Available online at *www.ujpronline.com*
Universal Journal of Pharmaceutical Research
An International Peer Reviewed Journal
ISSN: 2831-5235 (Print); 2456-8058 (Electronic)
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REVIEW ARTICLE

CARDIOVASCULAR COMPLICATIONS OF COVID-19 VACCINATION, ITS DIAGNOSIS, PATHOGENESIS, AND TREATMENT: A REVIEW

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Article Info:

Article History:
Received: 4 December 2024
Reviewed: 14 January 2025
Accepted: 18 February 2025
Published: 15 March 2025

Cite this article:
Fatima M, Ali E, Shafqat A, Tariq MT, Gulraiz L, Imran F, Hussain N, Awais J, Rasheed N, Mustafa MA. Cardiovascular complications of COVID-19 vaccination, its diagnosis, pathogenesis, and treatment: A review. Universal Journal of Pharmaceutical Research 2025; 10(1): 80-85.
http://doi.org/10.22270/ujpr.v10i1.1277

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Abstract

SARS-CoV-2 was the virus responsible for the COVID-19 pandemic that emerged in 2019. To date, over 670 million individuals have received mRNA-based COVID-19 vaccines. However, emerging evidence suggests a potential association between these vaccines and cardiovascular complications. Concerns have been raised regarding their possible contribution to underrecognized cardiovascular issues, such as arrhythmias and arterial hypertension. The individuals with pre-existing heart conditions are at a higher risk of adverse cardiovascular events and unfavorable clinical outcomes following vaccination. Reported complications include myocarditis, arrhythmias, acute coronary syndromes, heart failure, and thromboembolic events. This review discusses the underlying mechanisms, diagnostic techniques, strategies for treatment, and current limitations of the literature on the possible link between mRNA COVID-19 vaccinations and cardiovascular problems.

Keywords: Cardiovascular complications, COVID-19, COVID-19 vaccination, immunization, mRNA vaccine safety, public health, vaccine-related complications.

INTRODUCTION

The article explained the worldwide health crisis caused by SARS-CoV-2, which originated in Wuhan, China. Researchers have developed various vaccines and treatments, including adenoviral vector vaccines such as Ad26.COV2.S, mRNA-based vaccines like BNT162b2 and mRNA-1273, and others like Sputnik V, CoronaVac, and Oxford-AstraZeneca. Due to the urgent need for control, regulatory authorities granted emergency authorization for these vaccines[1].

The COVID-19 vaccine can cause mild side effects, but concerns persist about its lasting impact on the cardiovascular system. Despite the recovery, complications like multi-organ damage and secondary infections persist. Long-term effects can affect the cardiovascular, nervous, and mental health systems, increasing the risk of mortality. Patients with preexisting conditions, such as heart disease, diabetes, or neurological conditions, are more likely to experience prolonged symptoms despite most recovering within two to four weeks[2].

Healthcare professionals closely monitor cardiovascular complications associated with SARS-CoV-2, which tend to become more severe within the first six months after infection. These conditions include heart failure, myocardial injury, arrhythmias, and coagulation disorders, increasing the risk of mortality and poor health outcomes. COVID-19 can cause significant cardiovascular damage, as indicated by elevated levels of the cardiac biomarker troponin T. Men with myocardial injury often exhibit ST-segment elevation and obstructive coronary artery disease, while women are more likely to experience non-obstructive coronary artery disease. A growing number of patients report persistent chest pain months after their initial infection, raising concerns about long-term cardiovascular effects[3]. Scientific research is crucial for

identifying and addressing cardiovascular issues during the acute and post-acute stages of COVID-19 infection. This review aims to provide a concise yet comprehensive analysis of COVID-19 vaccine-induced complications, with a particular focus on cardio-vascular adverse events. It will examine the specific vaccines linked to these complications, elucidate the underlying pathophysiological mechanisms, discuss diagnostic approaches, outline treatment strategies, and highlight follow-up protocols for affected individuals.

METHODS

The study was conducted over four months, from July 28, 2024 – October 11, 2024 with ethical approval granted by the Ethics Committee for Research at the University of Biological and Applied Sciences (UBAS) in Lahore, Pakistan (Reference No. ERB-PHRMD-DPC/1517). The review primarily relied on PubMed and Cochrane databases, adhering to PRISMA flow statement guidelines. Relevant studies were identified using specific keywords, including COVID-19, COVID-19 Vaccinations, Vaccine-Induced Cardio-vascular Complications, mRNA Vaccines, and Vaccine-Induced Complications, covering research from 2010 to 2025. Additionally, supplementary searches were conducted across various electronic databases, such as Google Scholar. Only English-language studies published within the specified period were considered for inclusion. Figure 1 presents a PRISMA flow chart outlining the systematic review process.

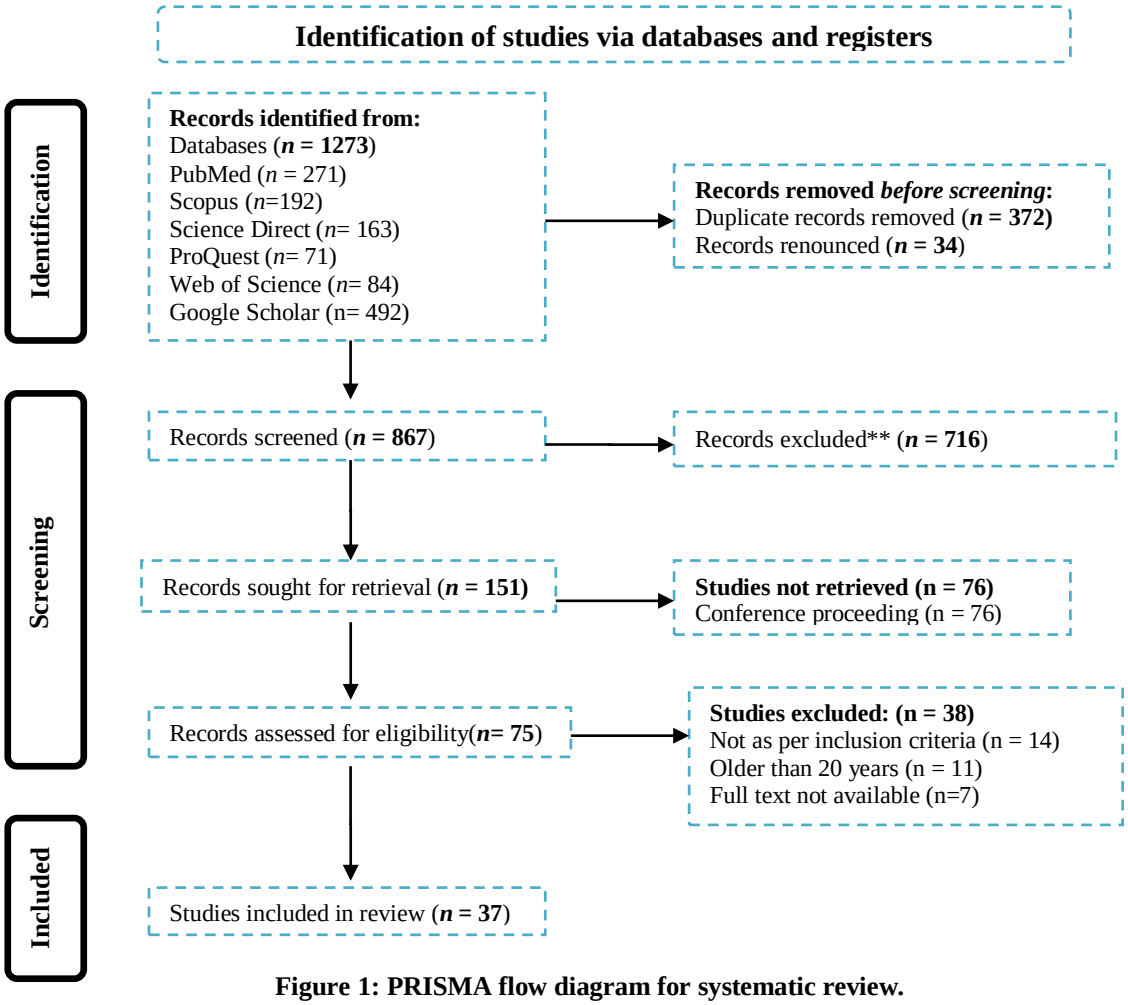

Figure 1: PRISMA flow diagram for systematic review.

Exclusion criteria

- Other related vaccinations for infections like influenza and asthma, etc.
- Other than cardiovascular complications.
- Research articles published in languages other than English
- Studies published before 2010

Data extraction

The extracted data included author details, the year of the study, COVID-19, COVID-19 vaccinations, vaccines induced cardiovascular complications, mRNA vaccines, diagnosis, pathogenesis, treatment, and limitations.

COVID–19, its vaccination, and their hazards

Vaccines play a crucial role in preventing infectious diseases and are developed using various technologies to ensure their effectiveness and safety. The main types include live attenuated, inactivated, subunit, toxoid, vector-based, and mRNA vaccines. Recently, mRNA vaccines, such as Pfizer-BioNTech and Moderna, along with vector-based vaccines like Oxford-AstraZeneca, have been designed to provide immunity by utilizing genetic material or harmless viral carriers. Despite their

benefits, vaccines may carry certain risks, including mild side effects like fever, soreness, and fatigue. In rare cases, adverse reactions such as allergic responses, CVS complications like myocarditis, or blood clotting disorders have been reported, particularly with some COVID-19 vaccines. However, the benefits of vaccination in preventing severe disease and death outweigh the potential risks, and ongoing research continues to improve vaccine safety and effectiveness.[4]

COVID-19 associated Cardiovascular (CV) Complications, mRNA vaccines and cardiac patient

COVID-19 CV complications

Myocarditis and pericarditis have been recorded in response to mRNA COVID-19 immunization, with young males aged 12 to 29 being more susceptible, especially after the second dose. However, the total incidence is still lower than the danger of myocarditis induced by SARS-CoV-2. Studies indicate that COVID-19 itself can lead to severe cardiovascular complications, including heart failure, arrhythmias, stroke, thrombosis, myocardial injury, and sudden cardiac death. These effects are linked to viral-induced epitheliopathy, hypercoagulation, and reduced fibrinolytic activity[5].

mRNA vaccine and CVS complications

Observational studies suggest that mRNA vaccines, particularly Moderna, have a slightly higher association with myocarditis than Pfizer-BioNTech. Additionally, vaccine-induced thrombotic thrombocytopenia and pulmonary embolism have been more frequently associated with mRNA and vector-based vaccines compared to inactivated vaccines. Elderly individuals, particularly those over 75, have also been reported to experience myocardial infarction and cardiac arrest post-vaccination[6].

Health concerns for cardiac patients

COVID-19 vaccination is crucial, especially for those with preexisting heart conditions, as it reduces the risk of severe illness and mortality. Cardiovascular complications following mRNA vaccination are rare and mild, but further research is needed to fully understand the long-term cardiovascular effects of both the virus and vaccination[7,8].

Identification and administration process of COVID-19 vaccination

The COVID-19 vaccination process involves identifying eligible individuals based on age, medical history, and priority groups, with registration conducted online or at centers. A pre-vaccination screening checks for contraindications. The vaccine is administered via intramuscular injection in the deltoid muscle, followed by monitoring for side effects. A vaccination certificate is issued, and follow-up reminders ensure complete doses. Adverse effects can be reported to health authorities. The Comparison of COVID-19 Vaccine frontrunners are given in Table 1.

Table 1: Comparison of COVID-19 vaccine frontrunners.

Vaccine Company	AstraZeneca	Moderna	Janssen	Pfizer/BioNTech
Type of Vaccination	mRNA	Vector-based	mRNA	Vector-based
Name of vaccine	Moderna COVID-19 Vaccine mRNA-1273	Ad26.COV2.S	Pfizer-BioNTech COVID-19 Vaccine mRNA-BNT126b	AZD1222
Number of Doses	2 doses 28 days apart	1 dose (potentially 2 doses)	2 doses 21 days apart	2 doses 28 days apart
Route of administration	IM	IM	IM	IM
Storage requirements	-20°C	2°C to 8°C	-70°C	2°C to 8°C
Projected availability	December 21, 2020	2021	December 15, 2020	Early/Mid 2021
U.S. Commitments	200 million doses	100 million doses	100 million doses	300 million doses
Projected/actual emergency use authorization (EUA)	December 18, 2020	Early/Mid 2021	December 11, 2020	Early 2021

* Only long-term (up to 6 months) storage requirements showdown

Race for a COVID-19 vaccine and CV case reporting

With the rising cases of COVID-19 deaths, vaccinations developed in the era were not fulfilled in all three steps of clinical trials, and this caused the reporting of multiple adverse events. One of the main adverse effects is myocarditis and other CVS-related events. The most used vaccines include (BNT162b2), Moderna Vaccine (mRNA-1273), AstraZeneca Vaccine (AZD1222), and Pfizer-BioNTech (BNT16 2b2 mRNA). The ratio of myocarditis to other adverse events of the vaccines is low, but there is still a need to analyze the vaccines further. In May 2021, the AstraZeneca vaccine company published their report with 6959 patients having cardiac AEs. Likewise, 2342 cardiac AEs were reported with Pfizer-BioNTech vaccines, and the Moderna vaccine has 0.03% cardiac AEs patients. Hypertension is most common among all vaccines[1].

Averted hospitalization and myocarditis cases of Covid-19 Vaccines

Averted hospitalizations and surplus vaccinations highlight the balance between benefits and risks in myocarditis cases associated with COVID-19 vaccines. While rare, vaccine-related myocarditis cases must be carefully monitored, ensuring effective risk mitigation strategies without compromising immunization efforts. This approach helps optimize public health outcomes by preventing severe COVID-19 cases while addressing vaccine safety concerns. Table 2 shows averted hospitalizations and myocarditis cases of different types of vaccines.

Table 2: Averted hospitalization and surplus vaccination regarding myocarditis cases of COVID-19 vaccines.

Hospitalization Prevention	Myocarditis Cases Reports	Vaccine Types
1799	47	Pfizer-BioNTech (BNT162b2 mRNA)
1903	68	Moderna (1273-mRNA)
2820	24	Pfizer-BioNTech (BNT162b2 mRNA)
2982	33	Moderna (1273-mRNA)

Pathogenesis of COVID-19 vaccine-induced CV complications

The SARS-CoV-2 vaccines contain variants of the Spike glycoprotein, which can cause myocarditis, an adverse effect resulting from immune reactions to both the vaccines and the mRNA substances. This inflammation is mainly seen in genetically vulnerable young males, suggesting sex hormones might be involved. Genetic factors, including HLA variations and heart-specific autoimmunity, increase the likelihood of developing severe myocarditis. The inflammation of myocardial tissue after vaccination can be life-threatening in those with autoimmunity affecting their hearts. The hypothesis suggests that certain vaccine substances, like Pfizer-BioNTech's mRNA vaccine components, may function as haptens to create new antigens causing immunological reactions. This theory could help healthcare professionals understand steroid treatment responses in selected patient groups. The pathological characteristics of myocarditis from SARS-CoV-2 infection or vaccination do not distinguish between the two forms. Research shows that both forms contain more macrophages than T-cells. A previous study found that 25 post-20-day mRNA COVID-19 vaccine receivers had substantial CD3-positive T-cell infiltration, with CD4-positive cells outstripping CD8-positive cells[12]. The data did not match demographic characteristics like age and sex. A previous study identified healed myocarditis as the main endomyocardial biopsy diagnosis in 25% of cases[9]. The presence of eosinophils suggests a hypersensitive response to vaccine ingredients. Severe myocarditis from any source identifies lymphocytic myocarditis, eosinophilic infiltration, mixed and giant cell infiltrations as typical histological features[10].

Symptoms of vaccine-induced CV complications

Vaccine-induced myocarditis symptoms often appear mild, with chest pain and elevated troponin levels being common symptoms. However, most cases of myocarditis following vaccination are gentle and heal without adverse effects. A previous study showed that 114 people died from myocarditis after vaccinations given to over 38 million people. Most people experience chest pain as a symptom, with dyspnea (29%), palpitations (8%), and adverse side effects of fever, myalgia, and chills. Medical experts suggest that the condition stems from immune reactions, such as cross-reactive antibodies or temporary inflammation, rather than myocardial tissue damage[9].

Diagnosis of cardiovascular complications after COVID-19 vaccination

Studies have shown abnormal ECG results together with elevated levels of D-dimer and C-reactive protein and troponin-diagnosed myocarditis after vaccine administration, particularly among certain age groups and gender demographics. The first diagnostic approach for biomarker evaluation includes electrocardiogram (ECG) and echocardiography. The diagnostic tools include cardiac magnetic resonance (CMR) in combination with nuclear imaging. Medical experts consider Endomyocardial biopsy (EMB) as the leading diagnostic testing method for myocarditis. Any detected ECG changes were non-discriminative because they included sinus tachycardia, mild diffuse ST-segment changes, and PQ segment depressions[11]. Table 3 presents the ways to diagnose CV Complications.

Treatment strategies for CV complications

The combination of intravenous immunoglobulins with corticosteroids shows promise in treating COVID-19 myocarditis, especially when dealing with fulminant myocarditis cases. Studies indicated that IVIG provided clinical advantages to patients with acute myocarditis, which exhibited left ventricular ejection fractional values while simultaneously reducing mortality rates. Studies have shown that corticosteroids do not reduce mortality rates in patients with viral myocarditis. Medical personnel addressed COVID-19 patient inflammatory responses through tocilizumab and favipiravir combined treatment. Additional research initiatives are necessary to determine properly the effects of IVIG treatment for CoVID-9 myocarditis[12,13]. Research has identified conservative vaccine-associated myocarditis prevention methods as consisting of supportive therapies with anti-inflammatory medications and pain mitigation strategies. Patients should also receive rest time[13].

Although scientific trials prove that COVID-19 vaccinations deliver both safety and effectiveness for healthy volunteers, there remains the potential for serious post-vaccination consequences, including hospitalization or death[14-16].

Follow-up CV complications

Follow-up is needed for each dose, and the person in person should be monitored to check any AEs. The dosage should be clearly mentioned. The time interval between the two doses should be monitored, and any AEs from the person taking vaccines should be asked about.

Limitation to report complications

The study on vaccine-related risks and COVID-19 mortality has several limitations, including a short observation period, a focus on younger males and single-dose vaccinations, and a lack of standardized diagnostic protocols. These factors make it difficult to distinguish vaccine-related effects from pre-existing health conditions and patient comorbidities.

Table 3: Diagnosis of CV complications.

	Strengths	Typical findings	Limitations
Cardiac Imaging Cardiovascular magnetic resonance (CMR)	High specificity and sensitivity of diagnosis for acute myocarditis	Usually, revised Lake Louise standards are used for evaluation.	Limited availability
	Helpful in excluding other conditions including stress-induced cardiomyopathy.	The criteria for myocardial edema based on T2 include both regional and high native T2 hypersensitivity.	Relatively long examination time
	Useful in risk stratification	Nonischemic pattern LGE, high native T1, and high ECV are T1-based indicators of myocardial damage.	
	Helpful in showing edema remission at follow-up	± Impaired regional and global ventricular function	
	High specificity and sensitivity of diagnosis for acute myocarditis	± pericardial effusion, edema, and enhancement Usually, the updated Lake Louise standards are used for evaluation. T2 based criteria for myocardial edema include high native T2 and regional T2 hypersensitivity	
Echocardiography	Widely available	Global and localized ventricular dysfunction	Low sensitivity and specificity for myocarditis
	Relatively low cost	Pericardial effusion	Operator dependent
	Relatively short examination time	± Myocardial wall thickening ± Left ventricular dilation ± Impaired strain	
Cardiac PET	Metabolic information Potentially helpful for tracking the effectiveness of treatment	Myocardial inflammation is indicated by focal FDG uptake.	Limited availability Exposure to ionizing radiations
Cardiac CT	Helpful in ruling out other potential diagnoses, such stress-induced cardiomyopathy	Pericardial effusion or thickening	Exposure to ionizing radiations
		± Myocardial wall thickening Late iodine enhancement	Low specificity for acute myocarditis
Chest radiography	Widely available Low cost Very short examination time	Possible cardiomegaly Pericardial effusion The presence of pulmonary edema in heart failure	The results are not specific to myocarditis
Other Investigations Troponin	Elevated in nearly all acute myocarditis patients. Widely available	Increased levels signify damage to myocytes	Blood must be drawn Not particular to acute myocarditis
BNP	Widely available	Increased levels are linked to heart failure.	Blood draw required Not particular to acute myocarditis
Endomyocardial biopsy	The reference for a conclusive myocarditis diagnosis High specificity	Inflammatory infiltrations in the heart linked to nonischemic myocyte injury or necrosis Newer criteria may use immunohistochemical techniques	Invasive with risk of complications Low sensitivity for acute myocarditis
Electrocardiogram (ECG)	Relatively quick Useful in ruling out another potential diagnosis that might present similarly	ST-segment and T wave abnormalities	Not specific for acute myocarditis

Variability in study designs, inconsistent reporting, and a lack of standardized diagnostic protocols contribute to potential inaccuracies and confounding results. Differences in study timelines, data collection methods, and reporting inconsistencies further complicate causal inferences. Despite these challenges, the study findings align with existing research and are supported by a substantial participant count.

CONCLUSIONS

Ongoing research continues to explore the potential link between mRNA based COVID-19 vaccines and cardiovascular complications, with findings indicating a rare but noteworthy association with myocarditis, arrhythmias, and other cardiac events. Effects are more frequently noted in younger males; however, their incidence is considerably lower compared to the cardiovascular risks posed by COVID-19. However, continuous monitoring and risk management strategies are essential. Future investigations should aim to enhance diagnostic accuracy, improve treatment protocols, and identify individuals at higher risk to maintain vaccine safety while upholding public health priorities.

ACKNOWLEDGEMENT

We sincerely appreciate the Faculty of Pharmaceutical Sciences at Lahore University of Biological and Applied Sciences (UBAS) Deanship for their support and resources, which were instrumental in facilitating this research. Their dedication to academic advancement is deeply valued.

AUTHOR'S CONTRIBUTION

Fatima M: conceived the idea, study design, methodology**. Rasheed N:** conceptualization**,** literature search. **Shafqat A:** concepts or Ideas**. Ali E:** formal analysis. **Mustafa MA:** editing. **Tariq MT:** review**. Gulraiz L**: collected and analyzed data**. Imran F:** methodology**,** experimental studies**. Hussain N:** collected and analyzed data**. Awais J:** data curation, investigation. Final manuscript was checked and approved by all authors.

DATA AVAILABILITY

Upon request, the accompanying author can furnish the empirical data used to bolster the findings of the study.

CONFLICT OF INTEREST

None to declare.

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