Impact of the serum and blood biomarkers on the severity and survival of the COVID-19 infected patients with dementia

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Research Article

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Abstract

Aim

Elderly population is categorized as a risk group for COVID-19 infection and dementia is the major cause of disability in elderly individuals and affects 70% of the elderly population. In this study, we evaluated blood and serum biomarkers of the patients with dementia infected by COVID-19 to evaluate possible indicators of the severity of COVID-19 infection.

Methods

Laboratory biomarkers of 11 dementia patients between the ages 85-96 infected by COVID-19 have been used for this study. Serum biochemistry and blood data of survived six patients were compared with the five patients who died because of COVID-19 to evaluate biomarkers correlated with COVID-19 severity and disease mortality.

Results

Fibrinogen, d-dimer, C-reactive protein (CRP), P, and Mg levels increased in the deceased dementia patients compared to the survived ones. Glucose, blood urea nitrogen (BUN), alanine transaminase (ALT), aspartate aminotransferase (AST), troponin, lactate, and procalcitonin levels significantly decreased in the deceased patients compared to the survived ones infected by COVID-19. %NEU, %LYM, MONO, %MONO, EOS, %EOS, %BASO, MPV, PT, INR, hematocrit (HCT), hemoglobin (Hb), total Hb, red blood cells (RBC), PDW, and ferritin levels decreased in the deceased patients compared to the healthy ones, where red cell distribution width (RDW), prothrombin time (PT), WBC and NEU levels significantly increased in the deceased patients infected by COVID-19.

Conclusion

Changes in the serum biochemistry and blood markers are correlated with COVID-19 infection severity and mortality that can be used to the prediction of disease progression in dementia patients.

Introduction

The world has been dealing with life-threatening human virus pandemics are increasing for years such as Crimean-Congo hemorrhagic fever, human immunodeficiency viruses (HIV), ebola virus disease, Marburg virus disease, Lassa fever, Nipah and henipaviral diseases, rift valley fever, chikungunya, zika, middle east respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV). However, novel coronavirus (2019-nCoV or SARS-CoV-2 or COVID-19) has become the major

public health problem since December 2019, since people are still infected and die by COVID-19 despite vaccination [1–3].

COVID-19 virus is transferred directly through infected person-to-person through coughing, sneezing, and breathing via droplets that come from mouth, nose, and eyes or through kissing or from secretions of various contaminated body fluids and close contact, by touching [1]. The COVID-19 infection can severely affect the people who have comorbidity and are older than sixty and several earlier studies suggested that elderly people are particularly at highest the risk from COVID-19 infection and fatality frequency is estimated about 2 to 3% [4, 5]. Because by aging most of the elderly have one or more age-associated diseases such as mental health, depression, and anxiety disorders, Alzheimer's disease, asthma or chronic lung diseases, severe kidney disease, moderate or severe liver disease, coronary artery disease, and diabetes mellitus, diabetes with end-organ damage, tumor and weak immune system [6].

Dementia is the major cause of disability among the elderly population and the prevalence of dementia is 5% of the population and 70% of the elderly population. Several studies have revealed that dementia increases the mortality risk of elderly people infected by COVID-19 [7], therefore evaluation of the clinical biomarkers are required to predict mortality risk and accurate decision for the treatment options In this study, we aimed to evaluate the correlation of the blood and serum biomarkers with the severity and mortality of COVID-19 infected dementia patients [8].

Methods

Diagnostic Criteria

New-onset fever and/or respiratory tract symptoms including cough or dyspnea and severe lower respiratory tract illness symptoms have been used as diagnostic criteria for patients infected by COVID-19. Other possible symptoms can be categorized as myalgia, diarrhea, and smell and/or taste disturbances as described previously by Aydemir et al. [11]. A Reverse-transcription polymerase chain reaction (RT-PCR) assay was used to detect SARS-CoV-2 RNA from the upper respiratory tract for the diagnostic test of COVID-19 [9].

Patients

This study was approved by the ethics committee of the Medical School of Katip Celebi University. Laboratory biomarkers of 11 dementia patients between the ages 85-96 infected by COVID-19 have been used for this study. Laboratory data of survived six patients were compared with the five patients who died because of COVID-19.

Data Collection

Biochemistry data were evaluated via Abbott c16000. Hormone analysis was performed via Siemens Advia Centaur XPT. Blood results of patients were collected by Sysmex XN1000. Urine analysis was performed via Sysmex UC3500+UF4000+UD10 and coagulation data were collected via ACL Top700.

Statistical Analysis

The statistical significance of the clinical data was evaluated via GraphPad Software, Inc., USA. An unpaired t-test was used to compare the two groups. All data were represented as the mean ± standard deviation (SD) as reported previously [10].

Results

In this study, blood and serum biomarkers have been investigated in two groups as survived dementia patients infected by COVID-19 and deceased dementia patients infected by COVID-19. Clinical data showed that fibrinogen, d-dimer, and C-reactive protein (CRP) levels increased in the deceased dementia patients compared to the survived ones (Figure 1). On the other hand, Na, K, Cl, Ca, P, Mg, and pH levels were measured in the blood samples of patients infected by COVID-19 as well. P and Mg levels increased in the deceased patients, where Ca levels significantly decreased (Figure 2). Among serum biochemistry parameters glucose, blood urea nitrogen (BUN), alanine transaminase (ALT), aspartate aminotransferase (AST), troponin, lactate, and procalcitonin levels significantly decreased in the deceased patients compared to the survived ones infected by COVID-19 (Figure 3). Direct bilirubin and indirect bilirubin levels increased, were protein, albumin, and globulin levels decreased in the deceased patients (Figure 4). Hematocrit (HCT), hemoglobin (Hb), total Hb, red blood cells (RBC), PDW, and ferritin levels decreased in the deceased patients compared to the healthy ones, where red cell distribution width (RDW) and prothrombin time (PT) levels significantly increased in the deceased patients infected by COVID-19 (Figure 5). WBC and NEU levels significantly increased in the deceased patients, controversially %NEU, %LYM, MONO, %MONO, EOS, %EOS, %BASO, MPV, PT, and INR levels significantly decreased in the deceased patients compared to the survived ones (Figure 6).

Discussion

The elderly population and people with comorbidities are categorized as major risk groups against COVID-19 infection. Dementia is the major cause of disability in the elderly population and accounting 70% of the elderly population [6, 11, 12]. On the other hand, several studies have revealed that people with dementia have severe symptoms and an increased risk of mortality compared to the patients infected by COVID-19 without dementia [7]. In our study, we compared serum and blood biomarkers of deceased and survived dementia patients infected by COVID-19.

COVD-19 induces thrombosis, coagulopathy, and cytokine storm that lead to severe symptoms and are associated with higher mortality risk [13]. Additionally, the COVID-19 virus triggers microglia activation, chronic neuroinflammation, and neurodegeneration in the central nervous system (CNS) and the virus shares molecular similarities with CNS protein epitopes leading to the autoimmune state triggering cytokine storm [14]. Therefore COVID-19 may severe the symptoms in patients with neurological disorders.

Several biomarkers have been associated with aging, for instance, leukocytosis, lymphocytopenia, neutrophilia, anemia, and severe inflammatory state were observed in the elderly patients characterized by enhanced levels of CRP, fibrinogen, ferritin, d-dimers according to the literature. Additionally, renal and hepatic function is impaired in elderly patients characterized by elevated levels of BUN, creatinine, AST, and PT [15]. Among those biomarkers, fibrinogen, d-dimer, and C-reactive protein (CRP) level indicating increased risk for thrombosis and mortality significantly increased in the deceased dementia patients compared to the survived ones according to our clinical data (Figure 1) [16].

Minerals such as magnesium (Mg), calcium (Ca), phosphate (P), and sodium (Na) play a vital role in the various biological functions including cell signaling, nervous system, reproductive metabolism, and detoxification system [17–20]. Additionally, impairment in the electrolyte levels has been reported in the patients infected by COVID-19 [21]. Ca is involved in the pumps and exchangers at the plasma membrane responsible for the signal transduction. Decreased levels of Ca levels have been reported in acute pulmonary infections, pulmonary disease, and viral infections including COVID-19 [22–24]. Ca is utilized by viruses for the internalization and regulation as key factors for viral replication in the host [25]. Deceased patients have lower Ca levels compared to the survived patients according to the clinical data (Figure 2). On the other hand, Mg is involved in the anti-oxidant metabolism, blood pressure homeostasis, muscle metabolism, neuronal system, and protein synthesis [21]. Several studies have been reported that serum Mg levels increased in the COVID-19 patients that correlate with our data (Figure 2).

Moreover, our clinical data have revealed that serum biochemistry biomarkers including glucose, BUN, creatinine, ALT, AST, troponin, lactate, and procalcitonin levels increased in the deceased dementia patients infected by COVID-19 compared to the survived ones (Figure 3). Increased level of blood glucose is tightly associated with COVID-19 progression and mortality risk [26]. On the other hand, increased levels of creatinine are associated with muscle loss and creatinine levels increased in the deceased dementia patients indicating excessive muscle loss compared to the survived dementia patients (Figure 3) [3]. Additionally ALT and AST levels increased in the patients with COVID-19 infections as indicators of liver damage, inflammation, hepatic ischemia, drug-induced liver damage, and muscle loss [27]. Additionally, renal and hepatic function is impaired in elderly patients characterized by elevated levels of BUN, creatinine, AST, and PT [15]. Our clinical data showed increased ALS, AST, direct bilirubin, indirect bilirubin, and BUN levels indicating enhanced impairment in the liver and kidney function in the deceased dementia patients compared to the survived ones (Figure 3, 4). Moreover, an increased level of troponin is an indicator of myocardial dysfunction and respiratory infection. Increased troponin levels in COVID-19 have been associated with increased inflammation-causing elevated levels of oxidative stress, myocarditis, myocardial infarction, and microangiopathy [28]. Troponin levels increased in the deceased patients compared to the survived ones indicating impaired myocardial function (Figure 3). On the other hand, increased procalcitonin levels are reported as bacterial co-infection in COVID-19 patients as we reported in our clinical study (Figure 3) [29]. Albumin is the most abundant protein in the serum and associated with increased inflammation in the body [3] and tightly associated with mortality risk and disease progression in patients with COVID-19 [30]. We have found decreased albumin levels in deceased

patients compared to the survived ones as a possible biomarker of increased inflammation and reduced anti-oxidant defense (Figure 4).

Anemia is associated with poor prognosis and increased risk of mortality in the patients infected by COVID-19. Increased RBC, decreased Hb, PDW, and HCT levels have been associated with anemia as we observed in the deceased dementia patients infected by COVID-19 compared to the survived patients (Figure 5) [30]. Moreover, our clinical data have revealed that increased NEU, decreased LYM, MONO, EOS, MPV, PCT, BASO, and INR levels in the deceased dementia patients infected by COVID-19 compared to the survived ones (Figure 6). Indicated changes in the blood biomarkers are tightly associated with a higher risk of mortality and disease progression [31]. Also with aging, leukocytosis, lymphocytopenia, neutrophilia, anemia, and severe inflammatory state were observed that are overlap with the COVID-19 pathology which may severe symptoms in the elderly patients [17].

In conclusion, elderly patients are in the risk group for COVID-19 infection, thus the prediction of disease severity and mortality risk should be tightly controlled in those patients. Blood and serum biomarkers could be used to predict disease severity in dementia patients and treatment options could be determined and applied for those patients.

Declarations

Acknowledgments

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Disclosure statement

The authors declare no conflict of interest. Study has been approved by a suitably constituted Ethics Committee of the institution within which the work was undertaken and that it conforms to the provisions of the Declaration of Helsinki. All authors have contributed significantly and that all authors are in agreement with the content of the manuscript. Each subject gave informed consent and patient anonymity is preserved.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contribution

MK and MY helped to collect data samples, conceptualization and writing ethic committee report. DA has performed analysis, written the manuscript and helped to conceptualization the data. NNU was responsible for the conceptualization, helping to write manuscript and discuss the results.

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Figures

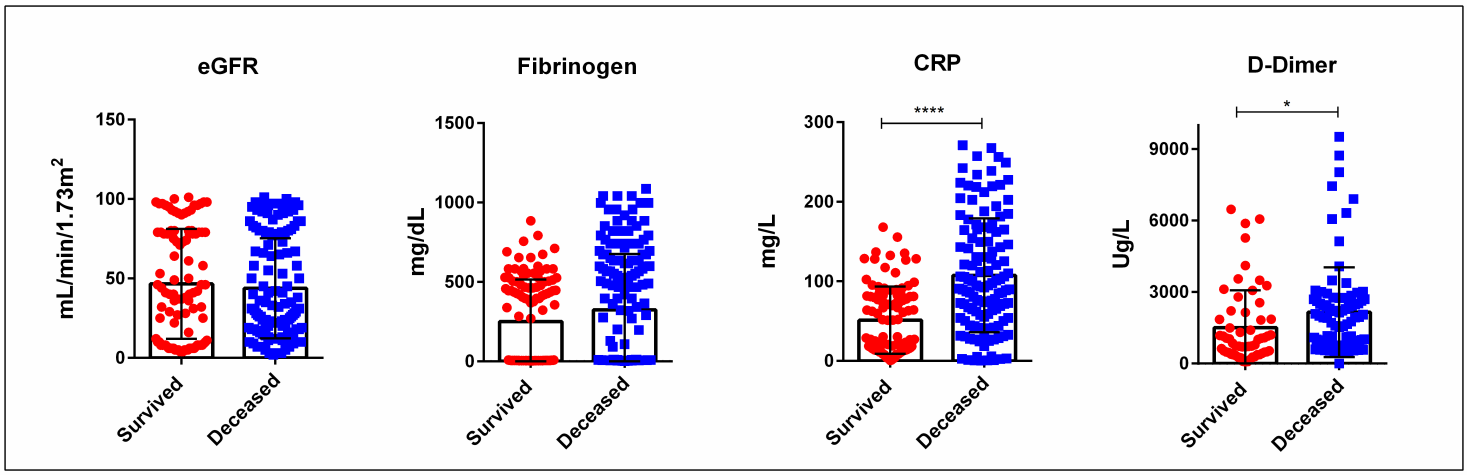

Figure 1

Serum immunological parameters in deceased and survived dementia patients infected by COVID-19

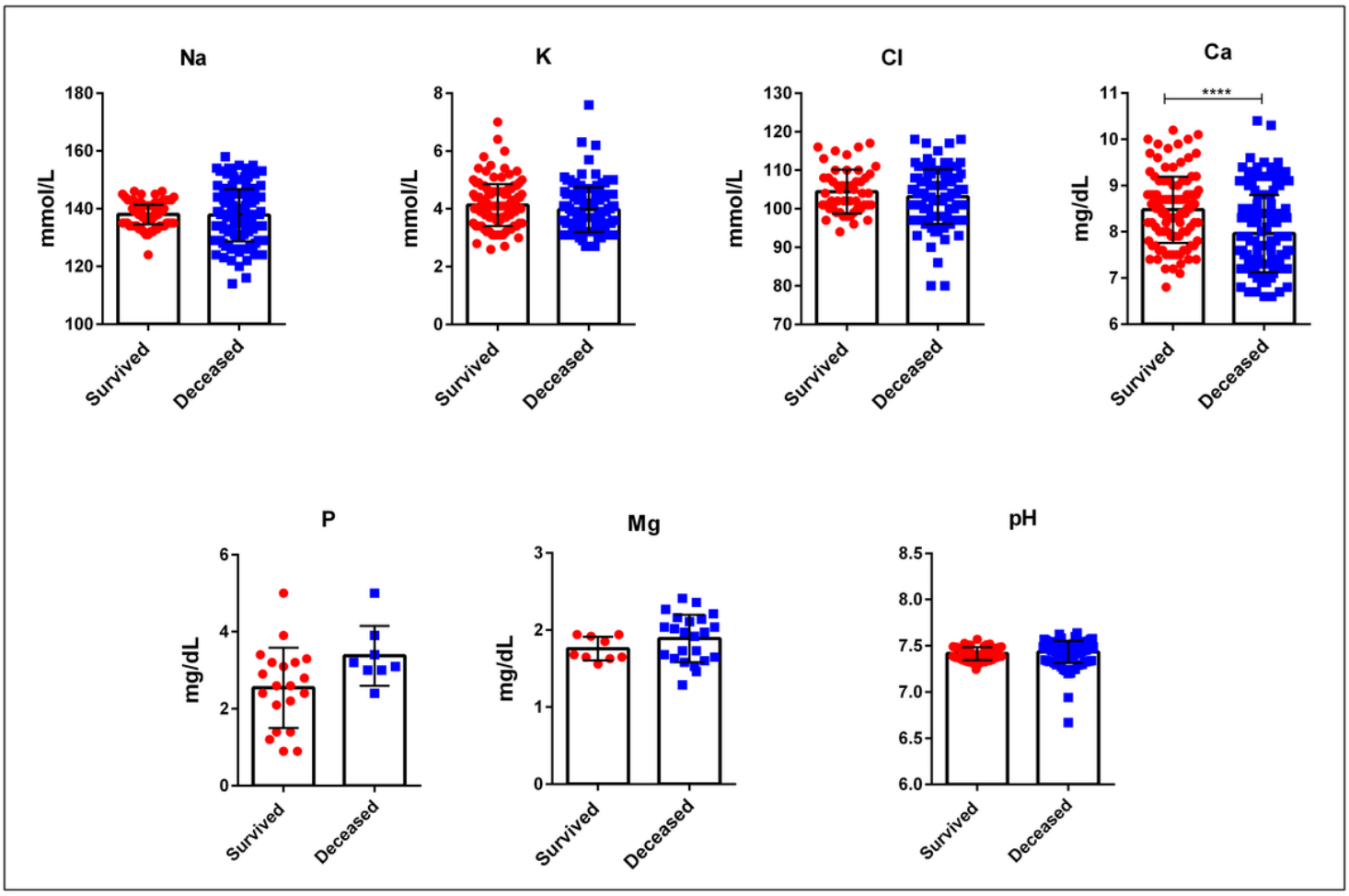

Figure 2

Changes in the serum electrolyte parameters in the deceased and survived dementia patients infected by COVID-19

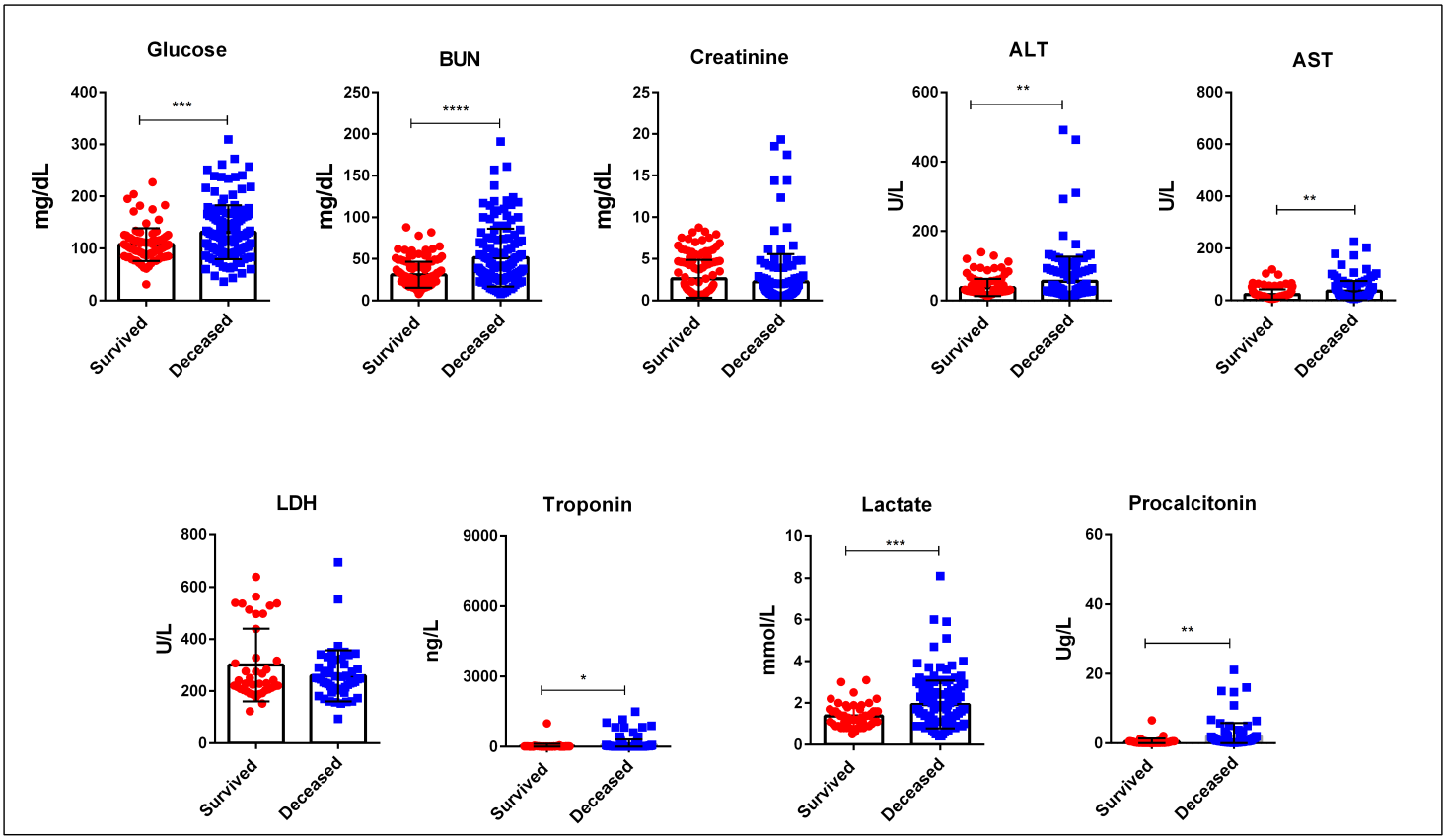

Figure 3

Changes in the serum biochemistry parameters in the deceased and survived dementia patients infected by COVID-19

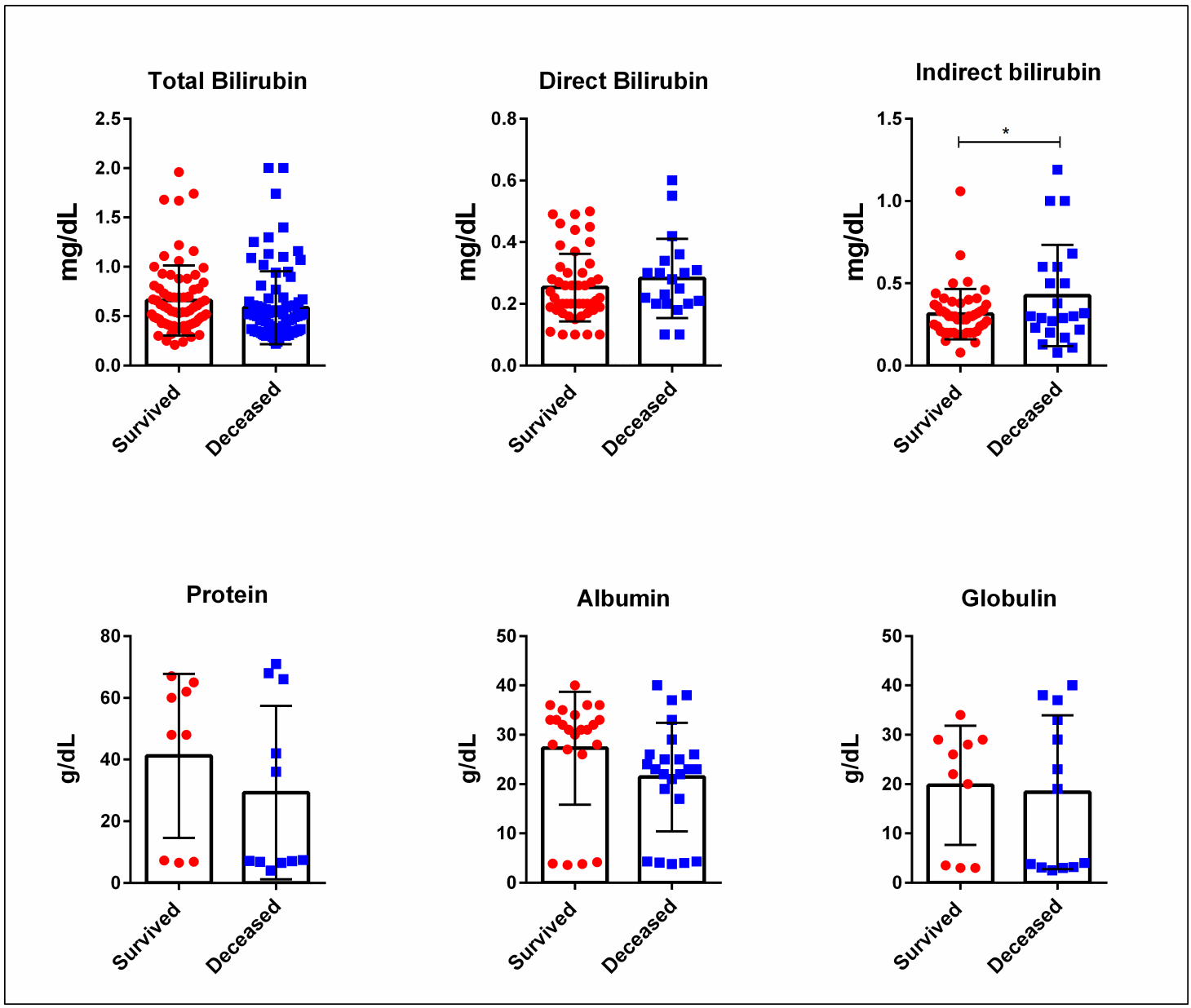

Figure 4

Changes in the serum biochemistry parameters in the deceased and survived dementia patients infected by COVID-19

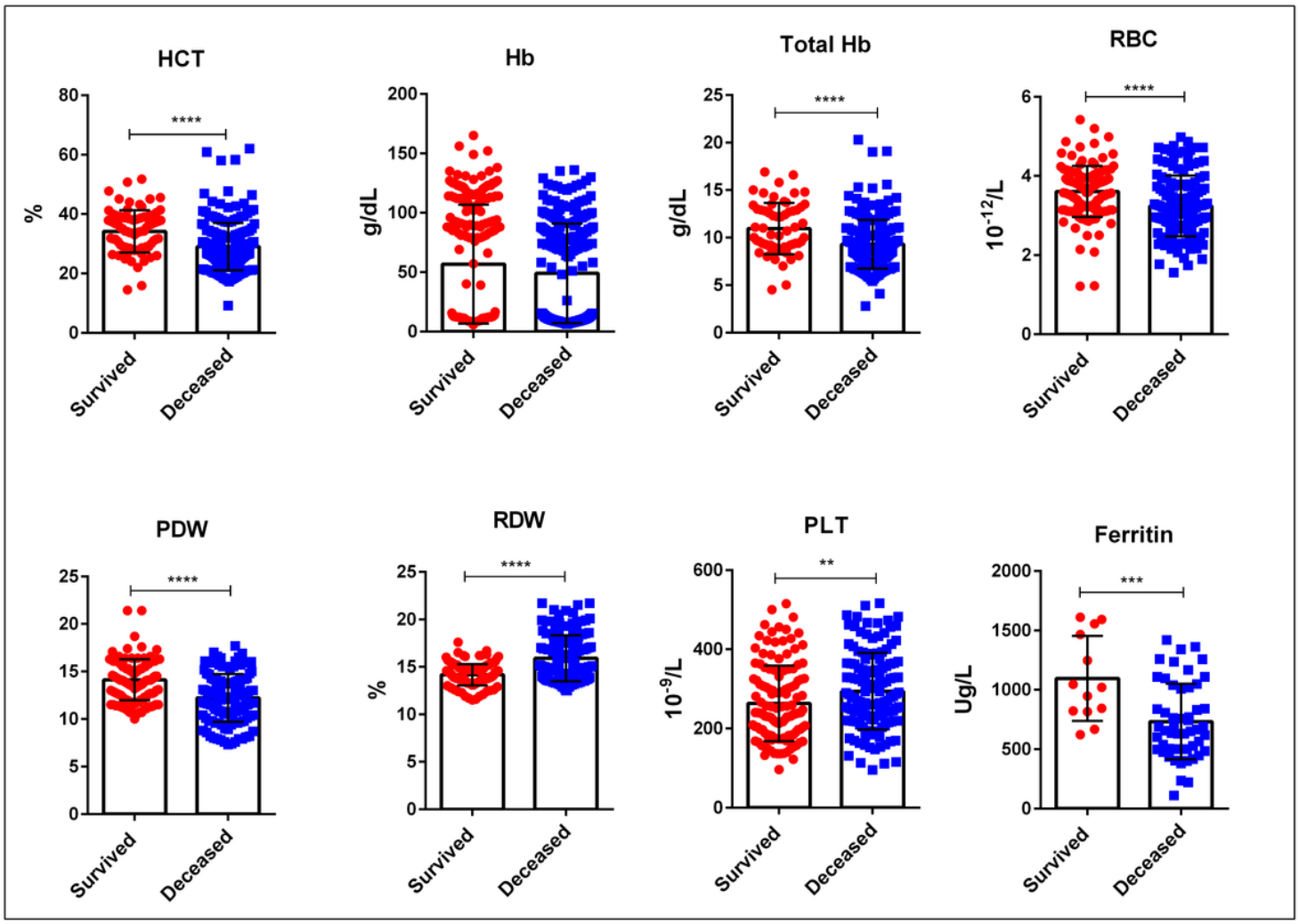

Figure 5

Changes in the hemogram parameters of deceased and survived dementia patients infected by COVID-19

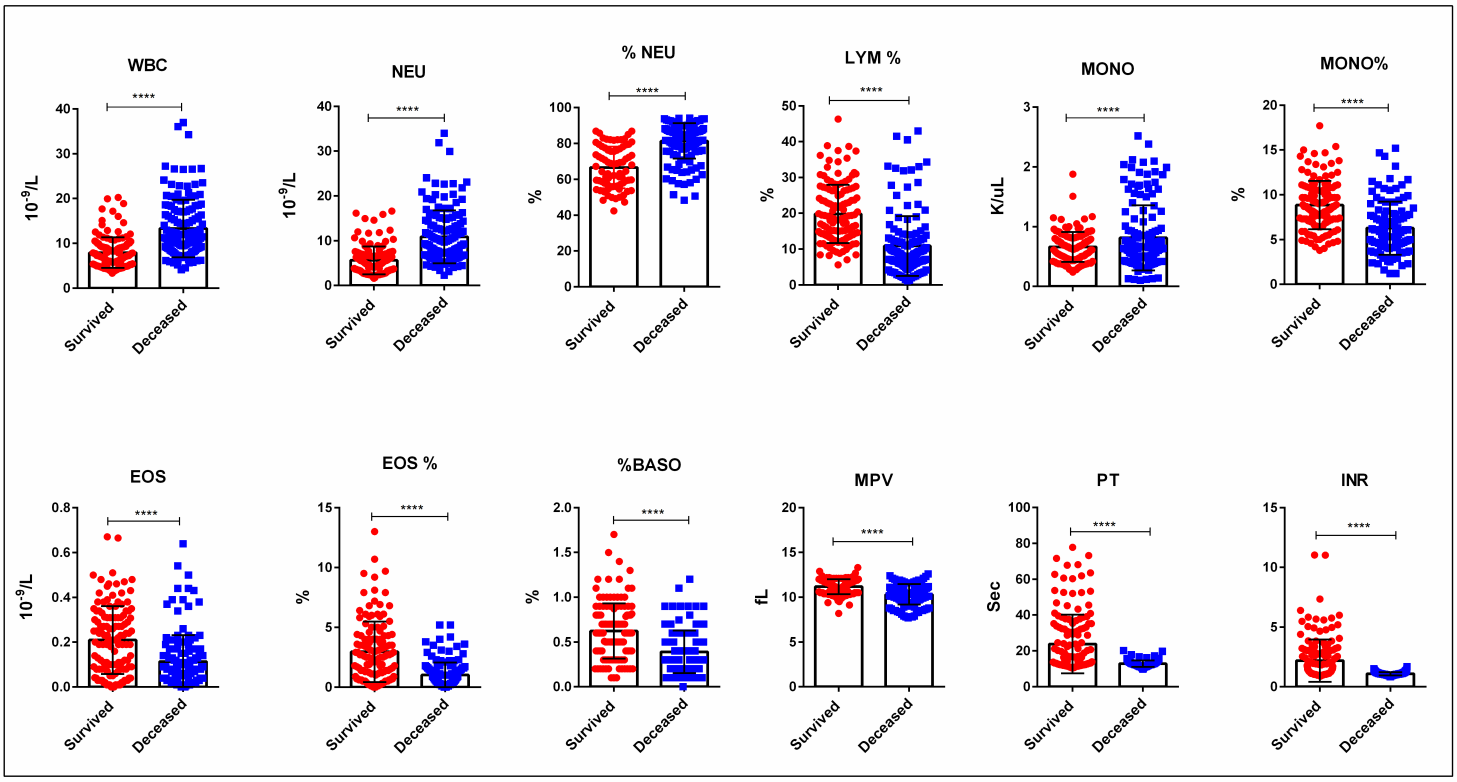

Figure 6

Changes in the hemogram parameters of deceased and survived dementia patients infected by COVID-19