Cardiac Health Indicators in Critical COVID-19 Cases

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ABSTRACT

Coronavirus disease-2019 (COVID-19) is an infectious disease that has spread worldwide and led to ongoing global concern. The pandemic prompted researchers to examine the impact of COVID-19 on human organs. The heart is one such organ. This study investigates the possible prediction of heart condition using some biochemical markers of particularly critically ill patients referred to an intensive care unit (ICU). Results of various serum biomarkers of patients infected with COVID-19 receiving treatment in the ICU, Asir Central Hospital, Asir Region, Saudi Arabia, were extracted and compared with healthy individuals using the Mann–Whitney U test. The study showed a distinguished increase in total Serum creatine phosphokinase-Total (CPK-Total), Serum creatine phosphokinase-MP (CPK-MP) levels among COVID-19/ICU patients. But, this increase was not statistically significant. Besides, aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase levels revealed a statistically significant increase in the infected group compared with controls. Examination of electrolytes showed a reduction in calcium median value in COVID-19/ICU patients. Data revealed a possible influence of COVID-19 on the heart. Herein, we observe significant parameters that may reflect cardiovascular injury elicited by the virus. These biomarkers possibly used to monitor the severity of disease on the cardiovascular system.

KEYWORDS: Cardiac Function; SARS-CoV-2; Intensive Care Unit; Cardiac Biomarkers; Disease Prognosis.

1. INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel pathogen that belongs to the genus Betacoronavirus [1]. This virus first originated in December 2019 in patients from Wuhan, Hubei Province, China, which led to ongoing pandemic worldwide [1]. Unfortunately, increase in the number of people diagnosed with COVID-19 has overwhelmed healthcare system of numerous countries [1]. Three factors helped to facilitate the dissemination of the virus: (1) the rapid transmission from human to human, (2) the novelty of the virus, and (3) international travel [2]. The current pandemic revealed a strong association between death in older people and chronic diseases. Diseases such as hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular disease, and cerebrovascular disease increase the chance of the complications and severity of COVID-19 in infected persons [3]. Respiratory failure was demonstrated as a cause of mortality in COVID-19 infection. However, COVID-19 fatalities have shown an association with cardiac signs. Although some patients exhibited symptoms related to heart concerns, including palpitations and chest pain, the relationship between heart disease and COVID-19 required further investigations [4]. Eight to 25% of overall patients infected with COVID-19 showed clinical symptoms of cardiovascular (CV) conditions, a high proportion of whom died [5]. Moreover, a diagnosis of the cardiac injury is included in patients with SARS-CoV-2 when troponin I, a cardiac biomarker, is higher than the reference interval [6]. Postmortem biopsy analysis of a COVID-19 patient has shown a linkage between COVID-19 and myocarditis. Myocarditis was confirmed by the presence of inflammatory infiltrates in the interstitial space of myocardium of patient diagnosed with COVID-19 [7]. Besides, acute heart failure can be the primary presentation among patients with COVID-19, and also the risk of venous thromboembolic event development may occur [8]. Thus, preexisting cardiac diseases in patients with COVID-19 predispose in developing severe complications [9]. The present study aimed to compare the biomarkers requested by health providers for COVID-19-positive patients admitted to ICU with normal individuals for investigating the possible alterations in

the biomarkers due to the virus in severe cases. This investigation may provide pathognomonic signs to the severity of the disease and the possible protection.

2. METHOD(S)

The present study was carried out in the Department of Clinical Laboratory Sciences, Faculty of Applied Medical Sciences, King Khalid University, Saudi Arabia. The study included results of 30 patients infected with COVID-19 receiving treatment in the ICU, Asir Central Hospital, Asir Region, Saudi Arabia, which were then compared with the selected healthy individuals. The age of patients ranged between 30 and 90 years old. Ethical approval {REC - No: (REC-11-1O-2020)} for this study was obtained from the Regional Committee for Research Ethics, Directorate Health Affairs - Asir Region, Ministry of Health, Saudi Arabia.

Blood samples of healthy individuals were collected from vein puncture of selected healthy participants and placed in plain tube without any anticoagulant for several biochemical tests. The serum was separated from the clot by centrifugation at 3,000 rpm for 10 minutes at room temperature. The clear supernatant was immediately transferred to another test tube and used for serum biochemical analysis. Patients' data were extracted from the Laboratory Information System exclusively, which provided information on the age, gender, ethnicity, and results of each patient.

Evaluation of biochemical tests was analyzed using a fully automated biochemical analyzer (Autoanalyzer, Bechman DXC 600). Serum creatine phosphokinase-Total (CPK-Total), creatine phosphokinase-MP (CPK-MP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), sodium, potassium, calcium, magnesium, and chloride were measured.

For statistical analysis, GraphPad Prism was used for analyses (GraphPad Prism version 9.00 for Mac, GraphPad Software, San Diego CA). The Mann–Whitney U test was used to compare COVID-19 patients with normal healthy individuals. To evaluate the degree of association between two variables, Spearman's correlation was used. A significant *P* value was considered when it is less than 0.05.

3. RESULTS

To investigate the association between SARS-CoV-2 infection and cardiovascular events, several cardiac biomarkers were investigated. The Mann–Whitney U test was used to examine the statistical differences between the two groups. CPK-Total level in COVID-19/ICU patients was statistically measured and showed a higher value than that of the control group (Figure 1). However, the Mann–Whitney U test was not significant between COVID-19/ICU patients (M = 119 U/L; p = 0.2311; U = 216.5) and the control group (M = 80 U/L; p = 0.2311; U = 216.5). Likewise, the median of creatine kinase-MP (CK-MP) (Figure 2) of COVID-19/ICU patients showed an elevation in the value (M = 35.40 U/L; p = 0.3833; U = 6) than the control group (M = 14.90 U/L; p = 0.3833; U = 6). However, the results were not statistically significant by the Mann–Whitney U test. In contrast, AST and ALT levels were significantly higher among patients than control (Figure 3). AST and ALT analyses by the Mann–Whitney U test were (M = 31.90 U/L; p < 0.0001; U = 179; *n* = 29) and (M = 50.70 U/L; p <0.0001; U = 174; *n* = 27) for ICU patients, respectively. Besides, LDH level revealed a roughly 2-fold increase in the patient group in comparison with controls (Figure 4). The Mann–Whitney U test was used to compare the median and showed significant values (M = 384 U/L; p = 0.0009; U = 52; *n* = 21) compared with control (M = 228.5 U/L; p = 0.0009; U = 52; *n* = 14). Additionally, electrolyte panel including Sodium (Na), Potassium (K), Magnesium (Mg), Chloride (Cl), and Calcium (Ca) was statistically analyzed (Figures 5 and 6). However, the Mann–Whitney U test at *P* < 0.05 was used to compare the median of two groups, and no statistical differences (p > 0.05) were observed. However, the Ca median value was significantly lower in COVID-19/ICU patients (M = 8.300 mg/dL; p < 0.0001; U = 52.50; *n* = 26) than the control (M = 9.295 mg/dL; p < 0.0001; U = 52.50; *n* = 28) as shown in Figure 5.

Figure 1: Comparison of CPK-Total levels between COVID-19/ICU patients and healthy controls. Mann–Whitney U test at P < 0.05 was used to compare the median between the two groups

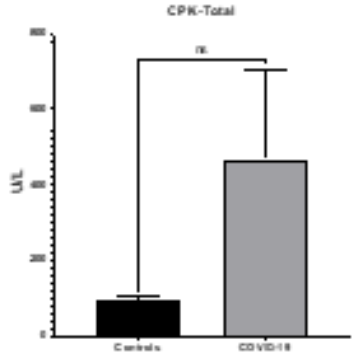


Figure 2: Comparison of CPK-MP levels between COVID-19/ICU patients and healthy controls. Mann–Whitney U test at P < 0.05 was used to compare the median between the two groups

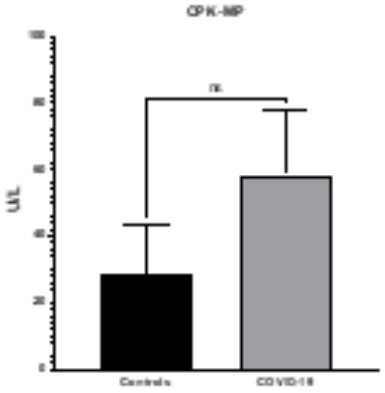


Figure 3: Comparison of AST and ALT levels between COVID-19/ICU patients and healthy controls. Mann–Whitney U test at P < 0.05 was used to compare the median between the two groups

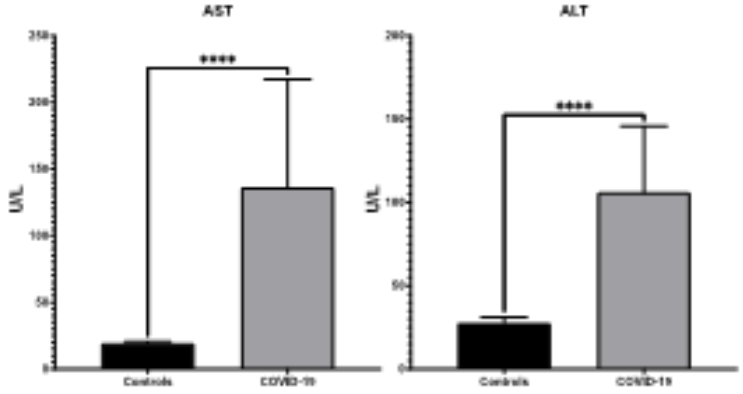


Figure 4: Comparison of LDH levels between COVID-19/ICU patients and healthy controls. Mann–Whitney U test at P < 0.05 was used to compare the median between the two groups

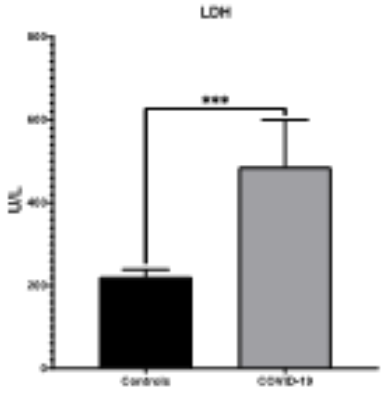


Figure 5: Comparison of Ca levels between COVID-19/ICU patients and healthy controls. Mann–Whitney U test at P < 0.05 was used to compare the median between the two groups

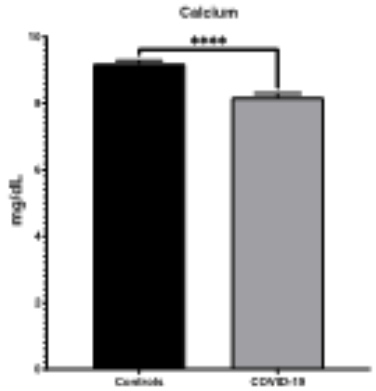
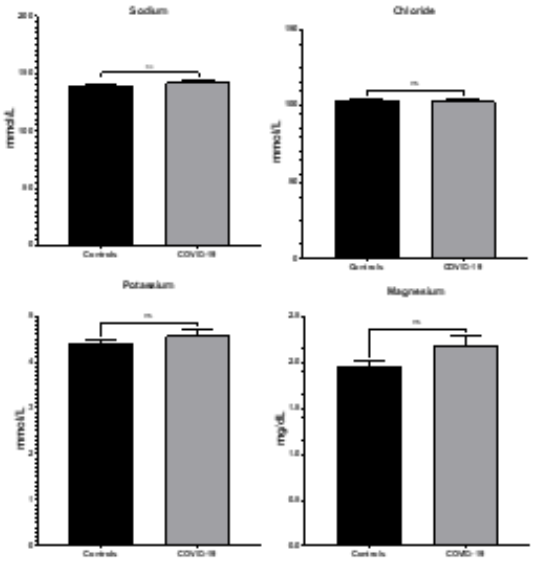


Figure 6: Comparison of sodium, chloride, potassium, and magnesium levels between COVID-19/ICU patients and healthy controls. Mann–Whitney U test at P < 0.05 was used to compare the median between the two groups



4. DISCUSSION

The association risk between the cardiovascular system and SARS-CoV-2 was determined by several studies [10–12]. However, the correlation remains limited [9]. Patients with cardiovascular disease infected with COVID-19 showed to worsen the cases of cardiovascular disease, contributing to the rate of mortality. On the other hand, myocardial injury, arrhythmia, acute coronary syndrome, and venous thromboembolism might be directly induced by COVID-19 in infected patients with no history of cardiac disease [1]. Therefore, the present study aimed to investigate the consequences of SARS-CoV-2 on the heart biomarkers for patients referred to ICU due to SARS-CoV-2.

Our study investigated CPK-Total and CPK-MP know as an indicator for cardiac injury [13]. Both biomarkers were high among COVID-19/ICU patients but were not statistically significant. However, the increase of CPK-Total and CPK-MP could indicate of a cardiac injury [13]. Cardiac injury might be due to the overactivity of immune system due to the attack by COVID-19 leading to ischemic injury [14].

Although the measurement of CPK-Total and CPK-MP is a valuable marker for acute myocardial infarction (AMI) diagnosis. Enzymes such as AST and LDH were historically used for AMI diagnosis. LDH is expressed by heart and can help in

diagnosis, particularly at the late stage of myocardial infarction disorder. and is a useful marker for AMI [15]. Additionally, AST/ALT ratio was recently stated to have predicted the risk of cardiovascular disease and mortality [16]. Thus, it is explaining the significant changes in AST and ALT of COVID-19/ICU patients when compared with the control group.

Additionally, a recent study has determined that LDH could serve as a prognostic biomarker for the disease severity [17]. The study showed that LDH is significantly high among dead COVID-19 patients than those who survived. The association of LDH with acute pneumonia was shown to be elevated [18]. Infection by SARS-CoV-2 could range from asymptomatic to atypical pneumonia [19]. Therefore, evaluating the level of LDH among COVID-19/ICU patients was of interest. Thus, we determined the level of LDH among COVID-19/ICU to examine that the LDH might predict the evaluation of the disease. As expected, the present study exhibited a significantly high level of LDH among patients with severe cases of COVID-19 referred to ICU compared with normal individuals.

The association between Ca and vascular health remained unclear. However, cardiovascular events may occur as an adverse effect due to the deposition of Ca in the vasculature, which is known to be a feature of vascular disease [20]. Additionally, Ca rule in heart is associated with myocardial contractility [21]. Reduction of Ca has shown to be a rare adverse cause of dilated cardiomyopathy [21]. Patient with dilated cardiomyopathy exhibited a fully recovery following Ca supplementation. Therefore, low or high level of Ca could contribute to heart diseases [22]. The level of Ca in a patient diagnosed with COVID-19 exhibited a reduction among mild/moderate and even severe cases in the early viral infection stage. But the reduction of Ca was even higher than that of early stage in severe/critical cases [23]. This is similar to our observation in ICU patients.

The theory discussing the relation between SARS-CoV-2 and cardiac biomarkers was illustrated previously and in our study. Infection with COVID-19 could induce heart-related diseases via several methods: (1) Direct alteration of angiotensin-converting enzyme 2 (ACE2) signaling pathway, (2) COVID-19 infection induces inflammatory response leading to organ damage, (3) COVID-19 impairs myocardial demand/supply ratio causing acute myocardial injury, (4) acute myocardial infarction developed due to plaque rupture, (5) therapies related, and (6) electrolyte disturbance [9].

The present study displayed that SARS-CoV-2 infection has a contribution to developing heart-related conditions. SARS-CoV-2 has direct and indirect involvement in the cardiovascular system. Biochemical screening tests to examine heart status could assess the estimation of a patient's critical severity and may further improve the treatment protocol carried out by clinicians to control the infection, preventing the interference of the virus or methods of therapy used, which could adversely lead to SARS-CoV-2-related complications. The limited access to the patient's file for monitoring preexisting medical history and the requested tests for COVID-19/ICU patients such as Troponin has limited the scope of the study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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