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ROS and cardiac function test in type 2 diabetes mellitus after Pfizer vaccination among Iraq patients

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ABSTRACT— Vaccination in diabetics is important to prevent cardiac complications that happen in type -2 diabetes mellitus after COVID-19 infections. Measurement of Reactive Oxygen Species (ROS) as indicators of oxidative stress in T2DM patients. and measuring variable of cardiac function test (Troponin-I, creatine kinase CK-MB) after the second dose of Pfizer vaccination. ROS (Reactive oxygen species) and cardiac function tests (Troponin-I, CK-MB) were determined by using an ELISA kit. The results revealed a higher level of ROS in both group of diabetic in comparison to controls elevated in diabetic (slightly higher in diabetics non vaccinated than vaccinated) I compare with healthy controls lower, while cardiac function tests including Troponin-I higher in diabetics (vaccinated higher than non-vaccinated) in compare with healthy control.CK-MB higher in diabetics and healthy vaccinated in compare with diabetics non vaccinated. ROS not changed after Pfizer vaccination. Vaccinated type 2 diabetes show marginal elevated in Cardiac function test and ALL Cardiac function test mean with normal range (diabetics show higher level of Troponin-I in compare with healthy control) while CK-MB higher in diabetics vaccinated and healthy control in compare with diabetics non vaccinated.

KEYWORDS: T2DM, Reactive oxygen species, troponin, creatine kinase(CK-MB).

1. INTRODUCTION

Diabetes Health problem that affects 463 million people worldwide, including 34.2 million Americans [1]. Pfizer's innovative mRNA technology-based SARS-CoV-2 vaccines are presently authorized, with effectiveness reaching 94–95 percent in clinical studies [2]. Despite the fact that vaccine safety profiles have been well researched and confirmed, the incidence and severity of adverse responses from immunizations may vary based on geography and ethnicity, and there is a chance of unreported side effects [3]. Patients with type 2 diabetes mellitus display substantial evidence of oxidative stress [4]. Superoxide anion (O2•-), hydrogen peroxide (H2O2), hydroxyl radical (•OH), and singlet oxygen are examples of reactive oxygen species (ROS) (1O2) [5]. The main mechanisms of elevated ROS formation in diabetes are altered glucose metabolism, oxidative damage to pancreatic -cells, and endothelial dysfunction [5- 7]. The primary mechanisms of altered glucose metabolism, oxidative damage to pancreatic -cells, and endothelial dysfunction are identified as drivers of elevated ROS formation in diabetes [8]. The development of type 2 diabetes mellitus is heavily influenced by oxidative stress (T2DM) [9].

Troponins are also important cardiac biomarkers for detecting myocardial damage [10]. CK-MB, an isozyme of CK (creatine kinase), is one of the best serum enzymology diagnosis indicators of myocardial infarction. Only myocardium contains more than 40% CK-MB with a high specificity of the Myocardial injury diagnosis [11]. The aims of this study is to investigate the effect of Pfizer on ROS release and cardiac function test (troponin-I, creatin kinase) in Type 2 DM after vaccination.

2. Material and methods

2.1 Ethical approval

The study was performed in accordance with the Institutional Board Review's ethical permission (IRB) in the College of Health and Medical Technologies at Middle Technical University. (date of sample collections during periods from December 2021 to march 2022) All subjects provided their informed consent before blood collection.

Inclusion Criteria divide into three group:

- Subjects with T2DM vaccinated with the Pfizer vaccine (age 20-70 years) (physician diagnosis of T2DM according to ADA,2021)
- Subjects with T2DM, unvaccinated; aged 20–70 years. (physician diagnosis of T2DM according to ADA,2021)
- Non-diabetic healthy controls who had been vaccinated; no hypertension; age > 20-55 years

2.2 Exclusion

- physician diagnosis type 1 diabetes; diabetic type 2 vaccinated with sinopharum and AstraZeneca and patient vaccinated with one dose of p-fizer vaccine; gestational diabetes mellitus renal, liver disease, cardiac disease and auto immune disease all are excluded.

2.3 Sample collection

2 mL venous blood fasting plasma glucose, and cardiac function test, Following the separation of plasma/serum from blood cells,5-10 minutes of centrifugation at 2500g, then place in ependroff tube and store at -80

2.4 Methods

Fasting plasma glucose (FPG) was determined enzymatically, ROS (Reactive oxygen species), and cardiac function tests (Troponin-I, CK-MB).all parameters were determined using the CUSABIO ELISA Kit from the United States of America.

3. Results

The data in table (1) revealed most of diabetic patient had higher level of FPG than control With highly significant differences (< 0.0001)

Table (1): Comparison of FPG levels in T2DM and healthy controls

Variables	Study Groups	N	Mean±S.E	T-Test	P-value
FPG 70-110(mg/dl)	Controls	50	92.77±1.45	3	<0.0001
	DM-2 non-vaccinated	50	191.2± 10.2		
	DM-2 vaccinated	100	169.8±6.59		

(P≤0.05)

The data in table (2) represent that most of diabetic patients has higher level of ROS in significant differences (< 0.0001) than control was lower

Table (2) comparison of ROS among studied group

Variables	Study Groups	N	Mean±S.E	T-Test	P-value

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ROS U/I	Controls	50	534.2±28.27	62.22	<0.0001
	DM-2 non -vaccinated	50	2150±425.9		
	DM-2 vaccinated	100	1648±44.28		

(P≤0.05)

The data in table (3) showed higher level of troponin in diabetic patients in significant differences (<0.0001)

Table (3) comparison of (Troponin) among studied group

Variables	Study Groups	N	Mean±S.E	T-Test	P-value
Troponin-I (68-110) ng/dl	Controls	50	78.20± 1.950	98.17	<0.0001
	DM-2 non -vaccinated	50	80.30± 1.552		
	DM-2 vaccinated	100	104.4±1.283		

(P≤0.05)

The data in table (4) revealed most of diabetic patient had higher level of Ck-MB than control With highly significant differences (< 0.0001)

Table (4) comparison of CK-MB among studied group

Variables	Study Groups	N	Mean±S.E	T-Test	P-value
CK-MB (1.5-4.5) μg/ml	Controls	50	3.250±0.980	1.192	<0.0001
	DM-2 non -vaccinated	50	2.29±0.070		
	DM-2 vaccinated	100	3.956±0.125		

(P≤0.05)

4. Discussion

This is a recent study in Iraq to assess level of ROS in type -2 diabetes mellitus after immunization with second dose of Pfizer vaccine. ROS elevated in two groups of diabetic (non -vaccinated diabetic slightly higher than vaccinated diabetics) in compare with control because Diabetes is a metabolic disorder defined by hyperglycemia caused by abnormal in insulin synthesis, activity, maybe both ROS, such as hydrogen peroxide and superoxide anion, cause chemical changes in nearly all biological components, including negative effects on -cell islets [12]. Chronic hyperglycemia causes a rise in reactive oxygen species (ROS) and oxidative stress, as a results of glucose intolerance in diabetic individuals which leads to insulin resistance, beta cell degeneration and dyslipidemia [13].

Free radicals, oxidative stress, and other metabolic stressors have been linked to the etiology of type 2 diabetes. Diabetes mellitus (DM) is profoundly influenced by oxidative stress according to new research [14]. Due to disrupting the immunological response of the host, oxidative stress causes immunopathological effects [15]. The pathology of diabetes is intrinsically linked to the generation and activation of oxidative stress (OS) [16]. Biochemical assays of cardiac function test showed a highly significant level of troponin-1 in both vaccinated and non-vaccinated (DM II) in compared with control group The pathogenesis of vaccine-induced myocarditis is unknown, however it might be connected to the vaccine's active component, the mRNA sequence that encodes for the spike protein of severe acute respiratory syndrome coronavirus 2(SARS-CoV-2), or the immunological response that occurs after vaccination [17]. Although the etiology of myocarditis is unknown, genetic mimicry of the virus spikes protein and a heart protein, as well as immunologic pathway activation and a non-specific innate inflammatory response, have all been observed [18].

mRNA vaccinations may produce an excess of the Severe acute respiratory-2 Spike protein S1 subunit, which may interact with toll-like receptor 4, activate NF-B (nuclear factor-B), and cause cardiac inflammation and myocyte injury [19]. Some people have a higher seroprevalence of SARS-CoV-2 even if they are asymptomatic during the COVID-19 pandemic due to cytokine activation of pre-existing autoreactive immune cells [18]. Among the mechanisms linked to cardiac injury in COVID-19 patients are direct viral myocardial injury, microvascular injury, stress cardiomyopathy (Takotsubo), acute coronary syndrome, myocardial injury due to an oxygen supply and demand imbalance, and systemic inflammatory response with myocardial injury [20].

Angiotensin converting enzyme -2, protein is present in cardiomyocytes and acts as a receptor for attaching to the spiking proteins of the Sever acute respiratory syndromes –corona virus-2 [21]. as a result, the virus may cause direct myocyte damage. However, in significant COVID-19 infections, immunological activation, and cytokine storm-induced multi-system inflammation can occur, which can lead to both immediate heart failure and the progression of delayed myocarditis [22- 24].

Zhu and colleagues, results showed a significant number of patients that have previously infected with COVID-19 had cardiac-related comorbidities and myocardial injury [25]. Another cause of elevation of cardiac troponin may be not from vaccine, Zhong and colleagues, demonstrate elevated troponin I levels were linked to a history of diabetes rather than a high blood glucose level [26]. Bashir and colleagues, show that elevated levels of troponin I are found in T2DM patients who do not have any early clinical evidence of active cardiovascular disease [10]. Elevated cTnI levels were linked to a history of diabetes rather than a high blood glucose level [26].

All results was unconfirmed from vaccine and this higher level transient and may be disappear according to the study of CDC studied reports of patients experiencing myocarditis after receiving an mRNA COVID-19 vaccination (Pfizer or Moderna). 52 percent of patients reported no symptoms in the previous two weeks following immunization. Understanding the long-term health impacts is vital for conveying the hazards and advantages to the general population [27].

creatine kinase was also observed to be constant at higher levels in diabetics vaccinated and healthy control vaccinated in compared with diabetics non- vaccinated. There is minor elevation of creatine kinase (CK-MB) the elevation is unknown, this may be due to the Immunogenic or inflammatory reactions to vaccine lipid nanoparticles or mRNA components are possible [28]. myocarditis is linked to the immunological response elicited by vaccination in a patient. A genetically vulnerable host as the host produces antibodies, in opposition to the viral particle formed in response to the mRNA The antibodies in the vaccination may cross-react with surface antibodies. On the cardio myocytes, causing an inflammatory response.in regard to cell damage, this cell damage appears as focal patchy damage. Based on our limited experience and recent vaccine-related events, we believe According to press sources, myocarditis may occur in conjunction with the BNT162b2 vaccination [29]. Talotta, explain that safety of autoimmune myocarditis caused by COVID-19 has been linked to an increased risk in young people, particularly those aged under < 55, and a higher risk for immunological adverse effects a Increased chance of immunological side effects due to increased reactogenicity [30].

5. Conclusions

The current study found that Pfizer vaccine not cause abnormal elevation of ROS in diabetic's patient and controls. the ROS level did not change following the Pfizer vaccination, ALL Cardiac function test means with normal range (diabetics show a higher level of Troponin-I while CK-MB is higher in diabetics

vaccinated and healthy control comparison with diabetics non-vaccinated.

6. Recommendations

COVID-19 is life-threatening and immunization is important to reduce death.2. A third booster dose should be taken and the study needs follow-up.

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8. Reference

[1] Chang M, Nguyen TT. Strategy for Treatment of Infected Diabetic Foot Ulcers. Accounts of chemical research. 2021;54(5):1080-93.

[2] Rabinowich L, Grupper A, Baruch R, Ben-Yehoyada M, Halperin T, Turner D, et al. Low immunogenicity to SARS-CoV-2 vaccination among liver transplant recipients. Journal of Hepatology. 2021.

[3] Bae S, Lee YW, Lim SY, Lee JH, Lim JS, Lee S, et al. Adverse Reactions Following the First Dose of ChAdOx1 nCoV-19 Vaccine and BNT162b2 Vaccine for Healthcare Workers in South Korea. Journal of Korean medical science. 2021;36(17):e115.

[4] Forman HJ, Zhang H. Targeting oxidative stress in disease: promise and limitations of antioxidant therapy. Nature reviews Drug discovery. 2021;20(9):689-709.

[5] Borisov VB, Siletsky SA, Nastasi MR, Forte E. ROS Defense Systems and Terminal Oxidases in Bacteria. Antioxidants (Basel, Switzerland). 2021;10(6).

[6] Al-Mashhadani HA, Alshujery MK, Khazaal FA, Salman AM, Kadhim MM, Abbas ZM, et al., editors. Anti-Corrosive Substance as Green Inhibitor for Carbon Steel in Saline and Acidic Media. Journal of Physics: Conference Series; 2021: IOP Publishing.

[7] AlMashhadani HA, saleh KA. Electro-polymerization of poly Eugenol on Ti and Ti alloy dental implant treatment by micro arc oxidation using as Anti-corrosion and Anti-microbial. Research Journal of Pharmacy and Technology. 2020;13(10):4687-96.

[8] Darenskaya MA, Kolesnikova LI, Kolesnikov SI. Oxidative Stress: Pathogenetic Role in Diabetes Mellitus and Its Complications and Therapeutic Approaches to Correction. Bulletin of experimental biology and medicine. 2021;171(2):179-89.

[9] Banik S, Ghosh A. The association of oxidative stress biomarkers with type 2 diabetes mellitus: A systematic review and meta-analysis. Health science reports. 2021;4(4):e389.

[10] Bashir A, Azharuddin M, Rashid I, Murti K, Pandey K. Predictors of cardiomyopathy in patients with type-2 diabetes mellitus with and without cardiovascular complications: A cross-sectional study. Diabetes Res Clin Pract. 2019;154:90-100.

[11] Sun Z, Wu W, Liu J, Ma N, Zheng Z, Li Q, et al. Influence of glucose-lowering rate on CKMB and

myoglobin serum levels in type-2 diabetes patients with coronary heart disease. Human immunology. 2014;75(12):1182-7.

[12] Singh A, Kukreti R, Saso L, Kukreti S. Mechanistic Insight into Oxidative Stress-Triggered Signaling Pathways and Type 2 Diabetes. Molecules (Basel, Switzerland). 2022;27(3).

[13] Kooshki F, Tutunchi H, Vajdi M, Karimi A, Niazkar HR, Shoorei H, et al. A Comprehensive insight into the effect of chromium supplementation on oxidative stress indices in diabetes mellitus: A systematic review. Clinical and experimental pharmacology & physiology. 2021;48(3):291-309.

[14] Qureshi K, Naeem N, Tariq J, Chaudhry MS, Pasha F. New-Onset Insulin Allergy After COVID-19 Infection in an Insulin-Dependent Type-2 Diabetic Patient: A Rare Complication. Cureus. 2021;13(9):e17879.

[15] Bakadia BM, Boni BOO, Ahmed AAQ, Yang G. The impact of oxidative stress damage induced by the environmental stressors on COVID-19. Life sciences. 2021;264:118653.

[16] Xu Y, Tang G, Zhang C, Wang N, Feng Y. Gallic Acid and Diabetes Mellitus: Its Association with Oxidative Stress. Molecules (Basel, Switzerland). 2021;26(23).

[17] Singh B, Kaur P, Cedeno L, Brahimi T, Patel P, Virk H, et al. COVID-19 mRNA Vaccine and Myocarditis. European journal of case reports in internal medicine. 2021;8(7):002681.

[18] Das BB, Moskowitz WB, Taylor MB, Palmer A. Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination: What Do We Know So Far? Children (Basel, Switzerland). 2021;8(7).

[19] Truong DT, Dionne A, Muniz JC, McHugh KE, Portman MA, Lambert LM, et al. Clinically Suspected Myocarditis Temporally Related to COVID-19 Vaccination in Adolescents and Young Adults: Suspected Myocarditis After COVID-19 Vaccination. Circulation. 2022;145(5):345-56.

[20] Mesquita ET, Jorge AJL, Villacorta H, Danzmann LC, Martins WdA. Heart Failure with Preserved Ejection Fraction and COVID-19: a Pernicious Relationship. International Journal of Cardiovascular Sciences. 2020;33:412-8.

[21] Goulter AB, Goddard MJ, Allen JC, Clark KL. ACE2 gene expression is up-regulated in the human failing heart. BMC medicine. 2004;2:19.

[22] Ishikura H, Maruyama J, Hoshino K, Matsuoka Y, Yano M, Arimura T, et al. Coronavirus disease (COVID-19) associated delayed-onset fulminant myocarditis in patient with a history of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy. 2021;27(12):1760-4.

[23] AlMashhadani HA. Synthesis of a CoO-ZnO nanocomposite and its study as a corrosion protection coating for stainless steel in saline solution. International Journal of Corrosion and Scale Inhibition. 2021;10(3):1294-306.

[24] Hayfaa AA, Khulood ASA, AlMashhadani HAY, editors. Study the Effect of Cyperus Rotundus

Extracted as Mouthwash on the Corrosion of Dental Amalgam. IOP Conf Series: Materials Science and Engineering; 2019.

[25] Zhu Z, Wang M, Lin W, Cai Q, Zhang L, Chen D, et al. Cardiac biomarkers, cardiac injury, and comorbidities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. Immunity, inflammation and disease. 2021;9(4):1071-100.

[26] Zhong B, Wang Y, Zhang G. History of diabetes mellitus is associated with elevated cardiac troponin I levels in patients with chest pain but no coronary heart disease. Cardiology journal. 2016;23(2):149-54.

[27] Kyaw H, Shajahan S, Gulati A, Synn S, Khurana S, Nazar N, et al. COVID-19 mRNA Vaccine-Associated Myocarditis. Cureus. 2022;14(1):e21009.

[28] Remmel A. COVID vaccines and safety: what the research says. Nature. 2021;590(7847):538-40.

[29] Park J, Brekke DR, Bratincsak A. Self-limited myocarditis presenting with chest pain and ST segment elevation in adolescents after vaccination with the BNT162b2 mRNA vaccine. Cardiology in the young. 2022;32(1):146-9.

[30] Talotta R. Do COVID-19 RNA-based vaccines put at risk of immune-mediated diseases? In reply to "potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases". Clin Immunol. 2021;224:108665.