

## THE PREVALENCE OF HIGH BLOOD GLUCOSE RATES AFTER VACCINATION WITH THE SPUTNIK V VACCINE

### RYAD ALATI

Department of pharmacology, faculty of pharmacy, alasmarya Islamic University, Zliten, Libya.  
Corresponding Author Email: ryadlatii@yahoo.com

### ASRAA ABUGHUWILAH

Department of pharmacology, faculty of pharmacy, alasmarya Islamic University, Zliten, Libya.

### FARDOUS FAED

Department of pharmacology, faculty of pharmacy, alasmarya Islamic University, Zliten, Libya.

### MARWAH ALAYAN

Department of pharmacology, faculty of pharmacy, alasmarya Islamic University, Zliten, Libya.

### NAFEESAH MOHAMMED

Department of pharmacology, faculty of pharmacy, alasmarya Islamic University, Zliten, Libya.

### ALSUNOUSI KASHLOUT

Department of pharmacology, faculty of pharmacy, alasmarya Islamic University, Zliten, Libya.

### Abstract

*Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus SARS-CoV-2. The virus was discovered in Wuhan, Hubei Province, China. There are many vaccines for COVID-19, including Russian Sputnik V (Gam-COVID-Vac). COVID-19 vaccination-induced hyperglycemia (ViHG) and sequelae have been documented in some cases. **Objective:** To determine that effect of Sputnik V vaccination on diabetic and non-diabetic patient. **Methods:** Blood samples were tested four times with the ACCU CHEK ACTIVE device, once before vaccination with the Sputnik V vaccine and three times after vaccination in diabetic and non-diabetic individuals. **Results:** all FBS were within the normal range for non-diabetic patient post vaccination ( $P$  value  $> 0.005$ ) and for type-I diabetes mellitus there were fluctuation in blood glucose levels during three time intervals ( $P$  value  $< 0.005$ ) and it is significantly increased. **Conclusion:** Individual patient knowledge and engagement remains the cornerstone of diabetes management. Therefore, it is important to educate patients with diabetes about the phenomenon reported here, and future studies may shed more light on the underlying mechanisms.*

**Keywords:** COVID-19, Post-vaccination, Sputnik V, Hyperglycemia

### 1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious illness caused by SARS-CoV-2, a new coronavirus. This virus was discovered in Wuhan, a city in China's Hubei Province [1]. Its fast spread in China has developed to an epidemic, which then turned into a pandemic, resulting in more than 118 million cases and 2.6 million fatalities [2]. COVID-19 is a multi-system illness that has been associated to the development of new onset diabetes [3]. The urgent need for a vaccine to help fight this pandemic has hastened the approval of the Sputnik V COVID-19 Vaccine in December 2020 [4].

Russia's COVID-19 vaccine, Sputnik V (Gam-COVID-Vac), is a two-part adenovirus vaccine against the SARS-CoV-2 coronavirus. Developed in Russia, Sputnik V uses an attenuated virus to deliver small amounts of pathogens and trigger an immune response. It is a DNA-based adenovirus vaccination vector that contains the SARS-CoV-2 coronavirus gene. The adenovirus acts as a "container" to transfer the coronavirus gene into the cell and initiate the synthesis of the envelope protein of the new coronavirus, thus "introducing" the potential enemy into the immune system [4].

The first case of COVID-19 in Libya was reported on March 24, 2020 and there are a number of concerns about the use of COVID19 vaccinations in Libya. Furthermore, there is an increase in reports of vaccination-related side effects throughout the world and there haven't been enough findings on whether vaccinations might worsen hyperglycemia [5].

Hyperglycemia induced by vaccination against COVID-19 (ViHG) and sequelae have been documented in some cases [6]. Post-vaccination hyperglycaemia in a diabetic woman and two diabetic men 1 to 6 days after the Covishield vaccine (AstraZeneca) [7].

In our study, we present here 26 cases reports of vaccinated patients with/without diabetes following vaccination with Sputnik V™.

## **2. METHODS AND MATERIAL**

**2.1 Study design:** This was a cross sectional study carried out at public health center of Zliten city-Libya between 11 and 17 July 2021. The number of patients is 26 and in two groups male and female who is more than 18 years, diabetic and non-diabetic and who were vaccinated with Sputnik V vaccine. The blood glucose levels were measure by Accu Chek active meter. The study was approved by the health services center of Zliten City, Libya. The approval was in 8- July 2021.

**2.2 Data collection:** All data was obtained from patients by completing questionnaires and reviewed by 4 pharmacy students (Asraa Abughuwilah, Fardous Faed, Marwah Alayan and Nafeesah Kashlout). Information extracted included age, gender, chronic disease, diabetes or not, type of diabetes, fasting blood glucose (FBG) before vaccination and fasting blood glucose measurements post/post vaccination Sputnik V.

**2.3 Sampling and sample size:** Fasting blood glucose levels measured by Accu Chek active glucometer (model GC), rapid result was obtained by this device, the number of random samples was 100 cases and 74 cases lost their result because we could not contact them.

**2.4 Accu Chek protocol and evaluation:** Fasting and non-fasting blood glucose tests were done by using Accuchek active meter devices (model GC), Germany manufacturing, serial number GB is 1519277, and blood volume 1-2 microliter. The Accu-chek active device is a handle device approved for diagnostic use that determines blood glucose level concentration by means of glucose test strip with a measuring interval 10600mg/dl or 0.6-33.3 mmol/L and time needed to give result is 5sec. The test principle of the Accu-chek active meter is based on direct measurement of glucose level in capillary blood sample [8].

**2.5 Statistical analysis:** The SPSS software version 26 (SPSS Inc., American Chicago) was used. The quantitative variables were shown by anova tests (repeated measure test). A p value of  $\geq 0.05$  was considered statistically significant.

## **3. RESULT**

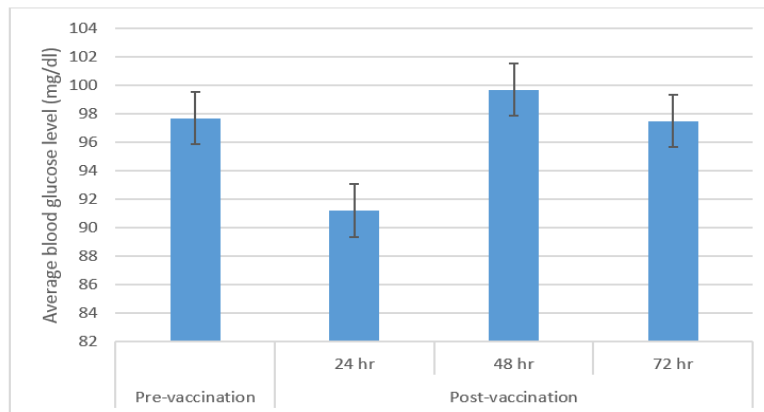
A total of 26 cases who were vaccinated with first dose of Sputnik V vaccine then blood glucose level was measured for them in three-time interval (24hrs, 48hrs and 72hrs). Of these, 15 female and 11 males > 18years old. Among of these cases, there are 4 cases were type 1 diabetes mellitus and 5 cases were Type II diabetes mellitus.

The average of FBG levels post-vaccination of healthy individuals were within the normal range (70-120mg/dl) and the average of RBG level post-vaccination of healthy individuals were within the normal range (80-140mg/dl).

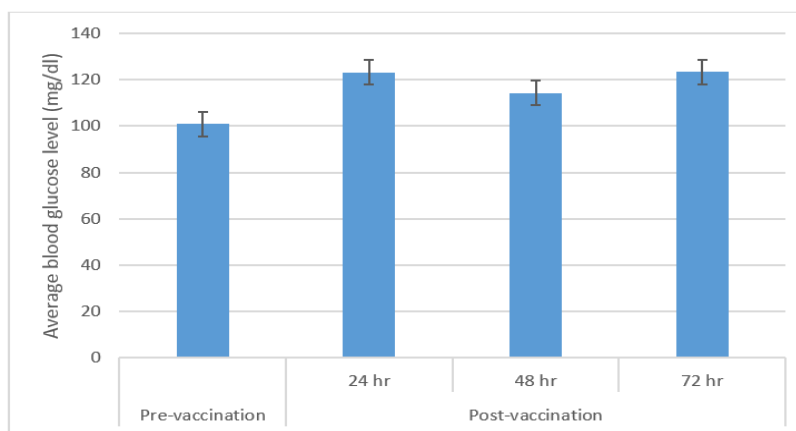
**Table 1: P value of blood glucose level**

Status	sig	Statistical result
Healthy individuals	.236	Not significant
DM-1	.673	Not significant
DM-2	.242	Not significant
Abnormal DM	.03	Significant

There are four cases of DM who have noticeable change in their blood glucose level after taking the Sputnik V vaccine.



**Figure 1: Fasting blood glucose level of healthy individuals**



**Figure 2: Random blood glucose level of healthy individuals**

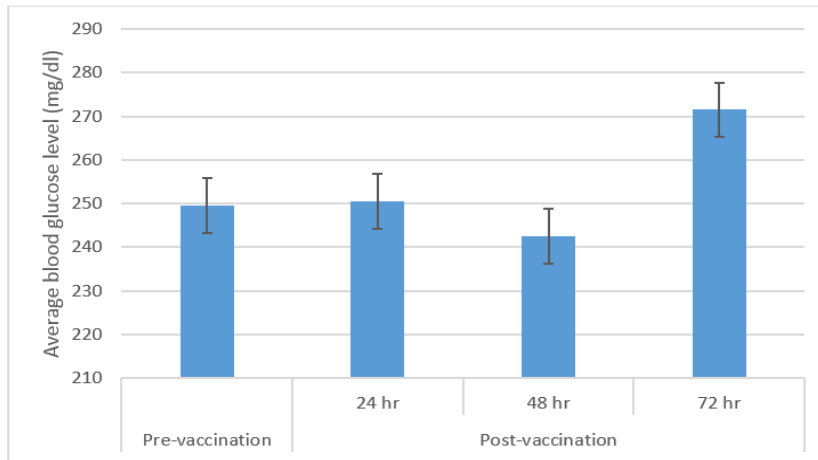


Figure3: Fasting blood glucose level of DM-1

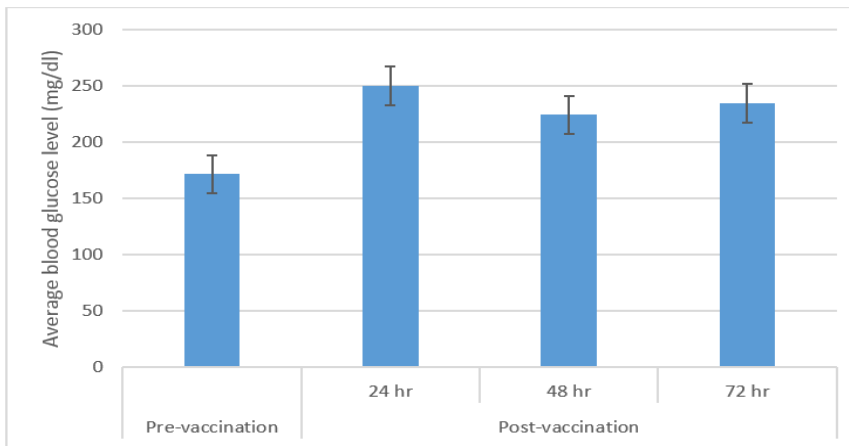


Figure 4: Fasting blood glucose level of DM-2

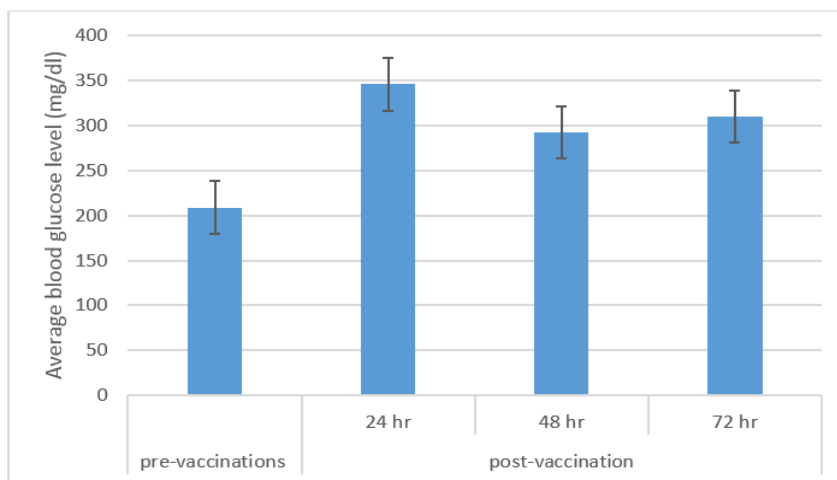
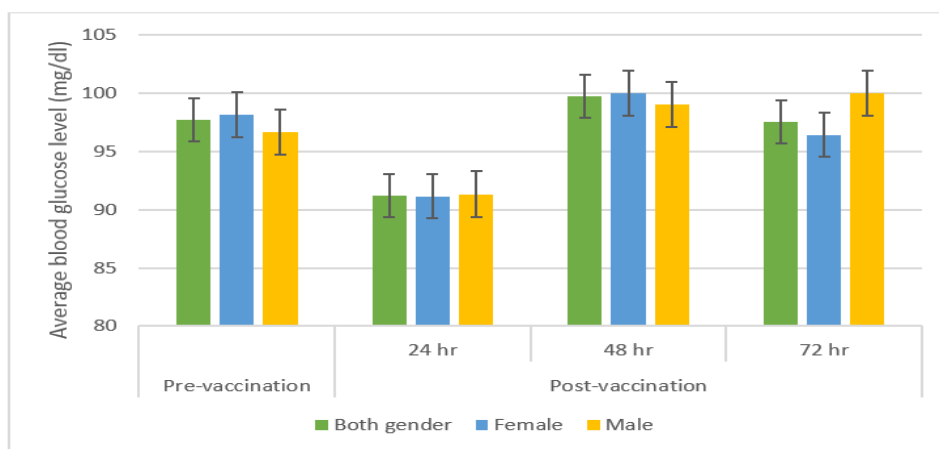


Figure 5: Abnormal blood glucose level of DM



**Figure 1: Fasting blood glucose level of healthy individuals with gender**

We found that there is no correlation between gender and FBG level post vaccination.

#### 4. DISCUSSION

Our cross-sectional study shows that there is no statistical significance of the abnormal change in the level of sugar in the blood in healthy people, and it also shows that there is no statistical relationship between diabetic patients and healthy people after the injection of Sputnik vaccination, but there is a clear statistical relationship and a clear change in the level of glucose in the blood of some patients with diabetes.

All corona vaccinations are considered safe and effective and have some rare side effects, and in this study, we described the possibility that there is a relationship between the Sputnik-COVID vaccinations with the change in the normal rates in the blood glucose level to compare it with the results obtained from previous studies regarding other vaccines that affect it.

In a previous study, they found that a group of people with type 1 diabetes had significant changes in their blood sugar levels, with FBG levels dropping significantly one week after vaccination. Additionally, in the same study, they found that those who received the Pfizer/BioNTech Oxford/AstraZeneca vaccine maintained their blood sugar levels within the normal range, with a significant drop in the second week. [9]. In a group of people with T1DM, we found that COVID-19 vaccination was associated with a temporary incremental change in interstitial glucose levels for many people. 58% of individuals with T1DM showed a reduction in time in target range in the week after vaccination [9].

The effect was more pronounced in individuals with better blood glucose control on the basis of estimated HbA1c. Importantly, there was no difference between the Pfizer/BioNTech Oxford/AstraZeneca vaccines in relation to their metabolic effect in the days after vaccination. The reduction in the proportion of interstitial glucose readings in the target range of 3.9–10 mmol/L persisted into the second week after vaccination, although to a lesser degree [9]. The percentage decrease in interstitial glucose readings over time is transient, but the percentage decrease in interstitial glucose readings below this range is clinically relevant in people with this disease. For many people with T1D, the effect on interstitial blood sugar was more pronounced in those who received dapagliflozin or metformin in addition than in those who received insulin alone. [9].

There was a significant variation in the change in the proportion of interstitial glucose readings in the target range as shown in Figure 1 with some individuals showing improved control on this measure, likely due to natural variation [9]. The 2-week post-COVID-19 vaccination period was taken based on patient reports of the period of time in which they were seeing perturbation of blood glucose. We, therefore, wanted to take a comparable period before the COVID-19 vaccination, that is, 2 weeks, hence, the period for which we looked at interstitial glucose levels [9].

The fact that although the proportion of interstitial glucose readings on target decreased for many individuals, but variability of interstitial glucose did not change suggests that for these people there was an overall shift upwards in interstitial glucose levels, rather than any significant change in variability [9]. The finding that there was a greater reduction in the proportion of interstitial glucose readings on target for people with a lower HbA1c may indicate that these individuals were more sensitive to the effects of vaccination on interstitial glucose levels. In essence they had 'More to lose' in terms of what in some individuals, was already a high proportion of interstitial glucose readings on target [9]. Clinical data support a strong neutralizing antibody response in diabetic patients with COVID-19 and vaccination should be advocated. However, our results suggest that patients with DM should be counseled and prepared for possible transient hyperglycemia after COVID-19 vaccination.

We are also not in a position as yet to appreciate whether such effects on interstitial glucose readings are seen in patients with T1DM following their second vaccination. The planning for these studies is underway. Furthermore, a question remains as to whether altered/reduced immunity to COVID-19 vaccination in those with diabetes. In relation to the rates of prescribing of dapagliflozin and metformin with insulin, the East Cheshire diabetes nurse (DSN) team have been very proactive about the use of adjunctive metformin and dapagliflozin in individuals with T1DM, with blood glucose levels consistently above target, and we have in fact reported the success of carefully considered dapagliflozin addition recently [9].

Sputnik V vaccine, also known as Gam-COVID-Vac, is a heterologous recombinant adenovirus vaccine that employs adenovirus 26 (Ad26) and adenovirus 5 (Ad5) as vectors for the production of the SARSCoV-2 spike protein. The administration of two different serotypes 21 days apart is designed to overcome any pre-existing adenovirus immunity in the population. Only GamCOVID-Vac employs this strategy among the various COVID vaccines currently under development [10] others, such as the Pfizer/BioNTech and Oxford/AstraZeneca COVID-19 vaccines work by stimulating the immune response to the virus' spike protein. Vaccines have different efficacy rates and minor side effects, as shown in a report through the Joint Committee on Vaccination and Immunization (JCVI) Independent report in April 2021 [11]. All the immediate notification data previously published by the UK government, on the Pfizer/BioNTech mRNA vaccine, due to hyperglycaemia, and this case is not limited to the patient's condition, healthy or suffering from both types of diabetes. Additionally, University of Oxford/AstraZeneca reported 54 additional COVID-19 vaccine cases between 01/04-2021 and 03/07-2021. Additionally, a series of three similar cases from India, followed by diet and exercise before the age of 25, followed by vaccination, had significantly elevated blood sugar levels after receiving the Covishield™ vaccine and had been vaccinated [7].

Our use of Accu Chek glucose monitoring allows identification of slight change in blood glucose level trends in dysglycaemia that may escape other forms of monitoring [12]. There are multiple reasons behind fluctuations in blood glucose level. With our analysis of our patient samples, there are no other contributing factors such as infection or intolerance to excipients, through which it can be said that the observed hyperglycemia was associated with sputnik V vaccination [13]. Transient fluctuations in blood glucose have many causes. With our analysis of the cases revealing no other contributory factors such as infection or hypersensitivity to the excipients, it seems likely that the observed relative

hyperglycemia was associated with the COVID-19 vaccination. One of the possibilities of the mechanisms of hyperglycemia after vaccination with Sputnik vaccine in patients with DM compared to healthy people is described here, that alerting the immune system in patients with DM raises sugar levels and this result differs from that in healthy people, although this response is still lower than in those with COVID19. Psychological stress and fear because they have chronic diseases has the ability to change the levels of regulatory hormones. Patients with DM may be less able to resist high glucose levels [13].

One possible mechanism for the hyperglycemia described here, is stimulation of the immune system resulting in a transient stress response, to a milder degree than would typically occur with a COVID-19 infection. Physiologic stress has the potential to increase counter regulatory hormone levels [11]. Most notable among these are adrenaline, growth hormone and cortisol and/or glucagon in those with alpha cell reserve. People with DM may be less able to rapidly counteract such elevations in blood glucose [12]. The series that we report comprises individuals having their first COVID vaccine.

It has been reported that people with prior COVID19 infection reported side effects from the vaccine more frequently after the first dose. Of course, vaccinations stimulate the immune system and cause an immune response. This response is to varying degrees within a person and between people, determined by a group of factors, including the vaccine. For instance, the type of adjuvant or within the host, for example, immune response genes [14]. Vaccinations, by nature of their intended purpose, elicit an immune response, often to varying degrees within and between individuals determined by a wide range of factors some of which reside within the vaccine, for example, the type of adjuvant or within the host, for example, immune response genes. Sestan et al. reported in 2018 that viral-induced inflammation leads to insulin resistance in the skeletal muscle, followed by compensatory hyperinsulinemia, which promotes the anti-viral effector response of CD8+ T cells [13]. Not surprisingly, this immune response has complex effects on metabolic processes, including blood sugar regulation. A group of cytokines produced by immune-mediated inflammation are known to affect blood glucose levels and insulin resistance in tissues. These actions can have complex biological interactions with other factors, including cortisol, adipokines, and other hormones. This may be more pronounced in people with poor blood sugar control [13].

It is not surprising that such immune responses have complex downstream effects on metabolism including regulation of blood glucose levels. A range of cytokines produced through immune-driven inflammation are known to impact on blood glucose levels and insulin resistance within tissues [14]. Such actions are likely to have complex and further biological interplay with factors including adipokines, hormones and cortisol. In 27 individuals with existing impaired glucose control, this is likely to be more pronounced. Knowing the patient's health status with diabetes and attempting effective treatment remains very important. Accordingly, it is important to inform people with diabetes in general about this phenomenon mentioned here, while we hope that other reports shed light on the basic mechanisms.

Individual patient knowledge and involvement remain the cornerstones of diabetes management. Therefore, it is important to inform individuals with DM about the phenomenon reported here, whereas future research may shed more light on the underlying mechanisms.

**Conclusion and suggestions:** Post-vaccination with Sputnik V has no effects on blood glucose level in healthy individuals but it may effect on diabetic patients. A larger, multi-site patient series is necessary to investigate this further. However, the results here raise the question of whether people with DM should be given specific advice in advance of COVID-19 booster vaccination in relation to potential temporary effects on their glycemic control.

**Strength of study:** Outcomes measure in random pathway (cross sectional study) and it is first time used after Sputnik V vaccination.

**Limitation of study:** Our cross-sectional study has several limitations and remains hypothesis generating. The sample of our study small and the sample should be more than 1000 of vaccinated cases, we were unable to follow up all the cases and we do not check the HbA1c for all patients before vaccination and after 3 months of Sputnik V vaccination. Moreover, our study is used Sputnik V to test the change in blood glucose level and in the future should use more than one type of vaccinations.

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