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The risk of adverse cardiovascular complications following covid-19 vaccination

Abstract

The current coronavirus disease 2019 (COVID-19) pandemic has urged the scientific community internationally to find answers in terms of therapeutics and vaccines to control SARS-CoV-2. SARS-CoV-2 is the 7th member of the human coronavirus (CoV) family to be implicated in this zoonotic outbreak. With the global popularity of immunization against COVID-19, reports of vaccine-related adverse events are rapidly growing. Local pain at the injection site is the most prevalent occurrence, as are unusual symptoms such as fever, headache, myalgia, and overall discomfort. Those with COVID-19 and pre-existing cardiovascular disorders (CVDs) are at an increased likelihood of severe morbidity and fatality, and the condition has been related to a number of both direct and indirect CVDs outcomes. As a result of acute coronary syndrome, COVID-19 produces CVDs such as arrhythmias, cardiac arrest, cardiogenic shock, myocarditis, stress-cardiomyopathy, and acute myocardial damage (AMD). Because of underlying chronic comorbidities or impaired immune systems, older persons and adolescents should be particularly cautious about vaccine-related CVDs.

Keywords: COVID, coronavirus, cardiovascular disorders, adverse effects, vaccine

Volume 11 Issue 1 - 2023

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Received: December 04, 2022 | **Published:** January 10, 2023

Introduction

India's Central Drugs Standard Control Organization (CDSCO) had given restricted emergency use authorization to seven COVID-19 vaccines; the Oxford-AstraZeneca adenovirus-vectored recombinant vaccine-AZD1222 and Covishield (ChAdOx1 nCoV-19), whole-virion inactivated coronavirus vaccine-Covaxin (BBV152) in January 2021, recombinant adenovirus-vectored vaccine-Sputnik V (Gam-COVID-Vac) in April 2021, Moderna's mRNA-1273 vaccine (June 2021), Zydus Cadila's DNA vaccine-ZyCov-D in August 2021 and Janssen's Ad26.COV2.S (August 2021). All these vaccines were rolled out to be given in two doses for optimum efficacy except Janssen's Ad26.- COV2.S and ZyCov-D that required one and three doses, respectively.[1,2]

Concerned about a pandemic of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), India has begun immunization in 2021. With the increased popularity of vaccination, there has been an increase in reports of various types of adverse effects, particularly the occurrence of CVDs, which should be monitored.[3] Currently, mRNA, viral vectors, virus-like particles, polypeptides, recombinant proteins, attenuated live viruses, and inactivated viruses are among the COVID-19 vaccines that have been licensed for emergency use or are being studied internationally.[4] The mRNA vaccine is the most concerning of these since it has been observed to elicit local allergic responses at the injection site as well as unusual symptoms such as fever, headache, myalgia, and overall discomfort in around 60% of patients following the second inoculation.[5] Pfizer-BioNTech (BNT162b1) and Moderna COVID-19 vaccines (mRNA-1273) are two of the most frequently used mRNA vaccines in the world, allowing RNA transport into host cells and production of the SARS-CoV-2 S antigen. To defend against COVID-19, the vaccinations provoke an immune response and create antibodies specific to the SARS-CoV-2 virus.[6] Because of their high potency, the potential for quick development, and cost-effective manufacture, mRNA-based vaccines offer several benefits over traditional vaccinations. They aggressively activate B cell responses and stimulate cytokine release by stimulating CD8+ and CD4+ T cells.[7] However, the physiochemical features of mRNA may impact its cellular transport and organ distribution, which produces mild to moderate local and systemic symptoms in the majority of vaccinated patients, casting a shadow on mRNA vaccine safety and dependability.[8] The majority of the symptoms may be attributed to the vaccine-induced in vivo overproduction of type I interferons and cytokines.[9]

Currently, the most extensively utilized COVID-19 vaccines in India, ChAdOx1 nCoV-19 and BBV152, are inactivated viral vaccines that stimulate an immune response against SARS-Cov-2 fast and efficiently. Furthermore, they may elicit a robust inflammatory response, leading to serious adverse CVDs.[10] Inactivated viruses are appealing because they can display numerous viral proteins for immune detection. Other proteins, in addition to the S protein, might function as possible antigens for SARS-Cov-2, including the N protein, M protein, non-structural proteins, and accessory proteins.[6] This raises the question of whether these insignificant antigens may change the immune system. Furthermore, more focus should be given to the antibody-dependent enhancement (ADE) of SARS-CoV-2 infection, because many severe patients with COVID-19 frequently exhibited more robust immunoglobulin G (IgG) responses and higher antibody titers, both of which are associated with poorer clinical outcomes.[11,12]

It is presently unknown if these vaccinations generate aberrant antibody responses, and further study is needed to address the possible harm associated with SARS-CoV-2 vaccines. Cardiometabolic disorders such as hypertension, atherosclerosis, heart failure, and diabetes are common problems in COVID-19 patients.[13-15] Populations with prior underlying disorders are at a higher risk of SARS-CoV-2 infection and a worse clinical outcome.[16-18] Vaccine immunity is known to be influenced by age. Following the first vaccination dosage, serum neutralization and levels of binding IgG or immunoglobulin A (IgA) were lower in older groups, with a significant drop in persons over the age of 80. Serum from participants over the age of 80 had reduced neutralization power against the B.1.1.7 (Alpha), B.1.351 (Beta), and P.1. (Gamma) variants and was more likely to lack any neutralization after the first dose.[19] After the first treatment, the frequency of SARS-CoV-2 spike-specific memory B cells fell in non-responders, and CD4 T cell production of interferon- and interleukin-2 was repressed in

older participants. 15 Furthermore, 9.7% of patients had COVID-19 in addition to diabetes.[20] The expression of the ACE2 receptor (total and glycosylated form) was elevated in diabetic cardiomyocytes, increasing vulnerability to SARS-CoV-2 infiltration by facilitating viral cellular entrance.[21] Furthermore, hyperglycemia reduced the efficacy of tocilizumab therapy in both diabetic and non-diabetic individuals.[22] Early glycemic management may be an appropriate treatment approach to improve outcomes in COVID-19 hospitalised patients with or without diabetes. Diabetes and hyperglycemia may impair responsiveness to anti-inflammatory and anti-viral medications. However, it is uncertain whether there is a comparable issue with the diabetes vaccine. Specific approaches are needed to increase vaccination response in the elderly and diabetic groups.[23]

There have been reports of serious adverse effects associated with the COVID-19 vaccination, including neuritis, facial nerve palsy, myocarditis, and thrombosis.[24-26] Myocarditis is an uncommon but significant consequence of vaccination that is usually self-limiting but can be fatal.[27] Recently, reports of vaccination-related myocarditis (Table 1) have largely been linked to the mRNA vaccine, which caused severe chest discomfort immediately after inoculation and was associated with elevated biomarkers for myocardial damage.[28-30] Cardiac magnetic resonance imaging reveals classic myocarditis signs including regional dysfunction, late gadolinium enhancement, and higher native T1 and T2 levels.[31] Thrombosis with thrombocytopenia syndrome (TTS) is a significant vaccination-related event that primarily affects women within 2 weeks after receiving the Chadox1 nCoV-19 or Ad26 vaccine.[32]

Table 1 Summary of cardiovascular adverse reactions and incidence rates after COVID-19 vaccination

Authors	Data sources	Vaccines names	Vaccine types	Cardiovascular adverse reactions
Abu Mouch et al.[24]	Case report	BNT162b2 vaccine	mRNA	5 patients presented myocarditis after the second and 1 after the first dose of the vaccine
Chamling et al.[28]	EudraVigilance	Pfizer-BioNTech and ChAdOx1 nCoV-19 vaccine	mRNA/adenovirus vectored	309 (18–64 years old) reported cases of myocarditis associated with Pfizer-BioNTech, 19 (65–85 years old) with ChAdOx1 nCoV-19 vaccine
Deb et al.[29]	VAERS and CDC website	mRNA-1273	mRNA	37 vaccine recipients developed myocarditis related to mRNA-1273 vaccine
Kim et al.[31]	Case series	2 received mRNA-1273, and 2 received BNT162b2	mRNA	7 patients with acute myocarditis over 3-months which 4 occurred within 5 days of COVID-19 vaccination
Lai et al.[32]	EudraVigilance	ChAdOx1 nCoV-19 and Ad26. COV2.S vaccines	adenovirus vectored	169 cases of CVST and 53 cases of splanchnic vein thrombosis following ChAdOx1 nCoV-19 vaccination out of 34 million people
Lai et al.[32]	VAERS	Ad26.COV2.S	adenovirus vectored	6 cases of CVST with thrombocytopenia following the administration of 6.86 million doses
Sessa et al.[33]	VAERS	Pfizer-BioNTech or mRNA-1273 vaccine	mRNA	68 thromboembolic events out of 13.6 million younger women
Welsh et al.[34]	VAERS	Pfizer-BioNTech or mRNA-1273 vaccine	mRNA	15 cases of thrombocytopenia were identified among 18,841,309 doses of Pfizer-BioNTech Vaccine and 13 cases among 16,260,102 doses of mRNA-1273 vaccine

Other vaccinations appear to be safe, with no abnormally high rates of thromboembolic events or thrombocytopenia reported.[33,34] In severe COVID-19 individuals, impaired type I interferon (IFN) activity was detected, which is characterized by a lack of IFN- and low IFN- production, as well as enhanced inflammatory responses.[35] Excessive immunological responses generated by vaccinations may increase myocardial ischemia and plaque development, resulting in myocardial damage and, in extreme cases, plaque rupture and acute myocardial infarction.[36] Because teenagers' immune systems are still developing, immunization may result in secondary myocarditis, cardiomyopathy, arrhythmia, and heart failure.[37] A recent phase I/II clinical research found that the CoronaVac vaccination was safe, tolerable, and immunogenic in children and adolescents aged 3-17 years, with injection site discomfort being the most prevalent adverse event.[38] Long-term immunogenicity and safety, on the other hand, were not available and must be carefully monitored. Furthermore, stressors such as anxiousness during immunization may cause hypertension, myocardial ischemia, and arrhythmias.[39]

Guidelines or recommendations on the use of COVID-19 vaccinations and the avoidance of adverse effects are becoming more common. According to the Centers for Disease Control and Prevention, vaccination sites should:[40,41]

a) Ensure that necessary supplies, particularly sufficient quantities of epinephrine in prefilled syringes, are available to manage anaphylaxis;

b) Screen potential vaccine recipients to identify people with contraindications and precautions, particularly those with CV metabolic comorbidities;

c) Implement recommended post-vaccination observation periods, either 15 or 30 minutes; and

d) Ensuring that healthcare personnel can identify the signs and symptoms of anaphylaxis and other life-threatening reactions as early as possible.

These restrictions should be vigorously enforced, particularly in rural settlements. Patients should seek emergency medical attention if they have signs or symptoms such as unrelenting chest tightness or palpitations during or after the observation period.[42] Clinicians should be on the lookout for vaccine-related CV complications such as myocarditis. Emergency electrocardiograms and myocardial damage biomarker tests are required, as does echocardiography if available. Consultation with hematology is recommended when TTS is highly suspected or proven. Intravenous immunoglobulin and anticoagulation

may be used, although heparin-based medicines and platelet transfusion should be avoided.[43] Finally, it is important to alleviate anxiousness and aid individuals in performing health management in their everyday lives, avoiding extreme variations in blood pressure or blood glucose, and emphasizing primary prevention of CVDs during immunization. Furthermore, infrequent and substantial side events following COVID-19 immunization emphasize the significance of building an effective vaccine safety monitoring system. National regulatory bodies should develop formal trans-regional cooperation to encourage vaccination safety data exchange.[44]

Acknowledgments

None.

Conflicts of interest

The authors declared no conflict of interest.

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Citation: Alam MT, Sharma R, Hussain MS. The risk of adverse cardiovascular complications following covid-19 vaccination. *Pharm Pharmacol Int J.* 2023;11(1):10–13. DOI: 10.15406/ppij.2023.11.00395