

ORIGINAL ARTICLE

# Evaluation of some cardiac markers in relation to COVID-19 mRNA vaccine

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## Abstract

**Background:** Acute myocardial infarction (AMI) is a dangerous cardiovascular illness that has a significant impact on people's health. Several biomarkers, including Myoglobin and troponin I (cTnI) were utilized to diagnose AMI in recent decades. The Troponin I (cTnI) was designated as the "gold standard" cardiac biomarker for the prediction of cardiomyopathy. It's a heart muscle regulating protein found on normal myocyte actin filaments. When cardiac muscles are injured, cTnI, one of the main subunits of the cardiac troponin complex, is released into the circulation (e.g., myocardial infarction). Myoglobin denoted by (symbols Mb and MB) seems to be an iron- and o<sub>2</sub>-binding protein present in the vertebrate heart and skeletal muscle tissues and, more specifically, nearly all mammals. In humans, MB is only present in the bloodstream following muscle damage. Its primary function is to supply myocytes with oxygen. Also essential to nitric oxide hemostasis was myoglobin. Additionally, it facilitates the detoxification of response oxygen molecules from the body. MB is accountable for most vertebrate muscles' red hue. The aim: To assess the difference in the level of (MYOGLOBIN and TROPONIN\_I) between patients with and without mRNA Vaccination.

**Methods:** This study included 125 patients (65 male and 60 female) with vaccinated and non-vaccinated covid-19 with an age range of 20–69 years. These patients are divided into two main groups: 1. vaccinated (vaccinated with COVID-19 infection, vaccinated without COVID-19 disease, vaccinated recovered from the CoV-19 virus), 2. unvaccinated (infected with the CoV-19 virus and non-vaccinated, recovered from covid-19 and unvaccinated). The outcome is measured using the Enzyme-linked immunosorbent assay (ELISA) technique. This study was conducted during the period from November 2021 to May 2022 at the Martyr Dr. Fairouz General Hospital, Wasit governorate, Iraq.

**Result:** Estimation of serum Troponin I and Myoglobin concentration showed that concentrations of Troponin I and Myoglobin were significantly higher ( $P < 0.0001$ ) in individuals infected with CoV-19 virus and unvaccinated higher than vaccinated with CoV-19 disease indicating the impact of the vaccine on the increment of both markers. However, the level of each marker was substantially higher ( $P < 0.0001$ ) in vaccinated with CoV-19 infection more than vaccinated without or recovered from COVID-19 illness.

**Conclusions:** The use of mRNA CoV-19 vaccination significantly modulate the increment of Troponin I and Myoglobin and improves the cardiac symptomatology in patients with CoV-19 infection.

**Keywords:** Covid-19, Covid-19 vaccination, Troponin I, Myoglobin

# 1 Introduction

In 1965, a novel protein component of the cardiac myofibrillar apparatus was found, and it was given the name troponin [1]. Troponins are found in the blood 4–10 hours after the beginning of AMI, according to several investigations [2]. Troponin levels reach their peak between 12 and 48 hours, but remain increased for four to ten days. When samples are taken 6–12 hours after the beginning of acute chest pain onset, the sensitivity for identifying troponin T and I reaches 100% [3]. Tn is a constituent of skeletal and heart myocytes' contractile device. Calcium ions and troponin protein regulate and increase the connection between the filaments of both actin and myosin during the sliding filaments mechanism of muscular contractions. The (cTn) complex is made up of 3 subtypes: 1. Troponin T: cTn complex is bound to the actin filaments by this protein. 2. Troponin C: provides a Ca<sup>+</sup> binding site. 3. Troponin I: As in absence of adequate Ca<sup>+</sup> ions, prevents interactions with myosin heads [4].

Cardiac troponins (cTn) (cTnI and cTnT) are indeed the gold standard for determining cardiac injury and cardiomyocyte necrosis, in addition to the most extensively used biomarker for identifying cardiac toxicity [5]. Myoglobin belongs to the globin family, along with cytoglobin, hemoglobin, and neuroglobin. Myoglobin has the closest evolutionary relationship to cytoglobin. In mammals, this cytoplasmic hemoprotein is highly produced in cells derived from striated muscles (example cardiomyocytes and oxidative skeletal muscles myofibers). Myoglobin is a hemoprotein that stores oxygen (O<sub>2</sub>), transports O<sub>2</sub> within cells, and controls the equilibrium of Oxygen and nitric oxide (NO) [6]. Any study of myoglobin functions should get started with Millikan's (1939) influential research, in which he establishes that Mb is generated adaptively in tissue in reaction to O<sub>2</sub> consumption and that it helps to the O<sub>2</sub> availability of these tissues [7]. MB, a mobile O<sub>2</sub> carrier, is produced in red muscles in reaction to mitochondrial oxygen consumption [8] and carries O<sub>2</sub> from the sarcolemma of the vertebrate cardiac and red muscles cell to the mitochondria [9].

Low tissue O<sub>2</sub> pressure can induce myoglobin production. Definitely, myoglobin messenger RNA is increased when myoglobin production is induced [10]. Myoglobin is crucial for sustaining fetal heart function [11]. In the past thirty years, developments in immunochemical methods have enabled quick detection of a range of markers signaling cardiac cell death achievable. Several blood proteins, such as myoglobin, creatine kinase muscle–brain type (CK-MB), and troponins, have demonstrated greater sensitivity in identifying Acute myocardial infarction than history and electrocardiogram (ECG) alone [12]. The evidence supporting cardiac necrosis indicators such as myo-

globin, CK-MB, and troponin is firmly established [13]. SARS-CoV-2 is the initial coronavirus to be found in Wuhan, China through 2019 and was responsible for the outbreak of a respiratory ailment that was subsequently designated COVID-19. Typically, the virus is transmitted through airborne droplets and quickly spreads through coughs, sneezing, speaking, and the contamination of hard surfaces with droplets. Infection people may exhibit moderate to severe illness symptomatology, and those with comorbidities are more prone to acquire serious diseases [14]. The Severe acute respiratory-CoV-2 is a single-stranded RNA viral surrounded by a capsid protein envelope [15]. COVID-19 could cause a fatal disease, similar to its precursor SARS-CoV. WHO had classed it as an epidemic afflicting the entire population due to its widespread geographical impact on a disproportionately large proportion of the global population [16]. COVID-19 seems to be an acute illness that can affect multiple organs via the lungs. The renal, hepatic, muscles, neurological system, and spleen are among these organs [17]. The SARS-CoV-2 utilized the angiotensin-converting enzyme 2 (ACE2) like its receptors on the surface of the cell targeted by the Coronaviruses. primarily their corresponding receptors onto target cells through their surface S proteins [18].

Over 39.7 million patients were infection with Severe acute respiratory-CoV-2 worldwide, and also higher than 1.1 million were killed in 2020. The incidence of illnesses is rising [19]. The vast majority of persons affected with coronavirus have mild to moderate respiratory difficulties and recover without extra treatment. Those who have ongoing health issues are more likely than the elderly to experience major diseases such as cardiovascular disease, diabetic, chronic respiratory diseases, and cancers [20]. Acute cardiac damage caused by COVID-19 has grown more common in recent years. Myocarditis is one of the most common kinds of heart damage. cytokine release syndrome, acute coronary syndrome, stress-induced cardiomyopathy, and sepsis-induced cardiomyopathy are all examples of COVID-19-related heart damage [21]. When it comes to patients with COVID-19, cardiovascular disease is a major cause of mortality and disability [22]. SARS-CoV-2 disease have been linked to an elevate in inflammation, which can lead to cardiac arrhythmia, myocarditis, and vascular inflammation, which can lead to heart failure [23]. Cardiac symptoms in COVID-19 appear at different times: through CoV-19 virus and/or subsequent to the apparent CoV-19 virus recovery [24,25]. Myocardial/pericardial inflammatory, arrhythmias, cardiac failure, and sudden cardiac fatality have been characterized as cardiac complications in the acute period (pre-recovery), that are more prevalent with increased COVID-19 intensity, co-

morbidities, and advanced age [26].

COVID-19 diagnostic, treatment, and prognosis may benefit from the use of cardiac biomarkers. Furthermore, cardiac biomarkers are often high in a variety of cardiac pathologies, and they're often elevated in pulmonary diseases. Cardiovascular indicators may indicate mixed disease if CoV-19 virus patients have a history of pulmonary comorbidity, which is prevalent [27]. These findings imply that increased cTn and myoglobin levels in CoV-19 virus patients may be attributable to direct myocardial damage and can be utilized to predict risk of mortality [28].

## 2 Methods and Materials

**The Subjects:** The study was approved by the Medical Human Research Ethics Committee at the Faculty of Medicine, University of Al-Qadisiyah, Iraq. A case-control study was conducted on 125 from Healthy individuals with a positive vaccine of CoV-19, patients with positive CoV-19 virus (vaccinated and non-vaccinated) having severe and mild COVID-19 symptoms and individuals with recovered COVID-19 (vaccinated and non-vaccinated).

The ages have included in the study and the control group has from 20 - 69 years. This study included two primary groups, one has included patients who have been mRNA vaccination of covid-19 and another one without mRNA vaccination of covid-19. The first main group was divided into the following subgroups: Group I: individuals with a positive vaccine of covid-19. [25] Group II: patients with positive COVID-19 and vaccinated. [25]

- Group III: patients with recovered COVID-19 and vaccinated. [25] The second main group also was further subdivided into:
  - Group IV: patients with positive COVID-19 but non-vaccinated. [25]
  - Group V: patients with recovered COVID-19 but non-vaccinated. [25]

About 5ml of venous blood was obtained from each participant. Blood samples were left for 15 minutes at room temperature to clot. Ten minutes of centrifugation at 3000 rpm were used to isolate serum after coagulation. Serum was aspirated and divided into small aliquots and the serum was converted into an Eppendorf tube, labeling of the tube, and stored at (-20 °C) until assayed for Myoglobin and Human Troponin I (Tn-I).

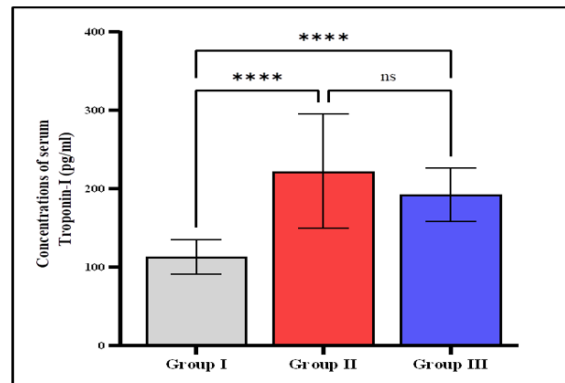
## 2.1 Determination of Myoglobin and Human Troponin I

Serum Myoglobin and Human Troponin I level were estimated by sandwich Eliza technique using My BioSource® kits.

**Inclusion criteria:** Individuals with a positive vaccine of the CoV-19 virus, patients with positive CoV-19 virus (vaccinated and non-vaccinated), and patients with recovered COVID-19 (vaccinated and non-vaccinated). **Exclusion criteria:** The research excluded all patients with - co-morbidity with chronic disease and hematological disease. - Hypertension. - Diabetes mellitus (type 1, type 2, pre-diabetes, gestational diabetes). - HIV/AIDS. - Cancers.

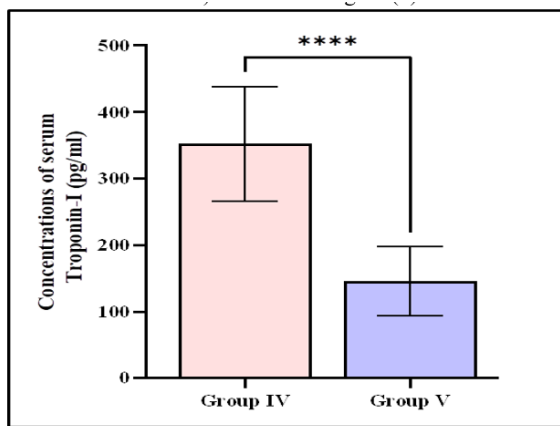
## 3 RESULT

**Estimation of Serum TROPONIN-I (TnI) Concentrations:** The measurement of serum troponin I level (pg/ml) for the vaccinated groups (I, II, and III) demonstrated that the concentration of troponin I was substantially higher ( $P < 0.0001$ ) in group II (vaccinated with COVID-19) more than group I and III as shown in Figure 1.



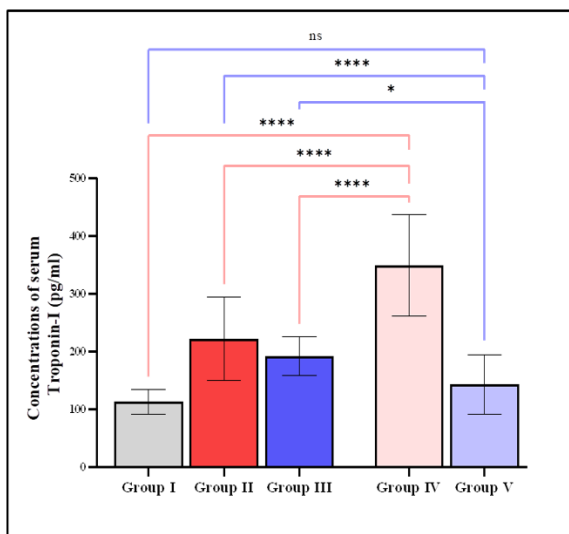
**Figure 1:** The measurement of serum troponin-I concentration (pg/ml). Group I (vaccinated without CoV-19 virus), Group II (vaccinated with CoV-19 virus) and Group III (vaccinated recovered CoV-19 virus). Troponin I was significantly higher in group II (vaccinated with CoV-19 virus) more than others in groups I and III. Data are expressed as means  $\pm$  SD. Indicates \*\*\*\*  $p$  - value  $< 0.0001$

For non-vaccinated groups (IV and V) the troponin I was significantly higher ( $P < 0.0001$ ) in group IV (no vaccine with COVID-19) more than group V (no vaccine recovered COVID-19) as shown in Figure 2.



**Figure 2:** The measurement of serum troponin-I concentration (pg/ml). Group IV (no vaccine with COVID-19) and Group V (no vaccine recovered COVID-19) Troponin I was significantly higher in group IV (no vaccine with COVID-19) more than in group V (no vaccine recovered COVID-19). Data are expressed as means  $\pm$  SD. Indicates \*\*\*\*  $p$ -value  $< 0.0001$

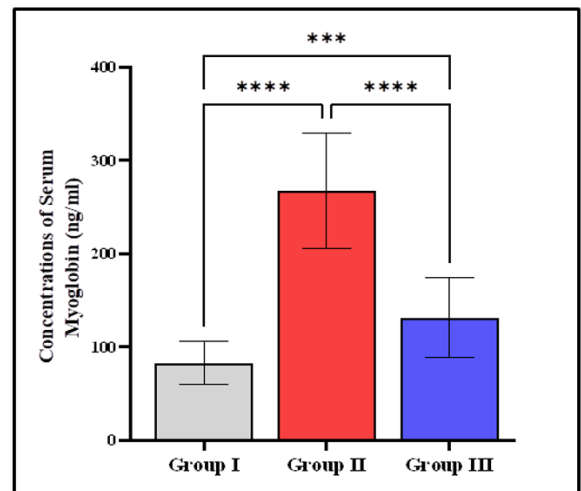
Figure 3 showed that group IV (no vaccine with COVID-19) has the highest troponin level among all the studied groups.



**Figure 3:** Estimation of troponin-I concentrations (pg/ml) for all study groups. The measurement of troponin-I was substantially higher in group IV (vaccinated with COVID-19) among all the studied groups. Data are expressed as means  $\pm$  SD. Indicates \*\*\*\*  $p$ -value  $< 0.0001$ .

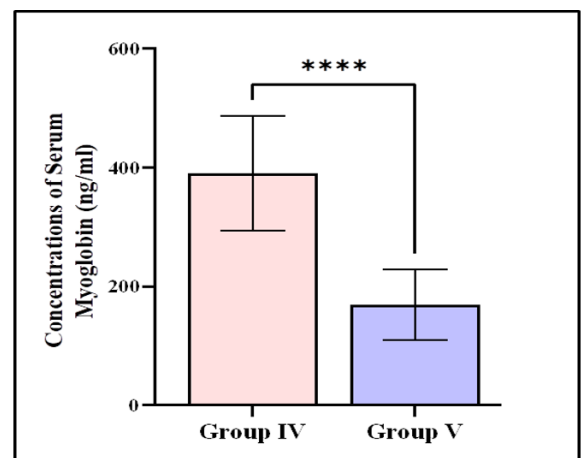
### 3.1 Estimation of Serum Myoglobin Concentrations

The measurement of serum myoglobin level (ng/ml) for the vaccinated groups (I, II, and III) showed that the concentration of myoglobin was substantially higher ( $P < 0.0001$ ) in group II (vaccinated with COVID-19) more than group I and III as shown in Figure 4.



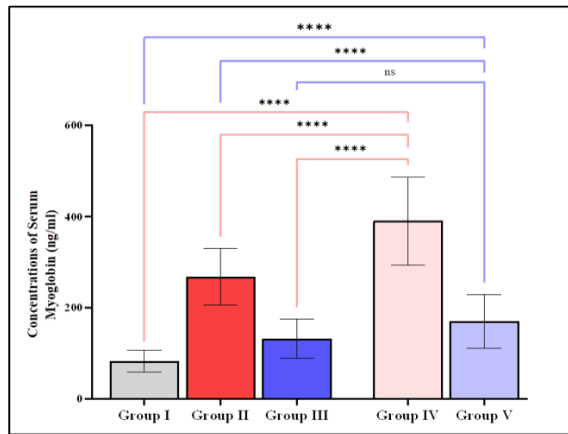
**Figure 4:** The measurement of serum myoglobin concentration (ng/ml). Group I (vaccinated without CoV-19 virus), Group II (vaccinated with CoV-19 virus) and Group III (vaccinated recovered CoV-19 virus). Myoglobin was significantly higher in group II (vaccinated with COVID) more than others in groups I and III. Data are expressed as means  $\pm$  SD. Indicates \*\*\*\*  $p$ -value  $< 0.0001$

For non-vaccinated groups (IV and V) the myoglobin was significantly higher ( $P < 0.0001$ ) in group IV (no vaccine with COVID-19) more than group V (no vaccine recovered COVID-19) as shown in Figure 5.



**Figure 5:** The measurement of serum myoglobin concentration (ng/ml). Group IV (no vaccine with COVID-19) and Group V (no vaccine recovered COVID-19) Myoglobin was significantly higher in group IV (no vaccine with COVID-19) more than in group V (no vaccine recovered COVID-19). Data are expressed as means  $\pm$  SD. Indicates \*\*\*\*  $p$ -value  $< 0.0001$

Figure 6 showed that group IV (no vaccine with COVID-19) has the highest troponin level among all the studied groups.



**Figure 6:** Estimation of myoglobin concentrations (ng/ml) for all study groups. The measurement of myoglobin was substantially higher in group IV (vaccinated with COVID-19) among all the studied groups. Data are expressed as means  $\pm$  SD. Indicates \*\*\*\* p-value  $< 0.0001$

## 4 Discussion

### 4.1 Estimation of Serum TROPONIN-I (TnI) Concentrations

cTnI is a component of the heteromeric proteins complex troponin (Tn), which is linked to the thin filament. (Tn) complex regulates the contraction of both skeletal and cardiac muscles. The TnI subunit inhibits actomyosin formation when intracellular  $Ca^{2+}$  concentrations are low [29]. The present study was to assess the levels of TROPONIN\_I in patients with mRNA Vaccination of Covid-19 and to the evaluation of the effect of the vaccine on the level of TnI. In this study, noticed that the concentration of Troponin I for the vaccinated groups was significantly higher ( $P < 0.0001$ ) in individuals infected with CoV-19 virus and vaccinated more than vaccinated, non-infected with covid-19 and patients that vaccinated, recovery from covid-19 as indicated in the Figure 1. The current results were consistent with the study of the [30–32] they during this huge case series from the United States, the authors describe 140 occurrences of clinically diagnosed myocarditis that were temporally associated to the COVID-19 vaccinated [32].

According to reports, myocarditis has become one of the symptomatology of CoV-19 virus infection. The suggested pathophysiology includes direct damage caused by (i) viral invasion of cardiac myocytes, (ii) the host immunity response of cytotoxic T cells, and (iii) the existence of acute inflammation and the cytokine storm [33]. Nevertheless, the connection between COVID-19 vaccinated and myocarditis remains anecdotal, and also no mechanism has been discovered. This is one of the initial cases of potential mRNA-based COVID-19 vaccinated myocarditis to be published in the medical journals, with extensive clinical

and translational evaluation and comparison to several control groups [34].

For non-vaccinated groups, the present study showed that troponin I was significantly higher ( $P < 0.0001$ ) in individuals infected with CoV-19 virus and unvaccinated more than patients that non-vaccinated and recovery from CoV-19 virus as indicated in the Figure 2. The current outcomes were consistent with the study of [35–37] They noted the elevation in (Tn) was associated with systemic illnesses and could be a cautionary indicator for the mortality of COVID-19 patients and that this deserves significant consideration in the context of clinical practise [38]. Through the numerous causes of cardiac damage addressed, it has been determined that high TnI in COVID-19 patients mostly results from three primary diseases: myocarditis, microangiopathy, and myocardial infarction (MI). MI is possibly the most well-understood cardiovascular contraindication of COVID-19 [39], Studies have also demonstrated that infection with COVID-19 provokes myocardial inflammatory and damage, and myocardial injuries are linked to increased occurrences of (ARDS), coagulopathy, and the requirement for noninvasive and invasive ventilation [40].

The results of the study were disagreed with those of Apple [41, 42] There are concerns that certain high-sensitivity myocardial troponin analyses do not match these criteria; nonetheless, the use of a high sensitivity ctnI test would not raise the percentage of with increased levels of cardiac troponin above the 99th percentile. In this research, noticed that patients infected with COVID-19 and non-vaccinated has the highest troponin I level among all the studied groups as shown in Figure 3. The current results were consistent with the study of the [43, 44] which Researchers discovered the likelihood of myocardia after a CoV-19 virus diagnostic is significantly higher than the incidence of myocarditis after a CoV-19 vaccinated, including all ages and gender. Altogether, the incidence within 30 days of a CoV-19 virus diagnosis was about 17 times greater than the rate among those who received the CoV-19 virus vaccine and also, they found that the risk of myocarditis in patients with the CoV-19 virus was roughly 16 times that of patients without the CoV-19 virus. The results of the study were disagreed with Ling RR et al. it was shown the risk of myocarditis wasn't really significantly different between persons who received COVID-19 immunizations and those who didn't get COVID-19 vaccines [45].

### 4.2 Estimation of Serum Myoglobin Concentrations

Mb is an essential intracellular oxygen-binding hemoprotein present in the cytoplasmic of vertebrate types I and IIa skeletal and heart muscle tissues. It is

widely recognised that Mb serves as an oxygen storage [46]. In this study, noticed that the concentration of Myoglobin for the vaccinated groups was substantially higher ( $P < 0.0001$ ) in individuals infected with CoV-19 virus, vaccinated more than vaccinated, non-infected with covid-19 and patients that vaccinated, recovery from covid-19 as shown in Figure 4. This result agreed with [47, 48] who found an elevated concentration of myoglobin for carditis after administration of the COV-19 mRNA vaccine. Moreover, this risk elevated was more probably to occur following the second vaccination dose compared to the first. In addition, none of the Twenty case patients with carditis following vaccination were transferred to the ICU or died during the observation period, whereas 14 of 133 unvaccinated individuals were sent to the ICU and 12 died. Our experiences and published studies have demonstrated that, to yet, the majority of reported episodes of carditis following immunization are self-limiting and have a favourable prognosis.

For non-vaccinated groups, the present study showed that Myoglobin was

significantly higher ( $P < 0.0001$ ) in individuals infected with CoV-19 virus and non-vaccinated more than patients that non-vaccinated and recovery from covid-19 as indicated in the Figure 5. The current results were compatible with the research of [49] that revealed the increased myoglobin was more prevalent in individuals with severe CoV-19 virus than in cardiac troponin I. Therefore, increased Mb may be used as a determinant of adverse COVID-19 outcomes. Also, [50] Who observed that the percentages of patients COVID-19 and unvaccinated with elevated MYO concentration were greater in the group with raised TnI. The biomarker was specific to MYO for the acute assessment of myocardial infarction and coronary heart disease. Following myocardial damage, the increase in serum MYO begins before the increase in TnI.

In this study, noticed that patients infected with COVID-19 and non-vaccinated has the highest Myoglobin level among all the studied groups as shown in Figure 6. The current outcomes were consistent with the research of [51] fully vaccinated individuals had considerably higher myoglobin levels than imperfectly vaccination and unvaccination patients. The results of the study were disagreed with [52, 53] it was shown which no clinical studies have reported the incidence of carditis following vaccination against CoV-19 virus. SARS-cov-2 is thought to be the cause of myocarditis, but only a few instances have been recorded following SARS-CoV-2 vaccinated. Possible causes include direct virus-induced damages to infect cardiac myocytes and T-cells-mediated cytotoxicity [54], in addition to immunological responses induced by vaccine viral components or immunostimulatory adjuvants [55], These rare events of myocarditis described following SARS-

CoV-2 vaccinated were characterized by a shorter, self-limiting course without permanently harm cardiac function, and affected mostly young men with a mean age of twenty-five [56].

## 5 Conclusions

Troponin I and Myoglobin concentrations were significantly increased in patients infected with CoV-19 virus and non-vaccinated in comparison with the rest of the groups vaccinated and unvaccinated. Patients who had the mRNA covid-19 vaccine exhibited a significant reduction in the concentrations of Troponin I and Myoglobin as compared with patients without mRNA covid-19 vaccine. Thus, covid-19 vaccination gives superior outcomes in reducing the inflammatory events of Troponin I and Myoglobin and improving symptoms in patients with covid-19.

**Conflict of Interest:** None

**Ethical consideration: from ethical committee in the Conflict of Interest:** None

**Ethical consideration:** from ethical committee in the University of Medical Laboratory Technician; the Martyr Dr. Fairouz General Hospital in Wasit city, Iraq.

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