



The potential influence of SARS-COV-2 infection on cardiac biomarkers in al-Madinah patient

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General Note



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ABSTRACT

Background and aim: There have been increasing evidence that some biomarker levels may be altered according to the severity of Covid-19. The largest datasets have been published in the Asian population, owing to the location of the original outbreak. However, it is possible that the clinical features of Covid-19 may be somewhat different in other populations around the world. Comorbidities that have been associated with severe illness and mortality include cardiovascular disease, chronic renal and chronic lung diseases. The current work aimed to evaluate the effects of Covid-19 on cardiac function by analyzing the levels of cardiac

enzymes and proteins in Saudi Covid-19 patients. *Methods and Results:* This was a prospective study was conducted between May 2020 to July 2020. A total of 100 adult Saudi Covid-19 patients were randomly collected from different hospitals (Ohud- King Fahd and Al-Madinah General hospitals) in Al-Madinah Al-Munawarah, Saudi Arabia. GraphPad Prism (version 5.01) was used to analyze the patient's data. Biochemical parameters were compared by unpaired t-tests and one-way ANOVA, and the data were represented as the mean (standard deviation). There were significantly increased levels of creatine kinase, lactate dehydrogenase, and troponin in severe Covid-19 cases compared with mild and asymptomatic cases. In addition, there were significantly increased levels of C-reactive protein and ferritin in Covid-19 patients. There were also strong positive correlations between cardiac biomarkers and inflammatory markers in severe Covid-19 patients. *Conclusion:* In Saudi Covid-19 patients, increased cardiac biomarker levels were correlated with increased levels of inflammatory markers (CRP and ferritin), suggesting that these patients are at high risk for cardiac damage and injury during the disease period.

Key words: Creatine Kinase, Covid-19, Coronavirus Disease, C-reactive protein, Cardiovascular Diseases, Troponin.

1. INTRODUCTION

The novel pneumonia known as coronavirus disease (Covid-19) has spread throughout the world including in the Kingdom of Saudi Arabia (Alhomayani & Alasmari, 2019). The epidemic has been confirmed by the World Health Organization as a public health emergency that needs to globally concern. The clinical and epidemiological data of Covid-19 patients from recent months have indicated that some diseases raise the risk of infection and can contribute to more severe lung injury and even death. These diseases are hypertension, cardiovascular diseases, and diabetes (Fang et al., 2020; Yang et al., 2006). Cardiovascular diseases (CVD) has shown a strong association with SARS (8%) and MERS (30%), (Gao et al., 2020; Madjid et al., 2020). Similarly, a high prevalence of CVD has been detected in Covid-19 patients; the majority of CVD patients who had Covid-19 experienced severe disease (Shi et al., 2020; Madjid et al., 2020). A study in Wuhan reported that 6.8% of 191 Covid-19 non-survivors had CVD; another study observed that 17% of Covid-19 non-survivors had CVD (Shi et al., 2020; Clerkin et al., 2020). However, the mechanism behind the association between CVD and Covid-19 is not clear - it could be a direct or indirect association. The majority of Covid-19 patients have a compromised immune system, which is common in patients with CVD (Hua et al., 2020). Patients with CVD have a higher risk of developing acute coronary syndrome in acute infections. This syndrome rises the myocardial demand, which finally causes myocardial injury or infarction (Zheng et al., 2020; Zhou et al., 2020). Cardiovascular comorbidities are common in Covid-19 patients who require urgent care to reduce morbidity and mortality (Zhou et al., 2020). Therefore, in this study, we investigated the association between Covid-19 and cardiovascular diseases (CVD) and the influence of infection on cardiac biomarkers.

2. PATIENTS AND METHODS

Subject and samples: This was a prospective study was conducted between May 2020 to July 2020. A total of 100 adult Saudi COVID-19 patients were randomly collected from different hospitals (Ohud- King Fahd and Al-Madinah General hospitals) in Al-Madinah Al-Munawarah, Saudi Arabia. All cases were reviewed based on the inclusion and exclusion criteria. Patients diagnosed with Covid-19 were included. Patients were excluded if they had a history of endocrine diseases or a history of major renal, liver, heart, or neurological disease. The laboratory data collected included the cardiac biomarkers creatine kinase, lactate dehydrogenase, and troponin. Based on the Saudi Health Ministry protocol, patients with confirmed Covid-19 were categorized as severe, moderate, mild, or asymptomatic according to the clinical characteristics and symptoms and chest radiography results (MOH, 2020).

Statistical analysis: The data were evaluated by GraphPad Prism program (version 5.01). Quantitative data that were normally distributed were expressed as percentages, mean, standard deviation, and range. The t-test was used for two variables, and one-way ANOVA was used to compare different categories of Covid-19 patients. Pearson correlation was used to investigate the association between the different variables and the severity of infection. Statistical significance was set at $P < 0.05$ and < 0.001 .

3. RESULTS

Baseline characteristics of patients with Covid-19:

In this study, the cohort of 100 patients diagnosed with Covid-19 had a mean age of 55.22 ± 13.58 years. Table 1 shows the baseline clinical characteristic of the study population. The subjects included 56 males and 44 females; 20% were smokers and 10% had diabetes as a chronic medical illness. The percentage of patients with severe Covid-19 was 50%; 31% had mild to moderate illness,

and 19% were asymptomatic. The data in Table 1 indicate that, compared with the normal range, the mean levels of CK, LDH, troponin, ferritin, and CRP were significantly higher in the Covid-19 patients.

Table 1: The Mean \pm SD for the biomarker's levels in Covid-19 patients.

Biomarkers	Covid-19 patients (n=100)	Comments	Reference Range
CK (U/L)	243.94 \pm 50.07	Elevated	22-198 U/L
LDH (U/L)	361.54 \pm 55.9	Elevated	98-192 U/L
Troponin (ng/L)	0.5 \pm 0.19	Elevated	0-0.4 ng/L
Ferritin (ng/mL)	1750.64 \pm 121.80	Elevated	20 to 250 ng/mL
CRP (mg/L)	29 \pm 9.35	Elevated	<10 mg/L

Data presents as Mean \pm SD for cardiac biomarkers levels that compared with normal reference range. CK = Creatine Kinase; LDH = lactate dehydrogenase; CRP = C-reactive protein.

Table 2: Correlation between cardiac biomarkers levels and inflammatory markers in severe Covid-19 patients

Parameter	CRP		Ferritin	
	<i>r</i>	<i>p</i>	<i>R</i>	<i>P</i>
CK (U/L)	0.622	0.004*	0.542	0.04*
LDH (U/L)	0.551	0.01*	0.531	0.01*
Troponin (ng/L)	0.332	0.05*	0.151	0.42

Data were analyzed by using Pearson correlation test, *r* is the correlation coefficient for each variable versus serum concentration of inflammatory markers. *P* < 0.05*, *P* < 0.001**

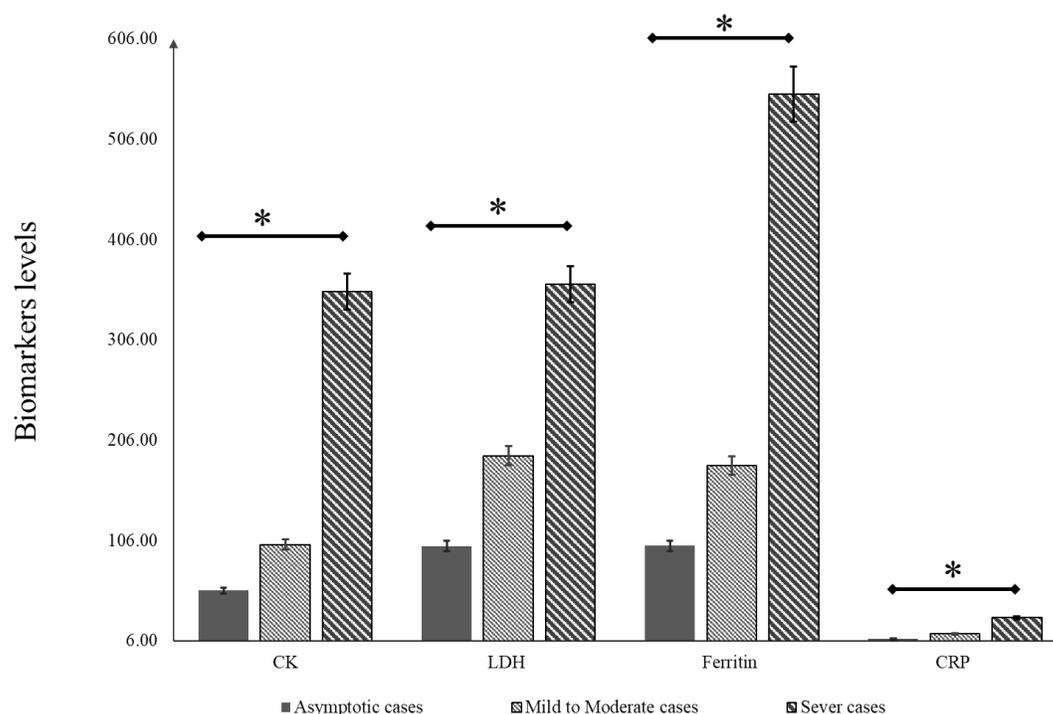


Figure 1: Laboratory features of the Covid-19 categories. Data was analyzed by One-Anova test to compare between three categories of Covid-19 patients and a statistical significance differences was considered as *P* < 0.001*

Laboratory features of the Covid-19 groups:

The cardiac enzyme concentrations were significantly increased in severe Covid-19 patients compared to the mild and asymptomatic patients ($P<0.001$) (Figure 1). Additionally, there were significantly increased levels of CRP and ferritin in the severe Covid-19 patients compared to the other two groups ($P<0.001$).

Relationship between cardiac biomarkers and inflammatory markers in severe Covid-19 patients:

A correlation analysis was performed to investigate the correlation between cardiac biomarker abnormalities and inflammatory markers in severe Covid-19 patients. CK ($r = 0.622$, $P = 0.004$), LDH ($r = 0.551$, $P = 0.01$), and troponin ($r = 0.332$, $P = 0.05$) were positively associated with the CRP level. Similarly, a significant positive correlation was observed between CK ($r = 0.542$, $P = 0.04$), LDH ($r = 0.531$, $P = 0.01$), and ferritin (Table 2).

4. DISCUSSION

People throughout the world have suffered from Covid-19. Some of these patients also have comorbidities, particularly pulmonary disease, hypertension, diabetes mellitus, hematological disorders, and cardiovascular diseases (Del et al., 2020; Yang et al., 2020; El-Malky et al. 2020). Biomarker evaluation is a useful tool in the early prediction and diagnosis of CVD. Cardiac markers such as CK, CKMB, troponin I/T, and LDH are commonly used to assess the level of damage caused by a heart attack (Henry et al., 2020). The aim of this study was to assess the levels of cardiac enzymes and to investigate the potential correlation between cardiac markers and inflammatory markers in patients with Covid-19. The results showed that the mean CK, LDH, troponin, ferritin, and CRP levels were significantly higher in Covid-19 patients when compared with the normal range. The clinical spectrum showed that cardiac enzyme concentrations were significantly increased in severe Covid-19 patients compared to mild and asymptomatic patients. Furthermore, the troponin levels were higher in the severe group compared to the other two groups. In agreement with our findings, previous studies have found similar results for cardiac biomarkers (Lippi et al., 2020; Madjid et al., 2020; Zhou et al., 2020).

Regarding the correlation between cardiac biomarker abnormalities and inflammatory markers in severe Covid-19 patients, the CK and troponin levels were positively correlated with the CRP level. Similarly, a significant positive correlation was observed between CK and ferritin, most likely due to pre-existing cardiac conditions or from myocardial dysfunction being triggered by Covid-19 (Henry et al., 2020; Madjid et al., 2020). Many studies have found that CVD complications can result from this viral infection, significantly impacting the high morbidity and mortality rates (Ruan et al., 2020; Zhou et al., 2020; Xiong et al., 2020). Myocardial injury was considered as a complication for patients with severe Covid-19 infection. An assessment of cardiac injury biomarkers may help to identify those patients at the highest risk, potentially leading to improved therapeutic approaches (Eman et al., 2020). Elevated troponin I combined with either advanced age or elevated aspartate aminotransferase (AST) was found to be the best model to predict poor outcomes in CVD, and an assessment of cardiac injury biomarkers may improve the identification of Covid-19 patients at highest risk (Qing et al., 2020). Elevated cardiac markers are probably due to secondary and systemic consequences and can be considered as a warning sign of recent adverse clinical outcomes of the patient (Driggin et al., 2020; Gergorio et al., 2020; PMCID, 2020). Elevated troponin and ferritin levels are an indication of severe disease, and ferritin in particular is elevated compared with non-severe patients. Therefore, it can be assumed that serum ferritin levels are strongly related to the severity of Covid-19. Troponin is also a useful marker of disease progression and prognosis in Covid-19 (Gergorio et al., 2020; Xu et al., 2020). Therefore, myocardial biomarkers should be evaluated in CVD patients who develop Covid-19 for risk stratification purposes; this could lead to earlier and more aggressive interventions in this patient group (Driggin et al., 2020). Researchers are actively investigating various aspects of this novel coronavirus to clarify the clinical manifestations of this disease and to improve patient management during this pandemic.

5. CONCLUSION

Our findings confirm the correlation between increasing the cardiac biomarker levels and the severity of Covid-19 infection in Saudi patients. Also, the positive associations between increasing cardiac marker levels and increasing the level of inflammatory markers (CRP and ferritin) in this study suggesting that Covid-19 infected patients are at high risk for cardiac injury during the disease period. However, the limitation of this study involves small sample size of only 100 infected cases. Therefore, current study encourages more research to clarify the complicated relationship between the severity of Covid-19 infection, and the risk of cardiac damage.

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Authors' contributions

WM: Conceptualization, study design, software, data curation, analysis and interpretation, original draft preparation and formal analysis, reviewing and editing. Author significantly contributed to this research and hold responsibility for its quality and content. Author has critically reviewed and approved the final draft and is responsible for the content and similarity index of the manuscript.

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Conflict of Interest

The author has no conflict of interest to be declared

Ethics approval

It was granted by the Ethics Clearance Committee of the Faculty of Applied Medical Sciences at Taibah University and Saudi Arabia Ministry of Health, General Administration for Researches & Studies (SREC/AMS 2020/63/CLD, IRB 452).

Data and materials availability

All data associated with this study are available upon request to the corresponding author.

Peer-review

External peer-review was done through double-blind method.

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