**Original Article**

# Evaluation Of Cardiovascular Complications In Patients With COVID-19 Admitted In Two Teaching Hospitals In North Of Iran During Three Months

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**Abstract:**

**Background**: COVID-19 patients with cardiovascular underlying disease have more severe problems.

**Methods and Materials**: This is a retrospective descriptive-analytical cross-sectional study based on the information in patients' medical records. From March 2020 to the end of April, patients with COVID 19 hospitalized in Razi and Fatemeh Zahra teaching hospitals were included in the study.

**Results**: In this study, 1501 patients were evaluated. Patients ranged in age from 21 to 76 years with a mean and standard deviation of 54±18.4 which 766 cases (51.0%) were female. Forty cases (2.7%) developed a severe form of the disease, and 1461 cases (97.3%) had a mild form of COVID-19. The final diagnosis of a heart disorders was acute myocarditis in 5.7%, arrhythmia in 9.5% and myocardial infarction in 3.6% cases respectively, which also had a statistically significant difference between severe and mild groups P<0.0001.

**Conclusion**: Underlying cardiovascular diseases are associated with a higher severity in COVID-19 patients.

**Keywords**: COVID-19, Myocarditis, Myocardial Infarction, Arrhythmia

Submitted: 7 November 2021, Revised: 2 November 2021, Accepted: 11 December 2021

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[ DOR: 20.1001.1.23222913.2021.10.4.11.1 ]

## Introduction

In early December 2019, the first cases of pneumonia of unknown origin were diagnosed in Wuhan, the provincial capital of Hubei Province, caused by a new beta-coronavirus (1-8). The World Health Organization declared the coronavirus, which it named COVID-19, first as an international public health emergency and then spread a pandemic and profound globalization (2).The disease's incubation period is from 2 to 14 (average 4 to 7) days . The initial manifestations of the disease are related to viremia, and then during days 5 to 7 in severe cases, the manifestations are related to the release of cytokines and cytokine storm syndrome. The clinical spectrum of the disease varies from asymptomatic or mild (in more than 80%) to severe cases leading to an acute respiratory syndrome, respiratory failure, and death. Clinical features include fever, sweating, myalgia, sore throat, dry mouth, dry cough, shortness of breath, chest pain, hemoptysis, abdominal pain, nausea, and diarrhoea (3). According to the time of disease onset, the most critical radiographic manifestations include scattered subpleural grand glass lesions, crazy paving lesions, and consolidation (1). Definitive diagnosis of the disease by virus detection by RT PCR is a sample of the pharyngeal swab, nasopharynx or oropharynx and a sample of tracheal secretions (3-18).The most crucial laboratory evidence in patients includes lymphocytopenia and increased CRP. The most important risk factors include old age, diabetes, high blood pressure, chronic heart, lung, liver and kidney diseases, cardiovascular disease, immunodeficiency and cancers(1) . The most important principle of treatment of patients is oxygen therapy and their respiratory support. So far, there is no conclusive evidence for the effectiveness of current antiviral therapies. Given the very high prevalence of the virus and its relatively high mortality rate, find factors that can prevent or accelerate the onset or exacerbation of the disease and its complications. It will significantly contribute to reducing the mortality of this disease in the continuation of the current pandemic and the possible seasonal epidemics.

The COVID-19 epidemic imposes a double burden on people with cardiovascular disease. About 40% of hospitalized COVID-19 patients have CVD, and the clinical course of COVID-19 is more severe in patients with hypertension, diabetes, and CVD. Evidence from experimental studies shows that a decrease in ACE2 is associated with the progression of type 2 diabetes and myocardial hypertrophy. Conversely, an increase in ACE2 improves glycemic control in diabetes, prevents myocardial fibrosis, and improves heart function after myocardial infarction. The SARS-CoV-2 infection triggers an enzymatic process that inactivates ACE2. This effect may partly explain the cardiovascular and respiratory manifestations of COVID-19 (4). The most critical cardiovascular complications of COVID19 are myocarditis, acute myocardial

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infarction, arrhythmias, venous thrombotic events, cardiomyopathy and heart failure, and cardiogenic shock and cardiac arrest. Electrocardiographic (ECG) changes can include a wide range that in some cases mimics the symptoms of an acute coronary syndrome (5-28). The present study was designed to investigate the rate and variety of cardiovascular complications in patients with COVID-19 admitted to Razi Hospital in Ghaemshahr during March 2020 and April 2020. The results of this study can be a helpful guide for the proper care of patients with COVID-19 in terms of cardiovascular problems and increase the ability to diagnose common or uncommon cardiovascular complications in these patients timely.

**Methods and material**

The present study is a retrospective descriptive-analytical cross-sectional study research on the information in the medical records of patients. This study was approved by the Ethics Committee of Mazandaran University of Medical Sciences (IR.MAZUMS..REC.1399.7835).

Sampling performed by census method. During the period from the beginning of March 2020 to the end of April 2020, 1501 patients with COVID 19 were admitted to Razi and Fatemeh Zahra teaching hospitals. The medical records of these patients were studied, and their clinical and laboratory characteristics, including troponin and Cardiac enzymes, were entered into a pre-prepared information form before the onset of the disease. Also, electrocardiography at the first visit (and subsequent ECGs in case of changes) was thoughtfully reviewed and reported by a qualified cardiologist. Definitions of COVID-19 severity were based on the World Health Organization COVID-19 clinical management guideline: 1- Mild stage (definitive COVID-19 patients without evidence of viral pneumonia or hypoxia); 2- Moderate disease (clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) but no signs of severe pneumonia, including SpO2 ≥ 90% on room air not requiring supplemental oxygen); 3- Severe stage (with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO2 < 90% on room air; 4- Critical (Acute respiratory distress syndrome (ARDS), sepsis/septic shock, acute thrombosis) or other conditions that would normally require the provision of life sustaining therapies such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy (6). Inclusion criteria was Patients with a definitive diagnosis based on virus isolation by RT PCR with a swab of the throat, nasopharynx or oropharynx, and a sample of tracheal secretions or typical radiological findings. Exclusion criteria included patients whose records were incomplete or who did not have a definitive diagnosis of COVID- 19. All data analysis was performed using SPSS software version 25. Significance level $p< 0/05$ was considered.

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**Results**

A total of 1501 patients with COVID-19 were admitted to Razi and Fatemeh Zahra teaching Hospitals from March to April, 2020. Among all hospitalized patients, 845 (56.3%) were over 50 years old and the rest were under 50 years old. Generally, 766 patients (51.1%) were female and the rest were male. Patients ranged in age from 21 to 86 years old with a mean and standard deviation of 0.54 ± 18.4 years. Also, the body mass index of patients with mean and standard deviation was 26.6 ± 4.6. Patients included in the study had a hospital stay of 1 to 18 days with a mean and standard deviation of 2.3 7 7.1 days. Recording the signs and symptoms of Covid-19 disease in patients showed that the patients' heart rate and respiration rate were 90.2 ± 24.5 and 23.4±5.5 per minute, respectively. The patients' blood oxygen saturation was between 73 to 97 with a mean and standard deviation of 89.7 ± 5.5. The mean fever of patients was 37.1 ± 1.1 ° C. Out of 1501 patients included in the study, 40 cases (2.7%) developed severe forms of the disease and 1461 cases (97.3%) had mild form. Examination of the studied variables in patients based on the severity of the disease shows that the age of patients with high severity (59.5 ± 14.2 years) was significantly higher than those with mild disease (53.8 ± 18.2 years) P = 0.019. But the body mass index between the two groups, no statistically significant difference was obtained P=0.869. There was no statistically significant difference of disease severity between male and female patients p = 0. 250. Laboratory findings of patients based on disease severity also shows that CRP, ESR and CKMB had a statistically significant difference between t mild and severe forms (P = 0.000). The underlying diseases in the patients showed that the highest frequency of underlying disease with 301 cases (20.1%) was related to hypertension and then with 110 cases (7.3%) was related to cardiovascular diseases. The underlying diseases in the patients based on the severity of the disease shows that in the severe group, hypertension (40% vs. 19.5%), diabetes (10% vs. 5.6%) and cardiovascular

**Table 1.** Final diagnosis of heart disorder based on age and gender

| | | Less than 50 years old N (%) | more than 50 years old N (%) | P | Male N (%) | Female N (%) | P |
|---|---|---|---|---|---|---|---|
| Final diagnosis of heart disorder | Acute myocarditis | 31(25.6) | 54(33.8) | 0.059 | 38(29.5) | 47 (30.9) | 0.005 |
| | Myocardial infarction | 19(15.7) | 35(21.9) | | 15(16.6) | 39(25.7) | |
| | Arrhythmia | 71(58.7) | 61(44.9) | | 76(58.9) | 66(43.4) | |

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disease (30% vs. 6.7%) have a higher frequency than the mild group and the history of underlying diseases between the two groups has a statistically significant difference P<0.0001. Final diagnosis of heart disorder based on patients' gender and age of patients is shown in table1.

The final diagnosis in patients with heart problems, based on the age group of patients, showed that there is no statistically significant difference. (P=0.059). In contrast based on the gender of the patients, there was a statistically significant difference between male and female P=0.005. Examination of ECG findings, troponin enzyme and final diagnosis of heart problems in patients showed that the highest frequency of abnormal ECG findings in patients with 111 cases (7.4%) was related to ST-segment changes and then 99 cases (6.6%) were related to heart rhythm changes. Of all COVID19 patients, the final diagnosis of myocardial infarction was acute myocarditis in 85 cases (5.7%), arrhythmias in 142 cases (9.5%), and myocardial infarction in 54 cases (3.6%). Cardiac troponin I levels also increased in 122 cases (8.1%). Examination of ECG findings, troponin enzyme and final diagnosis of heart problem in patients based on disease severity shows more abnormal findings in primary ECG of patients with severe disease; this difference is also statistically significant P<0.0001. Also, the frequency of problems Cardiac has a statistically significant difference between severe and mild groups P<0.0001. Evaluation of cardiac troponin enzyme Patients also showed that in the group with severe disease, 33 cases (82.5%) and

**Table 2.** ECG findings, troponin enzyme and final diagnosis based on disease severity

| Variables | | Severe form N (%) | Mild form N (%) | p |
|---|---|---|---|---|
| First ECG | Sinus rhythm | 0 (0/0) | 1215(83/2) | P<0.0001 |
| | Heart rhythm changes | 1(2/5) | 98(6/7) | P<0.0001 |
| | ST changes | 19(47/5) | 92(6/3) | P<0.0001 |
| | T changes | 20(50/0) | 56(3/8) | P<0.0001 |
| Final diagnosis of heart disorder | Acute myocarditis | 18(45/0) | 67(4/6) | P<0.0001 |
| | Myocardial infarction | 14(35/0) | 40(2/7) | P<0.0001 |
| | Arrhythmia | 8(80/0) | 134(9/2) | P<0.0001 |
| cardiac troponin | Normal | 7(17/5) | 1372(93/9) | P<0.0001 |
| | Increased | 33(85/5) | 89(6/1) | P<0.0001 |

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the group with mild disease, 89 cases (6.1%) had abnormal troponin levels P<0.0001 (Table 2).

**Discussion and Conclusion**

Cardiovascular disease is a common comorbidity observed in COVID-19 patients (29). A similar pattern has been reported in SARS and MERS (7), which reported simultaneous hypertension between 35% and 57%, coronary artery disease between 10% and 17% (8-10). On the other hand, the prevalence of cardiovascular diseases is higher in patients with high severity. Moreover, the relationship between COVID-19 is not clear whether the cardiovascular disease contributes to the worsening of cardiovascular disease. What is known is that cardiovascular patients are at a higher risk of developing the severe form of the disease, and 30 to 35% of deaths from COVID-19 are due to cardiovascular disease (11). In the study of Stefanini et al. (12), which examined myocardial infarction with elevated ST segment in COVID- 19 patients, the highest frequency of underlying disease was related to hypertension. Of the 1,501 COVID- 19 patients studied, about one-fifth had high blood pressure simultaneously, which was twice as high as 40 % in people with severe disease, which is consistent with previous findings. In a study performed in the United States, 2 to 5 % of patients needed to be hospitalized in an intensive care unit. On the other hand, 72 cases (4.8%) of patients needed to be admitted to the intensive care unit (13). Another result of the present study was the presence of 142 cases (9.5%) of arrhythmias in the studied patients. A more intimate look at this position among patients with severe and mild outcomes shows that the arrhythmia was 20% in deceased patients and 9.2% in recovered patients.

Study reports of early cases of arrhythmias in China Have shown 16.7% (14). Other reports have shown that arrhythmias in critically ill patients are 5.9%, which is significantly higher in people with myocardial injury (17.3% vs 1.5% in other patients P<0.001) was higher (15).These findings, which are consistent with the results of the present study, indicates that myocardial damage may cause secondary arrhythmias, while multiple arrhythmias in COVID-19 patients should raise the suspicion of inflammatory wandering. On the other hand, most of the cardiac arrests of inpatient patients have non-electroshock arrhythmias (16). In the present study, 54 cases (3.6%) had a myocardial infarction. The incidence of acute coronary syndromes in viral infections is probably increased due to the instability of plaques due to inflammatory processes. The risk of developing acute coronary syndromes in COVID-19 disease is unknown, but other viruses are three to ten times more common(17-19) Myocarditis has been reported clinically in Covid-19 disease and rarely reported in the endomyocardial autopsy; diffuse infiltration of T lymphocytes has been reported(20). In another report of the endomyocardial autopsy, the SARS-CoV-2 virus was found inside cardiac macrophages

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but not in cardiomyocytes (21). It is enough. However, the mechanism of its creation remains unknown. Despite the prevalence and lack of access to cardiac MRI and myocardial autopsy in most health care centres, the optimal method for diagnosing myocarditis are using tests (cardiac enzymes), ECG (segment changes), and echocardiography (abnormal wall movements, cardiac output and pericardial effusion) (22). In the present study, 85 patients (5.7%) had acute myocarditis. Cardiac troponin I was also elevated in 1222 patients (8.1%). The mechanism of direct myocardial damage includes plaque rupture and direct invasion of the virus. ACE2 receptors used by the SARS-CoV-2 virus to enter cells are widely expressed in the lung, myositis, and vascular endothelial cells(23). Recently, histological evidence of direct virus invasion of the endothelium with diffuse inflammation of the endothelium causing Covid-19-induced endothelium has been published (24). Endothelium, with impaired blood microcirculation, causes an inflammatory response of tissues and ischemia of organs (25). In addition, reports of COVID-19 patients presenting with prominent cardiac symptoms without underlying heart disease indicate a high risk of myocarditis (26-32). In addition, indirect myocardial damage can be caused by cytokine storm, microangiopathy, or an imbalance of myocardial oxygen supply and demand. The inflammatory response and cytokine storm are the hallmarks of severe Covid-19 disease, which can cause myocardial stress and injury, which in turn can indirectly affect cardiac dysfunction by affecting systemic peripheral vascular resistance and the effects of catecholamines, similar to that are seen in cardiomyopathy (28).The present study findings also show that in patients with severe COVID-19 inflammatory markers such as ESR and CRP are significantly higher than patients with mild form. One of the limitations of this study is the impossibility of investigating the mechanisms of cardiovascular problems in patients. Also, since the study was performed in the first wave of the disease, most patients were not in the excellent mental and physical condition and may not have been careful in answering some questions.

According to the results obtained in the present study, underlying cardiovascular diseases are associated with a higher severity than COVID-19. On the other hand, COVID-19 also causes or exacerbates cardiovascular diseases that require special attention of the staff. Treatment and follow-up of patients' clinical condition, especially regular use of ECG for early detection of arrhythmias.

Acknowledgment

This article was result of a specialty’s thesis of infectious diseases of Dr. Mousa Javadian and was supported by the Vice-Chancellor for Research at Mazandaran University of Medical Sciences (Grant Number: 7835).

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