Original Article

Prevalence of Pericarditis and Myocarditis after mRNA COVID-19 Vaccine

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Abstract

There are several researchers worldwide reported several cases of pericarditis and myocarditis following the administration of COVID-19 mRNA vaccines. This study aimed to assess the prevalence of pericarditis or myocarditis after receiving the COVID-19 mRNA vaccine, to identify the most susceptible age group, and to find the most common risk factors. It is a non-interventional cross-sectional study that will be conducted for 12 months. Data were collected from the patient's file and taking a direct history from the patient him/herself in the Makkah region. This study's success was possible due to ethical considerations observed by the researchers involved. To begin with, all the participants involved in the data collection process were informed of the study's objective to allow them to participate in the exercise voluntarily. A total of 10 patients who met the inclusion criteria were involved in the study. Among those involved, 70% 0f the population was female while the remaining 30% were male. The youngest patient in the sample population was 17 years whereas the oldest was 59 years of age. 70% of the respondents were diagnosed with pericarditis while 30% were diagnosed with myocarditis. Those who had received all the 3 doses were more likely to be affected by these health complications. A high number of the younger population were more likely to be diagnosed with either pericarditis or myocarditis events compared to older people. These health conditions often became prevalent 7 days after an individual has received the initial COVID-19 mRNA Vaccine.

Keywords: Pericarditis, Myocarditis, COVID-19, mRNA vaccine

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious illness caused by the SARS-CoV-2 virus [1-3]. On December 31, 2019, china reported that the first case of COVID-19 was discovered in a seafood market in Wuhan city. By January 30, 2020, the World Health Organization (WHO) announced that COVID-19 is an emergency and a global concern and by March 11, 2020, it was declared a serious global pandemic. As on November 15, 2021, there have been 253,163,330 confirmed cases of COVID-19 infection including 5,098,174 deaths reported to WHO. On March 02, 2020, the Ministry Of Health (MOH) of the Kingdom of Saudi Arabia reported the first case of COVID-19 infection. The MOH and the government of the Kingdom of Saudi Arabia imposed an obligatory curfew from March 23, 2020, to May 28, 2020. And by November 15, 2021, the total cases are 549,260 including 8,816 deaths. The symptoms of COVID-19 may include: fever, cough, shortness of breath, and sometimes develops into pneumonia. It may cause severe complications in persons with immunodeficiency, the elderly, and persons with chronic diseases [4].

Pericarditis is an inflammation of the outer layer of the heart (pericardium) it usually affects men more than women and the most common etiology is a viral infection. Signs and symptoms usually include acute sharp retrosternal chest pain increased by movement or inspiration and relieved by leaning forward, pericardium friction rub is found in approximately 85%, it is usually diagnosed by evidence of ST-Elevation, PR-Depression in ECG, ECHO also Cardiac MRI [5]. Myocarditis is an inflammation of the heart muscle, in most cases usually associated with viral infection as a primary cause, or secondary due to drugs or chemical agents. Signs and symptoms range from minor symptoms to cardiogenic shock, the diagnosis is based on clinical presentation and confirmed by Endomyocardial biopsy (EMB), via establishing Dallas criteria [6].

COVID-19 mRNA Vaccine: established in December 2020, by the Food and Drug Administration (FDA) issued Emergency Use Authorization (EUAs) of Pfizer-BioNTech

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COVID-19 (BNT162p2) Vaccine, Moderna COVID-19 (mRNA-1273) Vaccine, recommendations to vaccinate all persons above 18, In May 2021, FDA expanded the EUA for the Pfizer-BioNTech COVID-19 vaccine for adolescents aged between 12-15 years old [7]. In October 2021, the FDA also expanded the EUA for the Pfizer-BioNTech COVID-19 vaccine for children aged between 5-11 years old [8]. mRNA vaccines develop the cell to synthesize proteins that trigger an immune response inside the body, which produce anti-body to protect the body from getting infected by the real virus [9]. Since April 2021, there was an association between developing Pericarditis, Myocarditis, or both, after receiving the mRNA COVID-19 vaccine (Pfizer-BioNTech, Moderna), the prevalence was particularly increased among adolescents after receiving the second or third dose usually within several days [10].

Myocarditis and pericarditis have been linked recently to COVID-19 vaccines without recognizing the pathophysiology, after analyzing the adverse effects from Vaccine Adverse Event Reporting System (VAERS) with biology methods, the results revealed that myocarditis and pericarditis are induced by vaccines that are most frequently associated with mRNA COVID-19 vaccines, the incidence of pericarditis and myocarditis was to be found in males more than females, it is more common in adolescence, approximately 70% of cases associated with Pfizer-BioNTech COVID-19 vaccine, especially after the second dose [11]. According to vaccine adverse effect reporting system (VAERS) reported a rate of 0.41 cases per 100000 vaccination based on voluntary reporting of the event. There were 1,9 cases per 100000 among active military personnel. A large healthcare system estimates a rate of 1.0 myocarditis cases and 1.9 pericarditis cases per 100000 vaccination. In all reports, the clinical course of myocarditis and pericarditis after mRNA vaccination is usually resolved within days under appropriate treatment in most cases rarely linked to death. Although rare and self-limiting many individuals require hospitalization for management and to rule out other causes for their symptoms [12].

Myocarditis following vaccination with mRNA COVID-19 vaccines in members of our military between January 1 and April 30, 2021. More than 2.8 million doses of mRNA COVID-19 vaccine were administered in this period, although there were unexpectedly higher myocarditis cases among male personnel after the second dose of the vaccine. 23 male patients median age around 25 years experienced intense chest pain 4 days after receiving mRNA COVID-19 vaccines. All patients were medically free, BNT162b2-mRNA vaccine was administered to seven of them while the mRNA-1273 vaccine was administered to the other 16. 20 patients developed symptoms after receiving the second dose of the vaccine, cardiac troponin level was elevated in all patients, and magnetic resonance imaging confirmed the diagnosis in 8 of them. There was no additional etiology identified for myocarditis, all individuals received the right treatment and were recovered or recovering [13].

Materials and Methods

Study Design

It is a non-interventional cross-sectional study that will be conducted for 12 months. Data were collected from the patient's file and taking a direct history from the patient him/herself in the Makkah region. Data included personal data (Gender, nationality, age, route of admission), chief complaint, history of presenting illness (especially the duration between the onset of the disease and the last dose of COVID-19 mRNA vaccine), any associated symptoms, past medical history, and allergy, past surgical history, family and social history.

Inclusion and Exclusion criteria

Inclusion Criteria

Patients from both genders, Patients from all age groups above 5 years old, and Patients who are diagnosed with pericarditis or myocarditis after receiving the COVID-19 mRNA vaccine.

Exclusion Criteria

Patients who did not receive COVID-19 mRNA vaccine.

Ethical Consideration

This study's success was possible due to ethical considerations observed by the researchers involved. To begin with, all the participants involved in the data collection process were informed of the study's objective to allow them to participate in the exercise voluntarily. After doing so, the researchers then ensured that all the questionnaire components and items were thoroughly explained to avoid possible confusion while answering questions. The ethics committee of the Kingdom of Saudi Arabia Ministry of Higher Education Taif University approved this study.

Additionally, the participants have informed beforehand of the benefits and risks of participating in this study. The respondents were also notified of their right to abandon or withdraw consent at any given phase of the data collection exercise. Other prioritized elements include data integrity and privacy since this study involved confidential medical records. As such, the researchers assured the respondents that there would be no stigmatization and discrimination. Fairness and impartiality were also guaranteed in the survey questions.

Analyzes and Entry Method

The data collected was analyzed using SPSS® software (Statistical product and services solutions) for Windows® ver.21. Data was cleaned and entered into SPSS and analyzed for frequency, means, and CHI square or t-test for significance. For all statistical tests, the level of significance shall be fixed at p less than 0.05.

Results and Discussion

The study involved a sample of 10 patients who met the inclusion criteria outlined in this study. The analysis aimed to evaluate the demographic characteristics of the patients, their medical history, and the prevalence of various conditions as well as diagnoses of some conditions related to the COVID-19 mRNA vaccine exposure. Using predefined inclusion criteria from the data, 70% of the patients were female. Male patients were 30% of the entire group **Figure 1**.

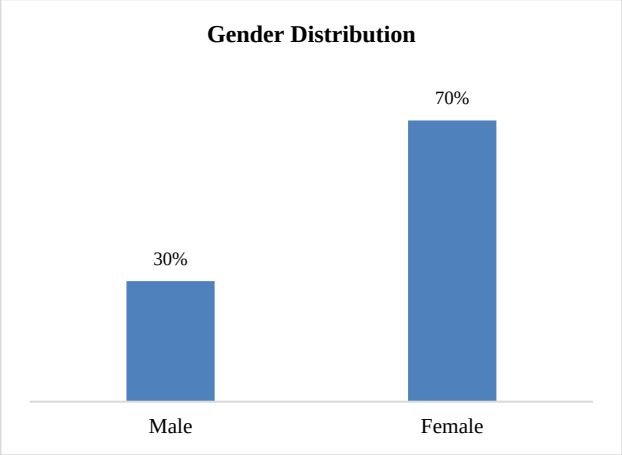

Figure 1. Demographic Statistics of participants

As shown in **Figure 2**, The age distribution of the patients varied widely with the youngest patient being 17 years old and the oldest being 59 years of age.

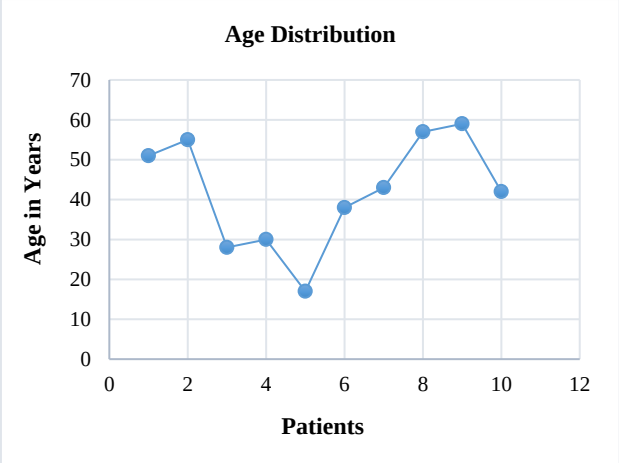

Figure 2. Age Distribution of participants

Figure 3 shows; Three of the ten patients indicated a history of smoking, two patients had a cardiac surgery history, 2 patients had a CAD history and no patients had a DVT or PE history. The results from this analysis are illustrated in the graph alongside.

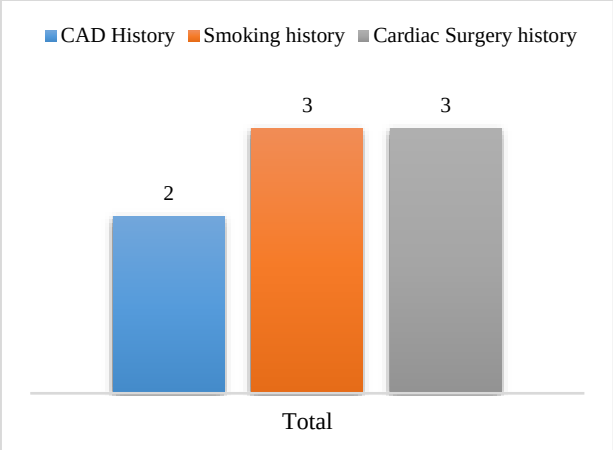

Figure 3. Patient medical history of participants

This study further sought to evaluate the prevalence of certain diseases among the patients. The study identified hypertension, diabetes, and dyslipidemia as common complications concerning the COVID-19 vaccine intake. Hypertension had a prevalence rate of 20%, one patient had dyslipidemia while no patient was diagnosed with diabetes. The results are illustrated in **Figure 4**.

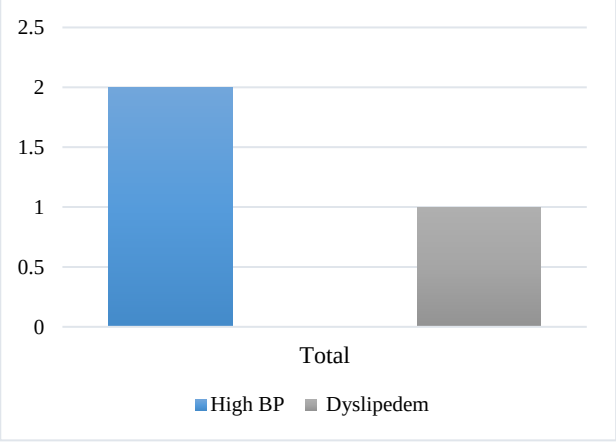

Figure 4. Prevalence of Hypertension, Diabetes, and Dyslipidemia among participants

As part of this study's objectives, we sought to identify patients who are diagnosed with pericarditis or myocarditis after receiving the COVID-19 mRNA vaccine. The two conditions have been reported to be on the rise, especially among people who received the COVID-19 mRNA vaccine. The results show that 70% of the patients were diagnosed with pericarditis while 30% were diagnosed with myocarditis as shown in **Figure 5**.

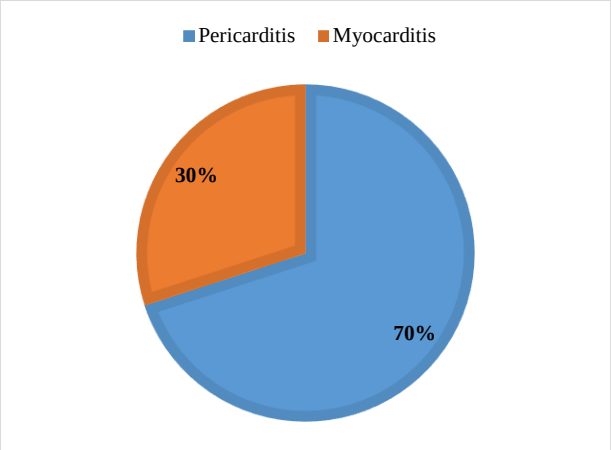

Figure 5. Pericarditis or Myocarditis diagnoses among participants

The study sought to establish a connection between the number of COVID-19 mRNA vaccine doses and the prevalence of Pericarditis or Myocarditis. Pericarditis was the most prevalent across the study sample and was diagnosed mostly in patients who had received more than one dose of the vaccine. Those who had received 3 doses of the vaccine were more likely to be diagnosed with Pericarditis while those who had received a single dose were more likely to be diagnosed with Myocarditis, as shown in **Figure 6**.

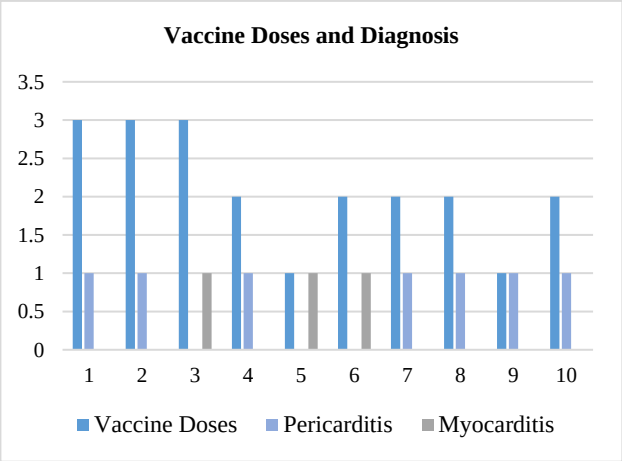

Figure 6. Vaccine Doses and Prevalence of Pericarditis or Myocarditis among participants

This study considered the participation of 50-75 participants to investigate the prevalence of pericarditis and myocarditis following their exposure to the mRNA COVID-19 vaccine. The success of this study involved 10 patients who were selected using predefined inclusion criteria. A majority of the participants were female (70%), whereas males were the minority making up 30% of the overall group involved. The study took into consideration the population where the youngest respondent was 17 years old, and the oldest was 59 years of age. As indicated earlier, the researcher was keen on considering the patient's medical history. Some of the critical issues that the study considered include the patient's history of smoking, DVT, PE CAD, and the history of cardiac surgery. With regard to this, about 3 out of 10 patients confirmed they had a history of smoking; none had DVT or PE history, while 2 of the respondents had CAD history [14]. The study also sought to look into other prevalent health conditions associated with the intake of the COVID-19 vaccine. Some of the issues identified include hypertension, diabetes, and dyslipidemia. However, none of the patients was diagnosed with diabetes, whereas one of the respondents had dyslipidemia, and 20% of the sample population was diagnosed with hypertension.

Based on this study's objectives, it was imperative to investigate the prevalence of pericarditis or myocarditis after receiving the COVID-19 mRNA vaccine. In this regard, it is fundamental to point out that many individuals affected by the same disease include persons who received the COVID-19 mRNA vaccine [14]. Among those involved in the study, 30% tested positive for myocarditis, while 705 were diagnosed with pericarditis. The high percentage of pericarditis was more prevalent among persons who had received more than a single dose of the vaccine [15]. On the other hand, those who had received one dose were more likely to be diagnosed with myocarditis.

Based on contemporary research studies, more people are likely to be diagnosed with myocarditis or pericarditis after 0-7 days following mRNA vaccination. This is more prevalent among persons aged 5-39 years. The rate is likely to be approximately 1 in 200,000 doses after the first dose and 1 in 30,000 doses after the second dose, and 1 in 50,000 doses after the initial booster [10]. Nonetheless, the variation with regard to those who were affected was based on sex and age. With was, however, more likely to affect ales more so adolescents after their second dose and first booster. This study also made a critical observation that one was likely to contract either of the two diseases after the first booster compared to dose 1 [15]. Centrally to this report, the researcher did not consistently observe lower incidence after the initial booster than dose 2in the primary vaccination series. The VSD population had more incidents of myocarditis or pericarditis, more so after the first booster compared to the observed internationally in countries such as the United States. This was similar to patterns noted by age groups and sex.

Myocarditis has been identified to occur after a series of viral infections, such as the coronavirus, which caused COVID-19 and Middle East respiratory syndrome [10]. The findings from this study provide sufficient evidence that young people who have received the mRNA COVID-19 vaccine are highly likely to contract pericarditis and myocarditis compared to older persons who have received the same vaccine. Throughout this study, the researcher was able to identify several strengths. The target population comprises patients from large commercial claims databases covering most parts of the KSA. In addition, this is one of the few observational

studies of persons who have received mRNA vaccines within the region with the name and number of doses of the different brands of mRNA vaccines. This was especially important as it enabled the researchers to compare head-to-head the pericarditis or myocarditis risks between BNT162b2 and mRNA-1273 vaccines among the highest-risk population within 1 to 7 days after vaccination [10]. Also, this study was able to identify potential confounding factors, which are the history of a COVID-19 diagnosis, demographic factors, and the week of vaccination.

Recommendations

Although the risks associated with pericarditis and myocarditis might be rare, clinicians must have such know-how. This should be considered in persons with chest-related pain seven days after vaccination, especially among the younger population. During the first evaluation, cardiac troponin level and ECG should be obtained, and inflammatory markers, including erythrocyte sedimentation rate and C-reactive protein, can also be helpful [10]. Cardiology evaluation and consultation with cardiac MRI and echocardiography should be considered where a suspected case exists. Also, it is crucial to evaluate for past disease (through Spike protein antibodies and ARS-CoV-2 nucleocapsid) and acute COVID-19 (through a polymerase chain reaction of samples of the respiratory tract sample) infection is also highly recommended [16]. This kind of management and evaluation may vary based on clinical course, rhythm stability, hemodynamics, comorbidities, potential other causes, clinical presentation, and the patient's age. Furthermore, Clinicians should hospitalize and maintain close follow-ups of patients with hemodynamic instability, arrhythmia, cardiac imaging abnormality, ECG change, evidence of myocardial injury, and those experiencing chest pain after COVID-19 vaccination [10].

CONCLUSION

In conclusion, some of the risks of pericarditis or myocarditis events among those who had received the COVID-19 m RNA vaccines were identified to be high among younger people. Still, the incidence was considered to be rare. Based on this study's findings from the collected data, after 1-7 days after receiving the second dose, the population considered to have the highest risk was males between 18 and 25. Based on a head-to-head comparison of risks associated with pericarditis and myocarditis with respect to the various vaccines available in the market, there lacked any significant difference, but this could not necessarily mean that there are no differences altogether. More studies need to be conducted with additional data sources to evaluate further the risks involved. Even though cases of myocarditis or pericarditis are rare, the risk-benefit assessment for COVID-19 vaccination indicates a satisfactory balance for all sex and age groups. Thus, it is recommended that only persons older than 12 years be allowed to receive the COVID-19 vaccination. Also, clinicians must be keen in assessing patients who contract various health complications a week after being vaccinated, including patients with hemodynamic instability, arrhythmia, cardiac imaging abnormality, ECG change, evidence of myocardial injury, and those experiencing chest pain.

Limitations

This study was reinforced by active surveillance of a more diverse population and by verifying cases through physician adjudication and the review of medical records. However, significant limitations, such as the lack of a control group, prevented causal inference. Additionally, the identified cases were mostly among patients who have received diagnosis codes that are less specific or within outpatient settings. Other limitations include ascertainment bias and potential reporting, possible differences among persons who received underreporting of SARS-CoV2 infection, and Moderna versus Pfizer vaccines.

This study's findings can inform risk-benefit analyses as there are greater benefits associated with mRNA vaccination which outweigh the associated risks. It is warranted to ensure continued communication with providers and patients regarding the risk for pericarditis or myocarditis following mRNA COVID-19 vaccination and ongoing safety surveillance among persons who have received the vaccination.

The researcher experienced some challenges with using publicly available data since the detail available in some data sources was limited. Additionally, there was insufficient data on vaccine doses related to pericarditis and myocarditis cases that were only available for distinguished populations such as the US VAERS. Thus, this made it difficult for the researcher to come up with conclusive data associated with this study's target population. Also, information from individual reports is rarely available to the public. However, they might contain key medical information that would have otherwise enabled the researcher to gain in-depth knowledge of each case. Details of this nature ought to be made available for public access. Transparency is crucial to enhance stout research through extemporaneous reporting to be carried out. Another limitation is that the use of most databases as the source of information for this study provides little or no clarification of the demographic composition of the target population with the absence of key information such as educational background, socioeconomic background, ethnicity, and race of the participants. Lastly, this study was not in a position to answer two major questions regarding the topic under discussion. The first is whether there are any long-term effects of vaccine-associated pericarditis or myocarditis. This is because there is limited literature on the well-being of patients who suffer from these conditions. Secondly, there is insufficient data on the biological mechanism linking myocarditis and pericarditis events to COVID-19 mRNA vaccination.

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CONFLICT OF INTEREST: None
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ETHICS STATEMENT: Ethical approval was obtained from the research ethics committee of Alhada Armed forces Hospital (application number: 2022-645). Informed consent was obtained from each participant after explaining the study in full and clarifying that participation is voluntary. Data collected were securely saved and used for research purposes only.

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