JOURNAL OF TECHNIQUES

Journal homepage: http://journal.mtu.edu.iq

RESEARCH ARTICLE - MEDICAL TECHNIQUES

Liver Functions in Type 2 Diabetes Individuals after Pfizer Vaccination in Iraqi Patients

Shrooq Ali Hussein[1*], Ahmed Abdul-Hussein Mohsin[1], Ahmed Ghazi Sabbar[1]

[1] College of Health & Medical Technology - Baghdad, Middle Technical University, Baghdad, Iraq.

[*] Corresponding author E-mail: shroqali33@yahoo.com

Article Info.

Article history:

Received
08 June 2022

Accepted
06 July 2022

Publishing
30 September 2022

Abstract

Coronavirus is a highly contagious disease, especially in diabetes mellitus type 2. It remains the main cause of death despite the availability of a vaccine. Coronavirus is transmitted via droplets from the nose, mouth, or throat. The study evaluates the biochemical parameters of liver function in patients suffering from type 2 diabetes and the correlation between D-dimer level and platelet count after a second dose of the Pfizer vaccine (14–21) days after vaccination. A study was carried out in al Suwayrah hospital, which included 300 patients aged 20 to 70 years old. one hundred were excluded from this study. A physician diagnosed with Type-2 diabetes mellitus (the ADA) (the American Diabetes Association, 2021) was involved in this study from December 2021 to March 2022. results showed that AST and ALT were normal, while ALP was higher in diabetics compared to controls (ALP was higher in both groups of diabetics vaccinated and non-vaccinated with Pfizer vaccine compared to controls). correlation with no significant effect on platelet count and D-dimer. The current research concludes that there is no effect of the Pfizer vaccine on a biochemical parameter of the liver.

Publisher : Middle Technical University

Keywords: Pfizer; T2DM; Liver parameters; D-dimer; Platelet.

1. Introduction

Diabetes affects more than 425 million people globally, and studies suggest that the number will rise to 629 million by 2045 [1]. The World Health Organization has estimated a viral pandemic on March 11, 2020, attributed to a disease caused by a new coronavirus 19 (COVID-19). The COVID-19 pandemic has led to a major increase in global death.[2]. On February 24, 2020, Iraq reported its first COVID-19 infection in Najaf city, followed by four instances in the Kirkuk governorate. COVID-19 (new coronavirus disease) is a highly contagious condition caused by SARS–coronavirus-2. (SARS-CoV-2) [3]. Diabetes has been linked to COVID-19 progression, and COVID-19 infection may predispose people to hyperglycemia. When combined with other risk factors, hyperglycemia may alter immunological and inflammatory responses, predisposing individuals to severe COVID-19 and potentially fatal outcomes [4]. On March 3, 2020, the Sulaymaniyah governorate, confirmed the death of a 69-year-old COVID-19 patient [5]. Diabetes has been identified as the most main risk factor for a severe COVID-19 outcome. Diabetes mellitus is distinguished by a variety of features, including advanced age, an inflammatory and hypercoagulable condition, and a high level of blood glucose [6]. Individuals with type 2 diabetes or type 1 diabetes are more likely to have a poor prognosis from COVID-19, thus immunization should be a priority for them [7].

A messenger RNA COVID-19 vaccine was discovered to be extremely effective in preventing symptomatic, asymptomatic, and severe SARS-CoV-2 infection [8]. Nanotechnology has accelerated the development of Pfizer/mRNA-based vaccines[9]. mRNA is delivered by chemically synthesized nanoparticles (NPs; i.e., liposomes) [10]. mRNA technology has the potential to revolutionize medicine, notably in the treatment of infectious diseases. A more complete understanding of the qualitative parameters that determine translating performance, as well as a better understanding of the relevance of mRNA delivery, are ushering in a new era of development activity investment [11]. The novel genetic technique of the mRNA vaccination (The anti-SARS-CoV-2 vaccine is based on messenger ribonucleic acid (mRNA) molecules), which are DNA repeats that produce proteins. It can stimulate the creation of responses that can neutralize the virus in clinical specimens [12]. Nucleic acid vaccines dependent on mRNA were developed more than three decades ago in the hope of developing vaccines that are both safe and simple to manufacture [13]. the Pfizer(BioNTech mRNA-based COVID-19) vaccines are approved for emergency use [14]. Vaccines were not related to facilitated death or serious hepatic responses in the preregistration studies. Even though there were rare reports of hepatic damage occurring within days or weeks after receiving the vaccine since the FDA's emergency use authorization (EUA) of Pfizer vaccine in December 2020 and approval in August 2021. There is only one rare case reported with a liver problem after the Pfizer vaccination, and it is uncertain whether it is caused by the COVID-19 vaccination or is a fortuitous, accidental relationship with a natural occurrence[15]. A two-dose regimen of Pfizer's vaccine provided 95% protection against COID-19 in those aged 16 and above. Local and systemic responses were dose-dependent, mild to moderate, and temporary [16]. The main goal of this study is to the possible effect of the

Nomenclature			
ADA	American diabetes association	EUA	EMERGENCY use authorization
ALP	Alkaline phosphatase	FDA's	Food and Drug Administration
ALT	Alanine transaminase	MRNA	messenger ribonucleic acid
AST	aspartate aminotransferase	SARS-CoV-2	SEVERE ACUTE RESPIRATORY SYNDROME corona virus-2
DM	Diabetes mellitus	WHO	WORLD HEALTH ORGANIZATIONS
DNA	Deoxyribonucleic acid	VWF	von Will brand factor

Pfizer vaccine on liver function among patients with type 2 diabetes mellitus and the relationship between D-dimer and platelet counts following the second dose of Pfizer vaccinations.

2. Materials and Methods

2.1. Sample

5 ml of venous blood was collected after fasting. Divide the blood into three parts: serum in a gel tube, whole blood in a prothrombin tube (D-dimer test), and whole blood in K3EDTA (completes blood count). The liver function tests (AST, ALT, and ALP) were measured by the linear Spanish kit colorimetric in Selectra Pro—XL. The D-dimer was measured by Hipro while the platelet count was determined in fully autosamsungs.

2.2. Study design

The current study investigated the effect of the Pfizer vaccination on the liver of patients with type 2 diabetes mellitus at al Suwayrah hospital from December 2021 to March 2022. Inclusion criteria two hundred include (100 patients with DM-2 and 50 Heathy with were previously vaccinated with two doses) (50 DM-2 nonvaccinated). The age range of 20-70. Diagnosis of type -2 diabetes mellitus by the physician according to ADA (American diabetes association, 2021).

2.3. Ethical approval

Before their blood was drawn for this study, all subjects provided written informed consent. Approval of this study was obtained from the ethics committee of AL Suwayrah hospital; on the date of 5/12/2021.

2.4. Statistical analysis

For Statistical analyses: Statistical Package of Social Science Software program, for windows version 24 (SPSS). Pre-coded personal information was entered into the computer and statistically analyzed using the .to compare DM-2 vaccinated and control groups used and one-way analysis of variance (ANOVA) to analyze three groups DM-2 vaccinated DM-2 nonvaccinated, and control. An independent sample t-test was used.

The comparison of significant (p-value) is done as follows:

- P value <0.05 was deemed statistically significant (S)
- P value< 0.01 was deemed extremely significant(HS)
- P value >0.05 There was no significant difference when the P value was greater0.05.

3. Results and discussions

3.1. Determination of Serum AST in study groups

The data revealed a non-significant difference between the three groups' p-value (0.5864).
In this current study (Table 1) in Iraq to investigate the effect of the Pfizer vaccine on patients with type -2 diabetes mellitus, our findings revealed no effect of the Pfizer vaccine on AST (Aspartate transaminase) Diabetes mellitus (DM) is a kind of metabolic disorder caused by an imbalance in insulin synthesis, insulin production, or both, which promotes persistent hyperglycemia, the major cause of diabetic complications such as failing over time and disruption to a variety of organ systems [17]. The liver is crucial in the pathophysiology of this illness [18]. AST is a pyridoxal phosphorus enzyme present in the cytoplasm as well as the mitochondria. Aspartate aminotransferase relates to both secretions of glucose from the liver throughout growth and fat cell glyceroneogenesis [19] .

Table 1 Comparison of AST among study groups

AST	Study Groups	Number	Mean± S.E	one way Anova	P-value
	Controls	50	22. 87±1.370		
	DM-2 non-vaccinated	50	21.71±1.126	0.358	0.5864
	DM-2 vaccinated	100	23.38±0.98		

Significant (P≤0.05)

3.2. Distributions of Serum ALT in study groups

The data represent a non-significant difference between the three groups' p-value (0.6527), Table 2.
alanine transaminase (ALT)is found primarily in the liver and catalyzes the reversible transformation of -keto-acids into amino-acids via amino group transfer, hence aiding fundamental metabolic pathways [21]. Serum alanine aminotransferase (ALT) is one of the most frequent biochemical tests acquired in clinical research, and it is widely employed in the screening and monitoring of liver failure. It is thought to be a reliable and sensitive indicator of liver disease.[20].This is a recent study in Iraq to investigate the effect of the Pfizer vaccine on patients with type -2 diabetes mellitus our finding revealed no effect of the Pfizer vaccine on (alanine transaminase).

Table 2 Comparison of ALT among studied groups

AST	Study Groups	Number	Mean± S.E	one way Anova	P-value
	Controls	50	27±1.195		
	DM-2 non-vaccinated	50	73±1.110	0.6527	0.2086
	DM-2 vaccinated	100	34±1.297		

significant (P≤0.05)

3.3. Estimation of Serum ALP

The data in Table 3 revealed that most diabetic patients had a higher level of alkaline phosphatase in significant difference ($p < 0.0004$) than controls.

Table 3 Comparison of ALP among study group**s**

AST	Study Groups	Number	Mean± S.E	one way Anova	P-value
	Controls	50	211. 7±8.3		
	DM-2 non-vaccinated	50	269.41±12.4	8.216	0.0004
	DM-2 vaccinated	100	252.2±7.5		

*significant (P≤0.05)

*3.4. Multiple Comparison of ALP among study group**s***

The data in Table 4 represent significant differences between controls and DM-2 non vaccinated in ($p < 0.0004$) .and significant differences between controls and DM-2 vaccinated ($p < 0.0060$). Non-significant differences between diabetics type 2 vaccinated and diabetes type 2 non vaccinated ($p < 0.3776$).

Table 4 Comparison of ALP among study group**s** (T-test)

ALP	Study Groups	Number	Mean± S.E	Compared with healthy P-value	DM-2 Vaccinated & DM-2 non vaccinated P-value
	Controls	50	211. 7±8.3		
	DM-2 non-vaccinated	50	269.41±12.4	0.0004	0.3776
	DM-2 vaccinated	100	252.2±7.5	0.0060	

*significant (P≤0.05)

ALP (alkaline phosphatase) **is** an enzymatic hydrolysis enzyme that removes phosphate groups from compound**s** [21]. Diabetics have greater levels of alkaline phosphatase (ALP), an enzyme found largely in bone and liver, than non-diabetics [22].ALP (alkaline phosphatase) represents a significant rise in both groups of diabetics in comparison with control this may be due that alkaline phosphatase has been linked to glucose metabolism, insulin resistance, and metabolic syndrome in several investigations [23].

3.5. Correlation between platelet and D-dimer

The results revealed their non-significant negative (inverse correlation) between platelet count and D-dimer (r=-0.06387at p-value =0.5475).

Table 5 The Simple correlation coefficient between D-dimer & platelet among DM-2 vaccinated

platelet & D-dimer	P-value	R
	-0.06387	0.5475

**. Correlation is significant at the 0.01 level (2-tailed).

Multiple mechanisms including metabolic and cellular problems have been proposed to explain the enhanced platelet reactivity seen in diabetic individuals. These pathways can be classified as aetiopathogenic in the following ways: a) hyperglycemia, b) insulin insufficiency and resistance, c) metabolic disorders linked with hyperglycemia, and d) additional cellular problems[24]. Hyperglycemia not only identifies diabetes, but it also plays an independent and significant role in the blood irregularities that contribute to a prothrombotic condition in diabetes patients [25]. D-dimer is a fibrinolysis product that is elevated in thrombotic events, suggesting fibrinolysis [26]. Dependent on instructions, downregulations of fibrin (ogen), D-dimer, von Will brand factor, and P-selectin produce hyper coagulatiolation, hemorrhaging, and low platelet count. Lower fibrinogen levels are related to a higher risk of bleeding during normal bleeding and altered clotting disorders, whereas high levels are linked to hypercoagulation [27].

Patients who do not get treatment have a quick increase in D-dimer, increased fibrinogen, VWF, and P-selectin levels, as well as hyperactivation of platelets. This is a symptom of thrombosis or excessive clotting. D-dimer and P-selectin levels are high in critically sick patients, but fibrinogen and VWF levels are low, as these molecules are depleted from circulation or the damaged endothelial cells and hyperactivated platelets that now display thrombocytopenia. The cytokine storm is most noticeable in the late phases of disease development. D-dimer assays are also highly useful since they detect D-dimer levels in the blood and act as an indirect marker of fibrinolysis and fibrin turnover [28]. The current study confirmed there is no effect of the Pfizer vaccine on type -2 diabetes mellitus that was previously vaccinated with 2 doses of Pfizer vaccine, Pfizer vaccine is completely risk-free [29]. In contrast to DNA vaccinations, mRNA does not integrate into the host's genome, reducing the risk of Geno toxicity. In comparison to inactivated virus or live vector-based vaccines, synthetic mRNA vaccine production is acceptable for quality control and has a lower risk of biological contamination during production [30].

4. Conclusions

The study found no side effects of the Pfizer vaccine on the liver functions tests after two doses of Pfizer vaccination enzymatic liver function with normal range (AST, alt). Except alp elevated in diabetic patients (vaccinated and non -vaccinated). And there is no significant between d-dimer level and platelet.

5. Recommendations

COVID-19 is life-threatening and immunization is saved to reduce death. A booster dose should be taken.

Acknowledgment

Thanks to the chemistry department and the blood collection unit at al Suwayrah Hospital.

Reference

[1] Erener, S., Diabetes, infection risk, and COVID-19. Molecular metabolism, 2020. 39: p. 101044.
[2] Suleman, S., Farooqui, A., Sharma, P., Malhotra, N., Yadav, N., Narang,j., Hasnain, M., Nayak, A., Borderline microscopic organism and lockdown impacted across the borders-global shakers. Environ Sci Pollut Res Int, 2022. 29(6): p. 8091-8108.
[3] Alzamora, M.C., Paredes,T.,Caceres d.,Webb,c.,Valdez,L.,Rosa,M., Severe COVID-19 during Pregnancy and Possible Vertical Transmission. Am J Perinatol, 2020. 37(8): p. 861-865.
[4] Lim, S., Bae, J., Sang Kwon, H., Nauck, M., COVID-19 and diabetes mellitus: from pathophysiology to clinical management. Nat Rev Endocrinol, 2021. 17(1): p. 11-30.
[5] Lami, F., Rashak, A., Khaleel, H., Mahdi, S., Adnan, F., Khader, Y., Alhilfi, R., Lehlewa, A., Iraq experience in handling the COVID-19 pandemic: implications of public health challenges and lessons learned for future epidemic preparedness planning. J Public Health (Oxf), 2021. 43(Suppl 3): p. iii19-iii28.
[6] Landstra, C.P. and E.J.P. de Koning, COVID-19 and Diabetes: Understanding the Interrelationship and Risks for a Severe Course. Front Endocrinol (Lausanne), 2021. 12: p. 649525.
[7] Pal, R., S.K. Bhadada, and A. Misra, COVID-19 vaccination in patients with diabetes mellitus: Current concepts, uncertainties, and challenges. Diabetes Metab Syndr, 2021. 15(2): p. 505-508.
[8] Spitzer, A., Angel, Y., Marudi, O., Association of a Third Dose of BNT162b2 Vaccine With Incidence of SARS-CoV-2 Infection Among Health Care Workers in Israel. Jama, 2022. 327(4): p. 341-349.
[9] Khurana, A., Allawadhi, P., Khurana, I., Allwadhi, S., Weiskirchen, R., Banothu, A., Joshi, K., Kumar, K., Role of nanotechnology behind the success of mRNA vaccines for COVID-19. Nano Today, 2021. 38: p. 101142.
[10] Constantin, C., Pisani, A., Bardi, G., Neagu, M., Nano-carriers of COVID-19 vaccines: the main pillars of efficacy. Nanomedicine, 2021. 16(26): p. 2377-2387.
[11] Jackson, N.A.C., Kent E. Kester, K., Casimiro, D., Gurunathan, S., DeRosa, F., The promise of mRNA vaccines: a biotech and industrial perspective. NPJ Vaccines, 2020. 5: p. 11.
[12] Chatterjee, R., Ghosh, M., Sahoo, S., Padhi, S., Misra, N., Raina,v., Suar, M., Ok Son, Y., Next-Generation Bioinformatics Approaches and Resources for Coronavirus Vaccine Discovery and Development-A Perspective Review. Vaccines (Basel), 2021. 9(8).
[13] Chaudhary, N., D. Weissman, and K.A. Whitehead, mRNA vaccines for infectious diseases: principles, delivery, and clinical translation. Nat Rev Drug Discov, 2021. 20(11): p. 817-838.
[14] Fox, A., Norris,C., Amanat, F., Zolla-Pazner,S., Powell,R., The vaccine-elicited immunoglobulin profile in milk after COVID-19 mRNA-based vaccination is IgG-dominant and lacks secretory antibodies. medRxiv, 2021.
[15] Covid-19 Vaccines, in LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. 2012, National Institute of Diabetes and Digestive and Kidney Diseases: Bethesda (MD).
[16] Mulligan, M.J., Kirsten E. Lyke,k., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Neuzil, K., Raabe, V., Bailey, R., Swanson, K., Li, P., Koury, K., Kalina, W., Cooper, D., Fontes-Garfias, C., Shi, P., Türeci, Ö., Tompkins, K., Walsh, E., Frenck, R., Falsey, A., Dormitzer, P., Gruber, W., Şahin, U., Jansen,k., Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. Nature, 2020. 586(7830): p. 589-593.
[17] Jaganjac, M., Tirosh, O., Cohen, G., Sasson, S., Reactive aldehydes--second messengers of free radicals in diabetes mellitus. Free Radic Res, 2013. 47 Suppl 1: p. 39-48.
[18] Alam, S., Raghav, A., Reyaz, A., Ahsan, A. Kumar, A., Jain, V., Agarwal, S., Tripathi, P., Prevalence of elevated liver enzymes and its relationship with type 2 diabetes mellitus in North Indian adults. Metabol Open, 2021. 12: p. 100130.
[19] Sookoian, S. and C.J. Pirola, Liver enzymes, metabolomics, and genome-wide association studies: from systems biology to the personalized medicine. World J Gastroenterol, 2015. 21(3): p. 711-25.
[20] Vespasiani-Gentilucci, U., Gaetano, P., Piccinocchi, G., Piccinocchi, R., Schene.E., Galati, G., Devincentis, A., Dell, C., Unto., Picardi, A., Determinants of alanine aminotransferase levels in a large population from Southern Italy: relationship between alanine aminotransferase and age. Digestive and Liver Disease, 2014. 46(10): p. 909-915.
[21] Kim, D.W., Hwang, S., Nam, Y., Kim, D., Shin, S., Yoon, H., The combined prognostic significance of alkaline phosphatase and vascular calcification in patients with end-stage kidney disease. Nutr Metab Cardiovasc Dis, 2020. 30(9): p. 1476-1483.
[22] Chen, S.C.-C., Tsai, S., Jhao, J., Jiang, W., Tsao, C., Chang, L., Liver fat, hepatic enzymes, alkaline phosphatase and the risk of incident type 2 diabetes: a prospective study of 132,377 adults. Scientific reports, 2017. 7(1): p. 1-9.
[23] Zhao, L., Li, L., Ren, H., Zou, Y., Zhang, R., Wang, S., Xu, H., Association between serum alkaline phosphatase and renal outcome in patients with type 2 diabetes mellitus. Ren Fail, 2020. 42(1): p. 818-828.

[24] Ferreiro, J.L., J.A. Gómez-Hospital, and D.J. Angiolillo, Platelet abnormalities in diabetes mellitus. Diab Vasc Dis Res, 2010. 7(4): p. 251-9.
[25] Schneider, D.J., Factors contributing to increased platelet reactivity in people with diabetes. Diabetes Care, 2009. 32(4): p. 525-7.
[26] Demelo-Rodríguez, P., Ortega ,L.,Virto, A., Macías,M., Samaniego,N., García,A., Bravo ,I., Diez,J., Walther,A., CerverA,J., Valle,j., Incidence of asymptomatic deep vein thrombosis in patients with COVID-19 pneumonia and elevated D-dimer levels. Thromb Res, 2020. 192: p. 23-26.
[27] Pillai, R.C., Fraser, F., Ph.D., Ziegenfuss, F., Bhaskar, B., Influence of circulating levels of fibrinogen and perioperative coagulation parameters on predicting postoperative blood loss in cardiac surgery: a prospective observational study. J Card Surg, 2014. 29(2): p. 189-95.
[28] Johnson, E.D., J.C. Schell, and G.M. Rodgers, The D-dimer assay. Am J Hematol, 2019. 94(7): p. 833-839.
[29] Pardi, N., Hogan, M., Porter, F., Weissman, D., mRNA vaccines—a new era in vaccinology. Nature reviews Drug discovery, 2018. 17(4): p. 261-279.
[30] Pardi, N., Muramatsu, H., Weissman, D., Karikó, K., In vitro transcription of long RNA containing modified nucleosides. Synthetic messenger RNA and cell metabolism modulation, 2013: p. 29-42.