosis[9]. It is possible to detect insulin autoantibody positivity and latent thyroid autoimmunity[10]. Ganakumar *et al*[11] advised that people with diabetes, particularly those with type 1 diabetes mellitus and inadequate glycemic control, be constantly monitored for hyperglycemia and ketonemia for at least two weeks after receiving the COVID-19 vaccine[11]. Autoimmunity and genetic predisposition may have contributed to the onset of the disease, even if the precise pathophysiologic mechanisms underlying type 1 diabetes are still unknown[12].

Table 1 Table summarizing the key information of coronavirus disease-19 vaccine related diabetic ketoacidosis in recipients with background type 1 and type 2 diabetes mellitus

Characteristics	Cases with background type 1 diabetes mellitus	Cases with background type 2 diabetes mellitus
Sex	Usually male	Usually male
Age group	Adolescent	Elderly
Background diabetes control	Poor control	No significant relationship
Duration of diabetic illness	Long	No significant relationship

According to Tang *et al*[12], vaccination could result in type 1 diabetes, irreversible islet beta cell loss, and autoimmunity in persons with susceptible genetic backgrounds[12]. The problem might be more serious and more likely to occur in situations where type 1 diabetes is already present. Yakou *et al*[13] advised that the immunization be cautiously administered to type 1 diabetes patients receiving strict insulin therapy and a sodium-glucose transporter[13] due to the increased risk of ketoacidosis. In the affected case, despite hyperglycemia and diabetic ketoacidosis (DKA) after SARS-CoV-2 immunization, low glycohemoglobin levels are a crucial indicator of COVID-19 vaccine-related DKA[14]. As a preventive measure, it is essential to counsel patients to continue getting insulin injections[13]. Due to the significant risk of ketoacidosis, the vaccination should be cautiously given to type 1 diabetes patients receiving rigorous insulin therapy and a sodium-glucose transporter[15]. When a patient becomes ill, it's crucial to remind them to continue taking their insulin injections and to drink enough fluids[13]. A similar preventative concern should be used in the case of the patient with poorly controlled type 2 diabetes, in addition to the patient with underlying type 1 diabetes. According to Kshetree *et al*[15], Type I or dysglycemia in Type 2 diabetes mellitus is becoming more frequently documented following COVID-19 vaccinations or infection[16]. The mechanisms could be autoimmunity following mRNA vaccinations, cytokine-mediated beta-cell injury, or as a component of an autoimmune syndrome brought on by vaccine adjuvants[15]. Further investigation into the negative effects of people prone to life-threatening illnesses is required, as suggested by Lin *et al*[14]. Also, there might be a need for postvaccination surveillance on both hyperglycemia and DKA problems[16].

Concerning the reported cases of a link between COVID-19 vaccination and diabetes ketoacidosis, an important clinical question is whether ketosis in type 1 diabetes is related to the use of sodium-glucose transport protein 2 (SGLT2) inhibitors. The clinical history of the vaccine recipients in the published articles on the clinical association usually revealed no use of SGLT2 inhibitors, which could be a clue to support the possible clinical association between COVID-19 vaccination and ketoacidosis. Last but not least, it should be noted that the mRNA COVID-19 vaccine is primarily associated with most findings on the relationship between COVID-19 immunization and diabetic ketoacidosis. There are, however, a few reports of clinical associations with other vaccination types (viral vector and inactivated COVID-19 vaccines) that have been documented[11]. The fact that the mRNA vaccination is currently the primary recommended COVID-19 vaccine may be the cause of the higher number of reported cases in the mRNA vaccine group. As previously stated, the COVID-19 vaccination may cause diabetic ketoacidosis in patients with type 1 or type 2 diabetes mellitus (Table 1).

There are significant differences in COVID-19 vaccine-induced diabetes ketoacidosis between recipients with type 1 and type 2 diabetes. COVID-19 vaccine induced diabetes ketoacidosis usually occurs in adolescent male cases with inadequate glycemic control in cases with background type 1 diabetes mellitus[11]. This is the same pattern seen in diabetic ketoacidosis caused by COVID-19 in type 1 diabetes patients[17]. There are fewer reported cases of COVID-19 vaccine-induced diabetes ketoacidosis in people with type 2 diabetes mellitus, and the patient is usually an elderly man with a long history of diabetic illness[15]. The background hemoglobin A1C level, on the other hand, has not been identified as a risk factor for the development of COVID-19 vaccine-induced diabetic ketoacidosis [18].

CONCLUSION

In general, the COVID-19 immunization should be given to the diabetic patient because it has been proven to be effective. Generally, it has been confirmed that it is secure. In exceedingly uncommon clinical situations, a COVID-19 vaccination recipient may experience diabetes-related problems such as hyperglycemia and ketoacidosis. Routine clinical care has a history of success in some situations. Users of vaccines who are more likely to develop problems, such as those who already have type 1 diabetes as an underlying illness, are advised to receive additional attention. Because there is a possible link between the COVID vaccine and ketoacidosis, the risk diabetic case must be closely monitored. There is still a need for more clinical research on this subject because there isn't any *in vivo* or *in vitro* experimental data at this time.

FOOTNOTES

Author contributions: Joob B and Wiwanitkit V contributed equally to this work; Joob B and Wiwanitkit V give the ideas; Joob B wrote and analyzed the data; Wiwanitkit V supervised; All authors have read and approve the final manuscript.

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