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Plasma brain natriuretic peptide, D-Dimer, and serum troponin-I as predictors for in-hospital death in patients with COVID-19

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Abstract

The severe acute respiratory syndrome coronavirus 2, first appeared in Wuhan, China, in December 2019. Since then, a variety of strains of the virus were spread throughout the world, prompting the World Health Organization to declare a pandemic in March 2020. Additionally, Coronavirus disease 2019 (COVID-19) can cause a variety of symptoms, ranging from fatigue and fever to severe respiratory and cardiovascular complications. This study evaluated the role of brain natriuretic peptide (BNP), troponin-I and D-dimer as biomarkers for death prediction in hospitalized patients with COVID-19. The study included 90 patients with COVID -19 diagnosed with PCR-RNA testing. They were divided into survivors and non-survivors. Also, 20 apparently healthy individuals age and sex matched were included as a control group. Plasma BNP and serum troponin-I were measured by enzyme linked immune-sorbent assay (ELISA) technique. D-dimer was measured by a turbidimetric technique. Patients with COVID-19 had significantly elevated levels of serum Troponin-I and plasma BNP in comparison to controls (p< 0.0001, for both). D-dimer, troponin–I and BNP levels were significantly higher in the non-survivors group when compared to the survivors group. Troponin-1 can predict COVID-19 severity with sensitivity, specificity, and accuracy of 55.1%, 66.7%, and 57.8%, respectively at a cutoff value of 0.075 (ng /ml); and area under the receiver operating characteristic (AUC) curve of 0.670 (95% CI: 0.551 – 0.790, p=0.018). BNP can predict COVID-19 severity with sensitivity, specificity, and accuracy of 98.6%, 71.4%, 92.2%, respectively at a cutoff value of 16.02 (Pg /ml) and AUC of 0.872 (95% CI: 0.778 – 0.965, p<0.001). Univariate and multivariate logistic regression analysis showed that only BNP level can significantly predict death among COVID-19 infected patients. In conclusion, plasma BNP and serum troponin-I could be used as prognostic biomarkers for determination of the severity of COVID-19 and BNP could predict mortality.

Keywords: COVID-19, BNP, Troponin-I, D-dimer

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Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), had been declared as a global pandemic since its first appearance in late December 2019.[1] Following the statistic from the World Health Organization (WHO), as of 22, December 2022, the cumulative number of confirmed COVID-19 cases exceeded 664 million, with more than 6.6 million deaths.[2] COVID-19 was found to interact with and affect the cardiovascular system, leading to myocardial damage, and there is an urgent need to better understand the cardiovascular consequences of COVID-19.[3] The following incident cardio-vascular diseases were identified to develop myocardial infarction, stroke, heart failure, atrial fibrillation, venous thromboembolism and pericarditis.[4] Coronavirus can cause cardiovascular injury via a variety of mechanisms, including increased cardiometabolic demand associated with systemic infection and ongoing hypoxia caused by severe pneumonia or acute respiratory distress syndrome, cytokines release and during ongoing severe inflammation, resulting in acute respiratory distress syndrome and other end-organ damage.[5]

Moreover, the interaction of SARS-CoV-2 with angiotensin-converting enzyme-2 can cause changes to the enzyme pathways, leading to acute injury of the lung, heart, and endothelial cells.[6] Coronary thrombosis has also been identified as a possible cause of acute coronary syndrome in COVID-19 patients.[7] As treatment in the intensive care unit (ICU) has become more difficult, timely triage of patients necessitates prompt recognition of severe forms of COVID-19. The evaluation of disease severity may be made easier by a number of laboratory parameters.[8]

Brain natriuretic peptide (BNP) is considered a biomarker for congestive heart failure.[9] In patients with COVID-19, the release of BNP may occur for a variety of reasons. First, the use of a mechanical ventilator and involvement of the respiratory system increase pulmonary vascular tone, resulting in right ventricular afterload and wall stretching; indicating the most potent mechanical stimuli that result in BNP release.[10] Second, the BNP release may be caused by direct myocardial tissue involvement caused by activation of the inflammatory system, oxidative stress, demand-supply mismatch, or direct virus-induced myocardial invasion and injury.[11] Moreover, cardiac troponin-I, a marker for myocardial injury, was frequently elevated in COVID-19 patients in hospitals.[12] Such patients frequently suffer from cardiac injury, which is linked to a higher death risk.[13] A fibrin degradation product known as D-dimer is also frequently used as a biomarker for thrombotic diseases.[14] In COVID-19, thrombotic consequences, and coagulopathies, such as disseminated intravascular coagulopathy, were frequent observed.[15] This study aimed to evaluate the role of two cardiac markers, BNP, troponin-I and D-dimer as biomarkers for death prediction in COVID-19 hospitalized patients.

Subjects and Methods

All patients were recruited from the ICU at Assiut University Hospital during the period between March 2021 to June 2021. The study protocol was reviewed and approved by the Institutional Review Board of the Faculty of Medicine, Assiut University, (November 2020). Also, the study was registered as a clinical trial (registration Clinical Trials ID: NCT04445415). Inclusion criteria included: patients with COVID-19, the infection was confirmed by the PCR-RNA testing, according to the standard method of the hospital. Exclusion criteria included: malignancy, acute myocardial infarction, and pregnancy.

The study included 90 COVID-19 patients (34 females and 56 males). Their ages ranged from 23 to 86 years. Based on the outcome of the studied patients, they were divided into two subgroups. The non-survivor subgroup, which included 69 patients (25 females and 44 males), and the survivor subgroup, 21 patients (9 females and 12 males). In addition, 20 apparently healthy individuals were included as a control group (10 females and 10 males).

All patients underwent a comprehensive medical history, clinical examinations, an

electrocardiogram, a computed tomography chest scan, and laboratory tests. Patient's data for erythrocyte sedimentation rate (ESR), diabetes mellitus, hypertension, liver and kidney diseases were collected from hospital records.

Methods

Whole blood samples (8 ml) were collected under complete aseptic conditions. Of these, an aliquot of 2 ml was added to a sodium citrated tube for assay of prothrombin time (PT), partial thromboplastin time (PTT), and D-dimer by full automated coagulation analyzer (Sysmex CS-5100®, Siemens-Healthineers, GmbH Henkestr. 127 91052 Erlangen, Germany) according to the manufacturer's instructions. Another aliquot of 2 ml was added to an EDTA tube for complete blood cell counting using fully automated hematology analyzer (ADVIA®2120i hematology system, Siemens-Healthineers, GmbH Henkestr. 127 91052 Erlangen, Germany), according to the manufacturer's instructions. The remaining sample (4 ml) was added to gel and clot activator tube for separating sera, used for routine chemistry investigations. These included serum ferritin and serum C-reactive protein (CRP), were done by a full automated blood chemistry system (ADVIA® 1800 chemistry system, Siemens-Healthineers, GmbH Henkestr. 127 91052 Erlangen, Germany), according to the manufacturer's instructions. Serum creatine kinase (CK), creatine kinase myocardial bound (CK-MB mass) and lactate dehydrogenase (LDH) were done using a chemistry analyzer (Dimension® Xpand® Plus Integrated Chemistry System, Siemens-Healthineers, GmbH Henkestr. 127 91052 Erlangen, Germany), according to the manufacturer's instructions. Finally, estimation of serum BNP and troponin I was done using the automated Immunoassay Analyzer (TOSOH AIA-360, TOSOH corporation, Shiba, Minato-Ku, Tokyo 105-8623, Japan) according to the manufacturer's instructions.

Statistical analysis

All statistical calculations were done using SPSS (statistical package for the social science; SPSS Inc., Chicago, IL, USA) version 22. Data were described in terms of mean ± standard deviation (±SD), or median and range when not normally distributed, frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative variables was done using student t test for normally distributed data and Mann Whitney U test for non- normally distributed data. For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlation between various variables was done using the Pearson correlation test. Receiver Operating Characteristic Curve (ROC) analysis was used to find out the best cut-off values to validate the prediction of COVID-19 infection and its mortality using different cardiac markers. Odds ratio (OR) with 95% Confidence Interval (CI) and Logistic Regression was calculated for prediction of development of COVID-19 infection and its mortality. Two tailed *p*-values were always calculated, set significant at 0.05 level.

Results

This study included 90 COVID-19 patients (group I) and 20 apparently healthy, age- and sex matched individuals as controls (group II). The patient group was classified into two subgroups non-survivors (subgroup Ia), which included 69 (76.6%) patients, 25 (36.2%) females, and 44 (63.8%) males, and survivors (subgroup Ib), which included 21 (23.2%) patients, 9 (42.9%) females, and 12 (57.1%) males. Clinical evaluation of the studied groups revealed that 56 (62.2%) of them were diabetic, 33 (36.7%) hypertensive, 3 (3.3%) had liver disease, and 13 (14.4%) suffer from renal disease (Table 1).

Table 1. Demographic and clinical data of the studied groups.

Variable name	Patient Group (I) (n=90)		Control Group (II) (n=20)		*p*-value
Age (years)					
Mean ± SD	56.73 ± 14.75		54.25 ± 12.03		NS
Median (range)	60 (23 – 86)		57 (30 – 70)		
Sex	N	%	N	%	
Male	56	(62.2)	10	(50.0)	NS
Female	34	(37.8)	10	(50.0)	
Comorbidities					
Diabetes mellitus	56	(62.2)			
Hypertension	33	(36.7)			
Liver disease	3	(3.3)			
Renal disease	13	(14.4)			

Quantitative data are presented as mean ± SD and median (range), qualitative data are presented as number (percentage), *P* > 0.05 is not significant (NS).

In the patient group (I), there was a statistically significant increase in total white blood cells (WBCs) count, absolute neutrophilic count and a significant decrease in absolute lymphocytic count compared to the control group (II) ($p <$ 0.0001). Serum ferritin, serum CRP, and ESR levels were also elevated in the patient group (I) when compared to the control group (II) ($p <$ 0.0001) (Table 2).

Table 2. Data of laboratory tests in the studied groups.

	Patient Group (I) (n=90)	Control Group (II) (n=20)	*p* -value
WBCs (10^3/ul)	10.6 (1.3 – 30.0)	6.4 (4.5 – 9.6)	<0.0001
Neutrophil (10^3/ul)	8.6 (1.1 – 28.5)	4.5 (2.4 – 6.5)	<0.0001
Lymphocyte (10^3/ul)	0.9 (0.03 – 5.0)	1.8 (1 – 3.1)	<0.0001
Serum Ferritin (ng/L)	570.5 (11.4 – 3816)	181 (67 – 298)	<0.0001
CRP (mg/L)	58 (2 – 273)	2 (1 – 6)	<0.0001
ESR (mm/hr)	61 (10 – 140)	6 (2 – 11)	<0.0001

CRP: C-reactive protein; ESR: erythrocytes sedimentation rate. Quantitative data are presented as median (range).
*$P \leq 0.05$ is significant.

There were statistically significant elevations of serum troponin-I, LDH, BNP, and D-dimer levels in COVID-19 patients (group I) when compared to control subjects (group II) ($p<$ 0.0001 for all). There were statistically significant increases in serum troponin-I, total CK level, CK-MB (Mass), and BNP levels in the non-survivors' group (group Ia) when compared to the survivors' group (group Ib) ($p=$ 0.018, p = 0.032, p = 0.043, and p = 0.000), respectively) (Table 3).

Table 3. Comparison of cardiac markers and D-dimer between the studied groups and between the subgroups of the COVID-19 patients (subgroups Ia and Ib).

Studied groups and subgroups	Cardiac markers					
	Troponin (ng/ml)	CK total (U/l)	CK -MB (Mass) (ng/ml)	LDH (U/L)	BNP (Pg/ml)	D-Dimer
Group I (n=90)	0.08 (0.0–15.03)	67.5 (10–3377)	1.9 (0.7 – 11.8)	575.2 (265.8–2301.0)	37.2 (0.02–820.2)	1.1 (0.19 – 14.9)
Group II (n=20)	0.01 (0.0 – 0.05)	54.5 (15–214)	1.8 (1.1 – 2.9)	161.0 (122 – 188)	10.6 (0.10–26.13)	0.15 (0.03–0.50)
p value	<0.0001	NS	NS	<0.0001	<0.0001	<0.0001
Subgroup Ia (Non-survivors) (n=69))	0.08 (0.0–15.03)	75.5 (10–3377)	2.0 (0.7–11.8)	599.5 (265.8 – 2301.0)	50.3 (14.2 – 820.2)	1.12 (0.19 – 14.9)
Subgroup Ib (Survivors) (n=21)	0.07 (0.01–0.70)	52.0 (15 – 214)	1.7 (0.9 – 2.9)	449 (274.4 – 1144.4)	10.0 (0.02 – 55.0)	1.06 (0.19 – 5.4)
p value	0.018	0.032	0.043	NS	<0.0001	NS

Quantitative data are presented as median (range), $P > 0.05$ is not significant (NS).

To determine the diagnostic ability of the studied cardiac markers for prediction of death among COVID-19 infected patients, the ROC curve analysis was performed. For troponin, the sensitivity, specificity, and accuracy were 55.1%, 66.7%, and 57.8%, respectively at cutoff value of 0.075 (ng/ml), and area under the ROC curve of 0.670. For the total CK the sensitivity, specificity, and accuracy were 55.1%, 66.7%, and 57.8%, respectively at cutoff value of 67.5 (U/L), the area under the ROC curve of 0.655. For CK-MB (Mass), the sensitivity, specificity, and accuracy were 55.1%, 57.1%, and 55.7%, respectively at cutoff value of 1.85 (ng/ml), and the area under the ROC curve of 0.646. Finally, for BNP, the sensitivity, specificity, and accuracy were 98.6%, 71.4%, and 92.2%, respectively at cutoff value of 16.02 g/mL, and the area under the ROC curve of 0.872 (Figure 1).

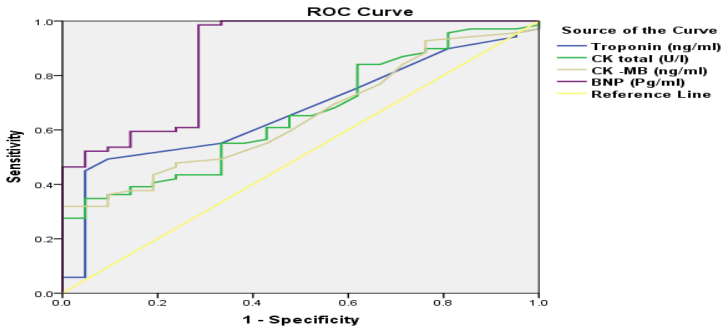

Figure 1. ROC curves for prediction of death among COVID-19 infected patients. Troponin (ng/ml) (blue), CK-total (U/L) (green), CK- MB mass (ng/ml) (brown), BNP (Pg/ml) (purple), and reference line (yellow). For Troponin, the area under the curve = 0.670 (0.551 to 0.790) *p*= 0.018. For CK-total, the area under the curve = 0.655 (0.531 to 0.779), p = 0.032. For CK-MB (Mass), the area under the curve = 0.646 (0.524 to 0.768), *p* = 0.043. And for BNP, the area under the curve = 0.872 (0.778 to 0.965), *p* < 0.000.

Univariate and multivariate logistic regression analysis for prediction of death among COVID-19 infected patients showed that only BNP level could significantly predict death among COVID-19 infected patients. Patients with BNP ≥ 16.02 were about 166 times more likely to die compared to patients with BNP < 16.02 (OR=166.19, 95% CI 17.289 – 1597) as shown in Table 4.

Table 4. Univariate and Multivariate logistic regression analysis for prediction of death among COVID-19 studied cases based on cardiac markers data.

Variables	N	Univariate analysis			Multivariate analysis		
		OR	95% CI	*p* value	OR	95% CI	*p* value
Troponin							
< 0.075	45						NS
≥ 0.075	45	2.452	0.881 – 6.825	NS	1.039	0.203 – 5.306	
CK total (U/l)							
< 67.5	45						NS
≥ 67.5	45	2.452	0.881 – 6.825	NS	1.039	0.203 – 5.306	
CK -MB (Mass) (ng/ml)							
< 1.85	43						
≥ 1.85	47	1.634	0.610 – 4.380	NS			
BNP							
< 16.02	16						
≥ 16.02	74	170.0	19.034 – 1518.359	<0.0001	166.19	17.289 – 1597.4	<0.0001

CI: Confidence interval; OR: Odds ratio. *P* > 0.05 is not significant (NS).

There was significant positive correlation between serum level of troponin and the CK-total (r= 0.704, $p < 0.001$), CK-MB (Mass) (r= 0.335, $p = 0.001$) and BNP (r= 0.316, $p = 0.002$) (Figure 2). Another significant positive correlation was observed between the serum level of CK-total and CK-MB (Mass) (r= 0.406, $p < 0.001$), and BNP (r= 0.224, $p = 0.034$) (Figure 3).

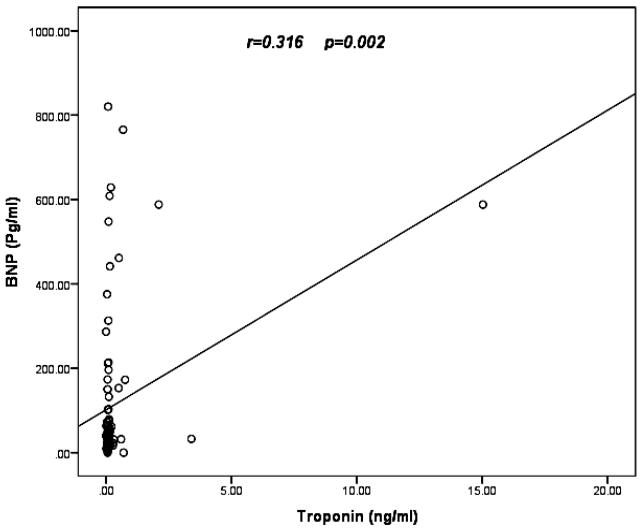

Figure 2. Scatter plot diagram showing the correlation between serum troponin (ng /ml) and BNP (Pg/ml) in COVID-19 cases.

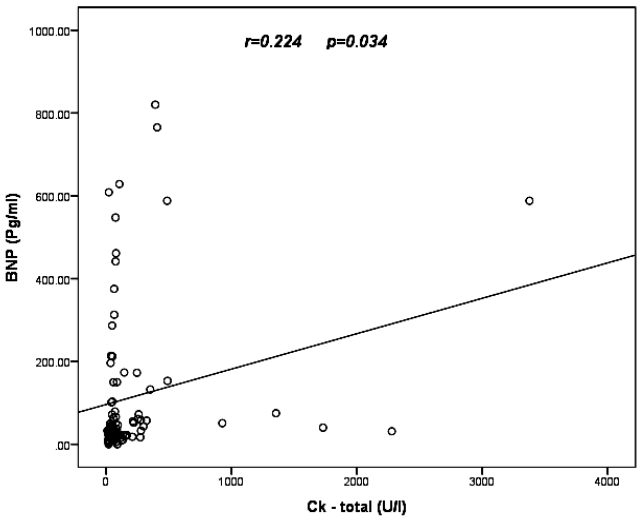

Figure 3. Scatter plot diagram showing the correlation between serum Ck-total (U/l) and BNP (Pg/ml) in COVID-19 cases.

Discussion

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in 2019 and resulted in a pandemic acute respiratory illness, called COVID-19.[16] Clinical symptoms can be varied from fever, cough, fatigue, headache, diarrhea, hemoptysis, dyspnea, ageusia, and anosmia. Cardiovascular manifestations play a significant role in predicting mortality among COVID-19 patients.[17] There is increasing evidence linking COVID-19 with increased morbidity and mortality from cardiovascular disease. Myocardial injury is common in COVID-19 hospitalized patients, usually accompanied by significant elevation of related cardiac biomarkers.[18-19]

This study aimed to evaluate the role of two cardiac markers, BNP, troponin-I and D-dimer as biomarkers for prediction of death in COVID-19 hospitalized patients. The study included 90 COVID-19 patients from the ICU at Assiut University Hospital during the period from March 2021 to June 2021. In this patient group, we observed a mortality rate of 76.6%. This finding agreed with observation of a study by Grasselli. et al., 2020, who reported that the overall mortality rate in ICU patients was somewhere between 16% and 78% and attributed this wide gap in reported mortality to different factors. These included the difference in the severity of disease at ICU admission time, availability of ICU beds, ICU admission criteria, sample size, underlying conditions, and length of follow-up.[20] A systematic review and meta-analysis study by Armstrong, et al., 2021, found that the mortality rate in 52 studies involving 43,128 patients admitted to ICU with COVID-19, was 35.5% (31.3–39.9%).[21] They also reported that the mortality rate was higher in the Middle East and lower in a single study from Australasia. Lower mortality rates of 19.8% and 23.8% were reported by Oliveira et al., 2021[22] who attributed these finding to the lower age of the studied group and higher proportion of non-African population.

The most common factors contributing to mortality in COVID-19 patients admitted in the ICU is the possible mechanisms of myocardial injury caused by COVID–19, termed acute COVID–19 cardiovascular syndrome, include heightened myocardial demand in response to the stress of infection, inflammatory cytokines creating a thrombogenic environment as the result of platelet activation and endothelial dysfunction, and direct myocardial damage.[23]

In the present study there was a significant elevations of serum troponin-I, CK-MB (Mass), LDH, BNP, and D-dimer levels in COVID-19 patients when compared to control subjects. Also, there were statistically significant increases in serum troponin-I, total CK level, CK-MB (Mass) LDH, and BNP levels in the non-survivors' subgroup when compared to the survivors' subgroup. These findings are supported by the findings of several studies. A study by Khan et al., 2021, who reported that

cardiac biomarkers can play an essential role in the diagnosis, management, and prognosis of COVID 19. However, cardiac biomarkers are usually increased in various cardiac pathologies, but they can be increased in some pulmonary diseases as well. They also reported that multiple preexisting or new-onset cardiac pathologies in COVID-19 can lead to increased cardiac biomarkers (especially in ICU patients). These comorbidities are also known as acute COVID–19 cardiovascular syndrome. They can be due to myocardial oxygen-energy demand-supply mismatch, direct viral infection, thromboembolic complications, or endothelial injury.[24]

Another study by Zhu et al., 2021, reported higher troponin levels among critically ill patients and in non-survivors compared to patients who were not critically ill or survived. In addition, they reported significantly elevated CK in non-survivors. Moreover, they reported that serum LDH was significantly higher in critically ill patients versus those who were not critically ill.[25]

The study by Li et al, 2020, also reported that the elevated cardiac troponin and CK in COVID-19 patients could be due to direct myocardial injury and can be used to estimate mortality risk[26] In addition, a study from Wuhan, China, reported higher CK-MB (Mass), LDH, myoglobin, and troponin-I among non-survivors when compared with survived patients.[27] Contrary to our findings, a study by Abdeen et al., 2021, found that BNP was not significantly higher in any of the groups of patients, whether survivors or non-survivors.[28] They attributed this finding to the wide plethora of pathophysiologic interaction of BNP which make it very difficult to extend its use beyond heart failure since the levels of BNP had been found to be elevated in non-dyspneic critical patients such as those with severe sepsis and septic shock. Also, they reported that BNP failed to predict length of hospital stay or long-term outcomes of morbidity and mortality.

In addition, Zinellu et al., 2021, found that COVID-19 patients with higher CK-MB concentrations had significantly higher rates of severe disease and death. This biomarker of myocardial injury may be valuable for risk separation in this gathering.[29] Furthermore, Ozdin et al., 2021, found that mortality was correlated with elevated levels of creatine kinase MB.[30] Similarly, previous studies showed that patients with COVID-19 and elevated CK-MB (Mass) levels were at higher risk of severe disease and mortality. Hence, elevated CK-MB (Mass) could be used as a predictor of adverse outcomes in COVID-19.[31,32]

A well-known indicator of myocardial injury is cardiac troponin.[33] It was reported that the troponin level of COVID-19 patients who did not survive was significantly higher than that of COVID-19 patients who survived, which is consistent with our findings.[34] Additionally, the study of Majure et al., 2021, found that COVID-19-infected hospitalized patients with elevated troponin had a significant increase in the risk of death and fared worse than patients with mildly elevated troponin.[35] Ali et al., 2022, reported that hospitalized COVID-19 patients with elevated cardiac troponin were more likely to die because cardiac biomarkers were typically elevated in COVID-19 patients.[36] Another study found that mortality was correlated with elevated levels of troponin, creatine kinase MB, and myoglobin.[30] The measurement of troponin can be used to predict the future of these patients as a sign of a worsening clinical situation.[37]

In the present study levels of D-dimer were significantly increased in the patient group compared to the control group. Despite that, we found no significant difference regarding D-dimer level between the non-survivors and survivors' groups. In agreement with that, Yao et al., 2020, stated that D-dimer levels were frequently elevated in SARS-CoV-2-infected patients.[38]

Acute lung injury or an increased rate of thromboembolic complications in COVID-19 patients may be the cause of elevated D-Dimer levels.[39] Aung et al., 2020, also reported that COVID-19 causes the body to become in a pro-inflammatory state, damaging the heart and lungs' tissue and increasing the risk of coagulopathy, or blood clots. Thus, COVID-19 patients are even more prone to experience a cardiovascular incident.[40]

Our findings are also supported by those of Soni et al., 2020, who reported that D-dimer levels at admission were not strong predictor of mortality,[40] and by Long et al., 2020, who found that D-dimer levels a few days after admission were found to have a stronger correlation with mortality than those at admission [42]. Their study demonstrated that patients with COVID-19 were likely to have hypercoagulation, and hypercoagulation, closely linked to disease progression and clinical outcome. To avoid thrombotic complications, coagulation indicators like D-dimer and prothrombin time should be monitored as soon as possible.[42]

On the other hand, Poudel et al., 2021, reported that the D-dimer value at admission was a reliable biomarker for predicting COVID-19 patient mortality.[43] According to a meta-analysis study by Simadibrata and Lubis, 2020,COVID-19 patients with elevated D-dimer levels at admission had a significantly increased risk of all-cause mortality.[44]

In the current study, the patient group's plasma BNP level was significantly higher than that of the control group. In line with that, Stefanini et al., 2020, demonstrated that critically ill COVID-19 patients had elevated BNP levels at admission.[45] According to the findings of our current study, the non-survivor group's BNP level was increased significantly in comparison to the survivors group. These was supported by Cilingir et al., 2022, who reported that mortality was significantly linked to higher BNP, which is in line with the previous findings.[48] Also, Zinellu et al., 2021, reported that patients with high severity or non-survivor status had significantly higher BNP concentrations than patients with less severity or survivor status ($p < 0.001$). As a result, in COVID-19, higher plasma BNP concentrations were significantly linked to increased disease severity and mortality.[49] In the clinical diagnosis of heart failure and cardiac dysfunction, BNP, and N-terminal-pro hormone BNP (NT-pro-BNP) are frequently used as significant indicators.[53]

In the current study, ROC curve analysis was used to determine the predictive ability of different studied cardiac markers for estimation of death among patients with COVID-19 infection. In addition, we performed univariate and multivariate logistic regression analysis for prediction of death among COVID-19 infected patients. It showed that only BNP level could be used as a significant predictor for death among COVID-19 infected patients. As, patients with BNP ≥ 16.02 were about 166 times more likely to die compared to patients with BNP < 16.02.

Higher plasma concentrations of BNP or NT-pro-BNP are essentially connected with higher sickness seriousness and expanded mortality in coronavirus disease.[49] COVID-19 patients who had higher BNP levels at the time of admission were found to have a higher risk of in-hospital mortality and other complications, both in patients who had heart failure and those who did not.[54]

Our current study showed significant positive correlation between the serum level of troponin-I, CK-total, CK-MB (Mass) and BNP. In line with this observation, measurably critical positive relationship was seen between high troponin-I and CK-MB (Mass).[55]

In conclusion, plasma D-dimer, serum LDH, troponin-I, and BNP variables were significantly elevated in patients with COVID-19 infection. Inflammatory markers including CRP, ESR and ferritin were significantly elevated in COVID-19 patients. Cardiac biomarkers could be used as prognostic factor for determination of the severity of COVID-19 and could predict mortality. Early detection of elevated BNP could be a significant predictor for mortality in patients with COVID-19. Thus, it should be assessed in patients with COVID-19 at time of hospital admission to optimize risk stratification.

Author Contributions

AAM, AOA and HAA, contributed to the study conception and design. AAM, AOA and MIS, contributed tomaterial preparation, data collection and analysis. AKMH provided clinical support. AAM wrote the manuscript draft. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

The study protocol was reviewed and approved by the Institutional Review Board of the Faculty of Medicine, Assiut University, (November 2020).

Informed consent

A signed consent form was obtained from each study participant.

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