Research Article

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Does COVID-19 infection alter serum biochemical and hematological biomarkers in deceased dementia patients?

https://doi.org/10.1515/tjb-2022-0206
Received September 15, 2022; accepted February 29, 2024;
published online May 20, 2024

Abstract

Objectives: The elderly population is categorized as a risk group for COVID-19 infection, and dementia is the primary cause of disability in elderly individuals and affects 70 % of the elderly population. In this study, we evaluated the blood and serum biomarkers of deceased dementia patients infected by COVID-19 compared to the survived dementia and non-dementia patients.

Methods: Laboratory biomarkers of 11 dementia patients infected by COVID-19 have been used for this study. The five patients' serum biochemistry and blood data were compared with the six patients who died because of COVID-19. Additionally, data from nine patients aged 85–96 infected with COVID-19 without dementia have been used to compare the difference between dementia and non-dementia individuals.

Results: D-dimer, C-reactive protein (CRP), glucose, blood urea nitrogen (BUN), alanine transaminase (ALT), aspartate aminotransferase (AST), troponin, procalcitonin, red cell distribution width (RDW), white blood cell (WBC), neutrophil (NEU) and %NEU levels significantly increased in the deceased dementia patients compared to the survived and non-dementia individuals. Calcium (Ca), hematocrit (HCT), red blood cells (RBC), lymphocyte (%LYM), monocyte % MONO, and basophil (%BASO) levels significantly decreased in the deceased dementia patients compared to the survived and non-dementia individuals infected by COVID-19.

Conclusions: Serum biochemistry and hematological biomarkers, including D-dimer, CRP, glucose, ALT, AST, BUN, troponin, procalcitonin, RDW, RBC, WBC, NEU, %NEU, Ca, HCT, %LYM, %MONO, and %BASO were significantly altered in deceased dementia patients infected by COVID-19 compared to the survived individuals.

Keywords: COVID-19; dementia; hematological biomarkers; serum biochemistry parameters

Introduction

The world has been dealing with life-threatening human virus pandemics 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, the novel coronavirus (2019-nCoV or SARS-CoV-2 or COVID-19) has become a major public health problem since December 2019 since people are still infected and die by COVID-19 despite vaccination [1–3].

The COVID-19 infection severely affects people, especially those older than 60, with comorbidities such as cancer, hypertension, obesity, metabolic syndrome, and cardiovascular diseases. Several earlier studies suggested that older adults are particularly at risk from COVID-19, and fatality frequency is estimated at 2–3 % [4, 5]. Most elderly have one or more age-associated diseases, such as cardiovascular diseases, asthma, dementia, chronic lung diseases, renal diseases, moderate or severe liver disease, diabetes, cancer, and immunological disorders, which overlap with COVID-19 risk factors. Dementia is the primary cause of disability among the elderly, with a 70 % prevalence, and the incidence of dementia is increasing worldwide because of the increased lifetime of the global population [6].

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People with dementia are the most vulnerable because of aging, chronic disorders, altered anatomy, vascular diseases, and weakened immune systems. According to epidemiological studies, dementia patients show worse clinical outcomes to infectious diseases, including COVID-19, influenza A, and respiratory syncytial virus disease, than non-dementia elders [7]. On the other hand, dementia increases the hospitalization and mortality risk of the elderly infected by COVID-19, according to the literature [8]. This study aimed to evaluate possible hematological and serum biomarkers in deceased dementia patients infected by COVID-19 compared to the survived dementia and non-dementia patients.

Materials and methods

Diagnostic criteria

New-onset fever and/or respiratory tract symptoms, including cough or dyspnea and severe lower respiratory tract illness, 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. [9]. Reverse-transcription polymerase chain reaction (RT-PCR) assay was used to detect SARS-CoV-2 RNA as a diagnostic test for COVID-19 [9]. The Blessed Dementia Rating Scale was used for the diagnosis of dementia. All patients in the study group scored 10 or more, which means severe impairment.

Patients

The Ethics Committee (Non-interventional Clinical Studies, Institutional Review Board) of the Medical School of Katip Celebi University approved this study with the number of IRB#179 on 18.06.2020. Laboratory biomarkers of 11 dementia and nine non-dementia patients infected by COVID-19 have been used for this study. The five surviving patients' serum biochemistry and hematological parameters were compared with the six deceased patients from COVID-19. Additionally, data from nine patients infected with COVID-19 without dementia have been used to compare the difference between dementia and non-dementia individuals. Information on the selected patients, including sex, age, and comorbidities, is given in the Supplementary Table 1. Data were collected from each patient after the first admission following COVID-19 diagnosis, and each data point in the graphs represents individual measurements of the indicated parameters.

Data collection

Biochemistry data were evaluated via Abbott Architect c16000 (Abbott, IL, USA), and hormone analysis was performed via Siemens Advia Centaur XPT (Siemens Healthineers AG, Hamburg, Germany). Patients' blood results were collected by Sysmex XN1000 (Sysmex, Norderstedt, Germany). Urine analysis was performed via Sysmex UC3500+U-F4000+UD10 (Sysmex, Norderstedt, Germany), and coagulation data were collected via ACL Top700 (Werfen, Warrington, UK). 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].

Statistical analysis

The statistical significance of the clinical data was evaluated via GraphPad Software, Inc., USA (9.0) via the Kruskal Wallis test with Dunn's multiple comparisons of continuous independent variables between groups. Data are presented as box and whisker plots showing the median, 25–75th percentiles (box), and the minimum-maximum values (bars). Statistically significant differences between groups are labeled with an asterisk (*), and a p-value ≤0.05 was considered significant.

Results

This study investigates hematological and serum biochemistry biomarkers in three groups: survived dementia patients infected by COVID-19, deceased dementia patients infected by COVID-19, and survived non-dementia patients infected by COVID-19. D-dimer, C-reactive protein (CRP), glucose, blood urea nitrogen (BUN), creatinine, alanine transaminase (ALT), aspartate aminotransferase (AST), troponin, procalcitonin, red cell distribution width (RDW), hemoglobin (HGB), white blood cell (WBC), neutrophil (NEU) and %NEU levels significantly increased in the deceased dementia patients compared to the survived and non-dementia individuals (Figures 1, 3, 5, 6, Tables 1, 2). Calcium (Ca), hematocrit (HCT), red blood cells (RBC), lymphocyte (%LYM), monocyte (MONO), %MONO, and basophil (%BASO) levels significantly decreased in the deceased dementia patients compared to the survived and non-dementia individuals infected by COVID-19 (Figures 2, 5, 6, Tables 1, 2). On the other hand, HGB, PLT, RBC, %MONO, eGFR, protein, albumin, globulin, and direct bilirubin levels were significantly high in non-dementia patients compared to the deceased and survived dementia patients infected by COVID-19 (Figures 1 and 4). Creatinine, ferritin, ALT, procalcitonin, ferritin, BUN, and LDH levels significantly decreased in non-dementia patients compared to the survived and deceased dementia individuals infected by COVID-19 (Figures 3 and 5, Table 1).

Discussion

The elderly and people with comorbidities, including cardiovascular diseases, diabetes, cancer, hypertension, diabetes, renal disease, and immune disorders, are categorized as major risk groups against COVID-19 infection. Dementia is

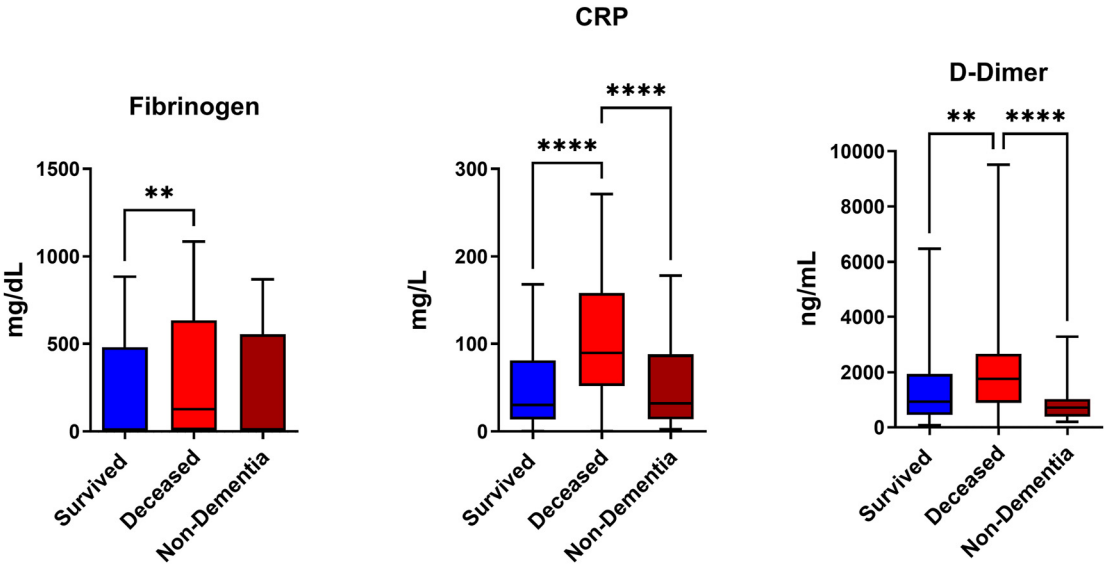

Figure 1: Serum immunological parameters in deceased dementia, survived dementia, and non-dementia patients infected by COVID-19. All data were analyzed by GraphPad Prism (9.0) via the Kruskal Wallis test with Dunn's multiple comparisons. Data are presented as box and whisker plots showing the median, 25–75th percentiles (box), and the minimum-maximum values (bars). Statistically significant differences between groups are labeled with an asterisk (*), and a p-value ≤0.05 was considered significant. eGFR, estimated glomerular filtration rate; CRP, C-reactive protein. *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001.

the primary cause of disability in older individuals and accounts for 70 % of the elderly population [10, 11]. Dementia patients are more vulnerable to infectious diseases, including influenza A and COVID-19, because of age, altered anatomy, decreased immune response, and vascular and renal disabilities overlapping with risk factors of COVID-19. Several studies have reported that people with dementia have an increased risk for severe symptoms, hospitalization, and mortality compared to non-dementia individuals [8]. This study evaluated possible hematological and serum biochemistry biomarkers in deceased dementia patients infected by COVID-19 in comparison with survived dementia and non-dementia patients.

COVID-19 induces thrombosis, coagulopathy, and cytokine storm associated with the increased risk of severe symptoms, hospitalization, and mortality in infected patients [12]. On the other hand, the COVID-19 virus triggers microglia activation, chronic neuroinflammation, and neurodegeneration in the central nervous system (CNS) since the virus shares molecular similarities with CNS protein epitopes associated with the cytokine storm [13]. That is the reason for the severe symptoms in patients with neurological disorders during COVID-19 infection. Elevated fibrinogen, D-dimer, and CRP levels are associated with the increased risk for thrombosis, severe symptoms, and fatality in COVID-19-infected patients [14] since indicated parameters are biomarkers for venous thromboembolism (VTE) and pulmonary embolism (PE). D-dimer, fibrinogen, and CRP levels significantly increased in deceased dementia patients compared to the survived dementia and non-dementia individuals (Figure 1, Table 1) [15].

Minerals such as magnesium (Mg), calcium (Ca), phosphate (P), and sodium (Na) play a vital role in various biological functions, including cell signaling, nervous system, reproductive metabolism, and detoxification system [16–19]. Additionally, impairment in electrolyte levels has been reported in patients infected by COVID-19 [20]. Ca is involved in the pumps and exchangers at the plasma membrane and is responsible for signal transduction. Decreased Ca levels have been reported in acute pulmonary infections, pulmonary disease, and viral infections, including COVID-19 [21–23], because Ca is utilized by viruses for internalization and regulation as critical factors for viral replication in the host [24]. According to our clinical data, deceased patients have significantly lower Ca levels compared to survived dementia and non-dementia patients (Figure 2). On the other hand, Mg is involved in antioxidant metabolism, blood pressure homeostasis, muscle metabolism, neuronal system, and protein synthesis [20]. Several studies have reported increased serum Mg levels in COVID-19 patients, and according to our data, Mg levels slightly increased in deceased dementia patients compared to the other groups (Figure 2, Table 1).

Increased blood glucose level is tightly associated with improved progression and disease severity in COVID-

Table 1: Serum parameters, including biochemistry and mineral values.

Serum parameters	Survived dementia	Deceased dementia	Non-dementia	p-Value
Fibrinogen, mg/dL	8.840 (4.80–480)	128 (6.34–634)^{a**}	5.460 (1.45–8.21)	a^{**} (0.0016)
CRP, mg/L	30.46 (13.8–81.32)	92.77 (54.04–163.8)^{a****,b****}	32 (14–88.19)	a^{****} (<0.0001) b^{****} (<0.0001)
D-Dimer, ng/L	933.5 (455.3–1934)	1762 (887–2,660)$^{a**,\ b****}$	715.5 (394.5–1,027)	a^{**} (0.0025) b^{****} (<0.0001)
Na, mmol/L	138 (136–140) ^{b**}	137 (132–144)	136 (133–139)	b^{**} (0.0056)
K, mmol/L	4 (3.7–4.55)	3.8 (3.4–4.5)	4 (3.52–4.3)	–
Cl, mmol/L	104 (100–108)	103 (98–108.5)	106 (102–108)	–
Ca, mg/dL	8.5 (8–8.8)	7.75 (7.3–8.52)$^{a****,\ b***}$	8.5 (8.1–8.9)	a^{****} (<0.0001) b^{***} (0.0003)
P, mg/dL	2.6 (1.57–3.2)	3.15 (3–3.77)	3.2 (3–4.25)	–
Mg, mg/dL	1.68 (1.64–1.93)	1.97 (1.63–2.14)	1.7 (1.69–1.79)	–
Glucose, mg/dL	103 (88–117)	122 (93.5–161.5)$^{a***,\ b*}$	98 (94–109)	a^{***} (0.0009) b^{*} (0.0198)
BUN, mg/dL	27 (19–40)	40.5 (28–69.5)$^{a****,\ b****}$	17 (10–31) ^{c*}	a^{****} (<0.0001) b^{****} (<0.0001) c^{*} (0.0005)
Creatinine, mg/dL	1.31 (0.81–4.47)	1.08 (0.61–2.05) ^{a***,b***}	0.68 (0.62–1.07) ^{c****}	a^{***} (0.0003) b^{***} (0.0009) c^{****} (<0.0001)
ALT, µ/L	29 (23.75–39)	30 (23–70) ^{b****}	16 (13–20) ^{c****}	b^{****} (<0.0001) c^{****} (<0.0001)
LDH, µ/L	230 (204–328)	245 (204–287)^{b***}	211 (180–248) ^{c*}	c^{*} (<0.0001)
AST, µ/L	18 (11–24)	19 (14–43.5)$^{a**,\ b**}$	19 (15.25–16)	a^{**} (0.0036) b^{**} (0.0046)
Troponin, ng/L	3.02 (0.01–13)	1.5 (0.03–36)$^{a***,\ b**}$	3 (0.01–14)	a^{***} (0.0007) b^{**} (0.0084)
Procalcitonin, µg/L	0.19 (0.09–0.58)	0.68 (0.33–2.04)$^{a****,\ b****}$	0.06 (0.04–0.14)^{c***}	a^{****} (<0.0001) b^{****} (<0.0001) c^{***} (0.0009)
Protein, g/dL	48 (7.1–63.5)	7.4 (6.8–66)^{b**}	68 (66–70)^{c*}	b^{**} (0.0046) c^{*} (0.0198)
Albumin, g/dL	31 (27–34)	23 (17–26)^{b****}	36 (34.25–39)^{c**}	b^{****} (<0.0001) c^{**} (0.0061)
Globulin, g/dL	24 (3.37–29)	19 (3.1–35)^{b*}	33 (30–35)^{c*}	b^{*} (0.0457) c^{*} (0.0189)
Direct bilirubin, mg/dL	0.21 (0.18–0.3)	0.26 (0.2–0.33)	0.41 (0.18–0.66)^{c**}	c^{**} (0.0040)
Total bilirubin, mg/dL	0.55 (0.42–0.78)	0.48 (0.34–0.64)	0.38 (0.28–0.91)	–
eGFR, ml/min/1.73 m^2	41 (8–79)	31 (18–79)^{b****}	81 (54–88.5)^{c****}	b^{****} (<0.0001) c^{****} (<0.0001)

All data were analyzed by GraphPad Prism (9.0) via Kruskal Wallis test with Dunn's multiple comparisons and shown as median (25–75th percentiles). [a]Different from the survived group, [b]different from the non-dementia group, and [c]different from the deceased group. *Represents the significant value of the indicated groups (a, b, c). *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001. CRP, C-reactive protein; Na, sodium; K, potassium; Cl, chlorine; Ca, calcium; P, phosphor; Mg, magnesium; BUN, blood urea nitrogen; ALT, alanine transaminase; LDH, lactate dehydrogenase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate.

19-infected patients same as our clinical data (Figure 3) [25]. The exact mechanism behind the elevated glucose levels during COVID-19 infection remains unclear; however, virus-induced cytokine storm and pancreatic cell dysfunction are suggested as the main contributors to the dysregulation of glucose metabolism. COVID-19 virus has been found in the pancreatic β-cells in the post-mortem tissues, and *in vitro* studies revealed that COVID-19 can enter and proliferate in the human primary islet cells [26]. On the other hand, ALT, LDH, and AST levels increased in patients with COVID-19

Table 2: Hematological parameters.

Hematological parameters	Survived dementia	Deceased dementia	Non-dementia	p-Value
HCT, %	34.25 (28.75–38.78)	27.6 (23.9–32.4)^{a****}	35.9 (32.9–38.3)^{c****}	a^{****} (<0.0001) c^{****} (<0.0001)
HGB, g/dL	11.3 (5.7–14.9)	9.3 (6.3–15.35)$^{a**, b****}$	11.85 (8.4–89)^{c*}	a^{**} (0.0033) b^{****} (<0.0001) c^{*} (0.0159)
RDW, %	14 (13.4–14.8)	15.05 (13.73–17.5)$^{a****, b****}$	13.35 (13.1–13.73)^{c*}	a^{****} (<0.0001) b^{****} (<0.0001) c^{*} (0.0223)
PLT, 10^{-9}/L	239 (183–325)	277.5 (221.5–363.3)^{a*}	287 (234.8–378.5)^{c**}	a^{*} (0.0121) c^{**} (0.0060)
Ferritin, µg/L	1,021 (818.5–1,510)	660.5 (500.3–1,016)$^{a*, b****}$	112 (53.5–144)^{c****}	a^{*} (0.0338) b^{****} (<0.0001) c^{****} (<0.0001)
RBC, 10^{-12}/L	3.68 (3.17–3.95)	3.17 (2.73–3.75)$^{a***, b****}$	4.14 (3.94–4.45)^{c****}	a^{***} (0.0002) b^{****} (<0.0001) c^{****} (<0.0001)
PDW, %	14.1 (12.3–15.8)	12.2 (10.5–14.03)^{a****}	12.2 (10.9–13.48)^{c****}	a^{****} (<0.0001) c^{****} (<0.0001)
WBC, 10^{-9}/L	7.2 (5.34–9.31)	11.5 (8.77–17.09)$^{a****, b****}$	7.72 (5.3–8.73)	a^{****} (<0.0001) b^{****} (<0.0001)
NEU, 10^{-9}/L	4.95 (3.36–6.89)	9.02 (6.58–14.39) $^{a****, b****}$	4.87 (3.31–6.02)	a^{****} (<0.0001) b^{****} (<0.0001)
%NEU	67.2 (56.8–77.2)	84.7 (77.85–88.2) $^{a****, b****}$	66.3 (60.65–71.55)	a^{****} (<0.0001) b^{****} (<0.0001)
%LYM	18.2 (13.4–26.3)	8.65 (6.42–12.2) $^{a****, b****}$	21.4 (14.7–27.5)	a^{****} (<0.0001) b^{****} (<0.0001)
MONO	0.65 (0.47–0.81)	0.63 (0.45–0.94)	0.72 (0.53–0.88)	–
%MONO	8.5 (7.1–10.7)	5.6 (4.1–7.8) $^{a****, b****}$	10.5 (8.5–11.9) ^{c**}	a^{****} (<0.0001) b^{****} (<0.0001) c^{**} (0.0046)
EOS, 10^{-9}/L	0.2 (0.08–0.31)	0.08 (0.03–0.14) $^{a****, c****}$	0.05 (0.01–0.13)	a^{****} (<0.0001) c^{****} (<0.0001)
%EOS	2.5 (0.9–4)	0.7 (0.3–1.4) $^{a****, c****}$	0.75 (0.2–1.6)	a^{****} (<0.0001) c^{****} (<0.0001)
%BASO	0.6 (0.4–0.8)	0.3 (0.2–0.6)$^{a****, b****}$	0.5 (0.4–0.8)	a^{****} (<0.0001) b^{****} (<0.0001)
MPV, fL	11.3 (10.5–11.8)	10.5 (9.6–11.2)$^{a****, c****}$	10.4 (10–10.9)	a^{****} (<0.0001) c^{****} (<0.0001)
INR	1.27 (1.05–2.92)	1.07 (1–1.16) $^{a****, c****}$	1.07 (1–1.12)	a^{****} (<0.0001) c^{****} (<0.0001)

All data were analyzed by GraphPad Prism (9.0) via Kruskal Wallis test with Dunn's multiple comparisons and shown as median (25–75th percentiles). [a]Different from the survived group, [b]different from the non-dementia group, [c]different from the deceased group. *Represents the significant value of the indicated groups (a, b, c). *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001. HCT, hematocrit; HGB, hemoglobin; RDW, red cell distribution width; PLT, platelet; RBC, red blood cell; PDW, platelet distribution width; WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; MONO, monocyte; EOS, eosinophil; BASO, basophil; MPV, mean platelet volume; INR, international normalized ratio.

infections as indicators of liver damage, inflammation, hepatic ischemia, drug-induced liver damage, and muscle loss [27]. Additionally, impaired renal and hepatic function in elderly patients has been characterized by elevated BUN, creatinine, and AST levels [14]. eGFR is a clinical marker of renal function, and lower levels of eGFR are associated with acute kidney injury (AKI), renal dysfunction, and increased mortality risk and disease severity in COVID-19-infected individuals. On the other hand, lower eGFR levels have been observed in dementia patients and individuals having comorbidities, including cardiovascular diseases, vascular disorders, infections, and anemia [28]. BUN, ALT, and AST

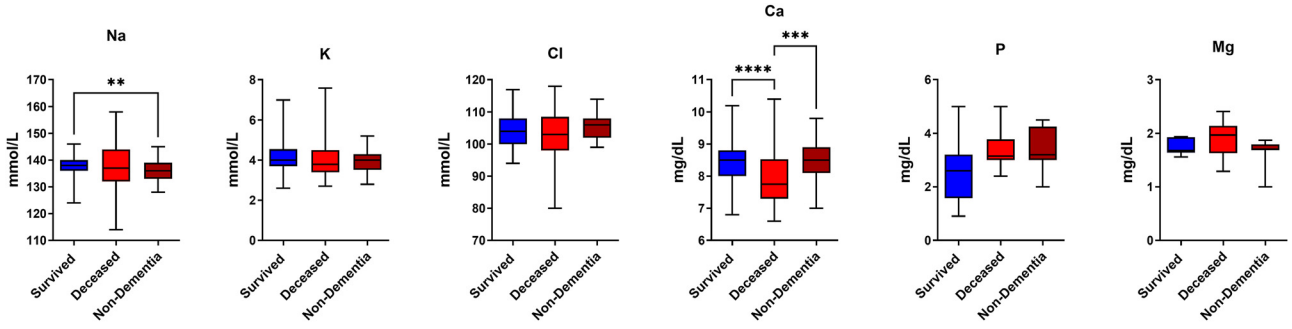

Figure 2: Serum electrolyte parameters in deceased dementia, survived dementia, and non-dementia patients infected by COVID-19. All data were analyzed by GraphPad Prism (9.0) via the Kruskal Wallis test with Dunn's multiple comparisons. Data are presented as box and whisker plots showing the median, 25–75th percentiles (box), and the minimum-maximum values (bars). Statistically significant differences between groups are labeled with an asterisk (*), and a p-value ≤0.05 was considered significant. Na, sodium; K, potassium; Cl, chlorine; Ca, calcium; P, phosphor; Mg, magnesium. *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001.

levels significantly increased in deceased patients compared to surviving and non-dementia individuals (Figure 3). On the other hand, creatinine, LDH, and eGFR levels were markedly lower in the non-dementia patients compared to the deceased and survived dementia patients infected by COVID-19 (Figure 3, Table 1).

Elevated levels of troponin are indicators of myocardial dysfunction and respiratory infection. Increased troponin levels in COVID-19-infected patients have been observed with increased inflammation, triggering oxidative stress, myocarditis, myocardial infarction, and microangiopathy [29]. On the other hand, increased procalcitonin levels are reported as bacterial co-infection in COVID-19 patients and associated with increased risk for fatality according to the clinical data [30]. Troponin and procalcitonin levels increased dramatically in deceased dementia patients compared to survived dementia and non-dementia individuals (Figure 3). Protein, albumin, globulin, and direct bilirubin levels were significantly elevated in the survived non-dementia individuals compared to the deceased and survived dementia patients, according to our clinical data (Figure 4). Albumin is the most abundant protein in the serum and is produced by the liver. Altered albumin levels are associated with increased inflammation in the body [3] and increased mortality risk in patients with COVID-19 [31]. Moreover, albumin and globulin are two significant biomarkers for inflammation status; on the other hand, albumin, globulin, bilirubin, and albumin/globulin ratio are biomarkers for liver function besides ALT and AST [32]. As a possible biomarker of increased inflammation, reduced antioxidant defense, and altered liver function, indicated parameters altered in dementia patients compared to the non-dementia individuals (Figure 4).

COVID-19 infection alters hematological parameters associated with disease progression, severity, and mortality. Lymphopenia, abnormal coagulation profile, PE, thrombocytopenia, sepsis-induced coagulopathy, thromboembolism, and arterial thrombotic complications have been observed in COVID-19 patients. Indicated disorders should be closely followed up via evaluation of the D-dimer, CRP, ferritin, and complete blood count to predict disease severity [33]. HCT, HGB, RBC, %LYM, %MONO, and %BASO levels significantly decreased in the deceased dementia patients compared to the survived dementia and non-dementia individuals (Figures 5 and 6). On the other hand, RDW, WBC, %NEU, NEU, and MONO levels significantly increased in the deceased dementia patients compared to the survived dementia and non-dementia individuals (Figures 5 and 6, Table 2). COVID-19 infection induces oxidative stress and inflammation, causing the death of RBCs associated with decreased HCT, HGB, and increased PDW levels that we observed in our data (Figure 5) [34]. Neutrophil to lymphocyte ratio (NLR) is a significant biomarker of systematic inflammation used to predict the severity of bacterial infections, especially pneumonia. On the other hand, the NLR ratio provides considerable information about inflammatory disorders, including cancer and acute coronary syndrome. Our clinical data observed that increased LYM and NEU levels are associated with disease severity and mortality in COVID-19 infection (Figure 6) [35]. Increased NLR has been associated with the risk of Alzheimer's disease (AD) because of inflammation-induced neuronal death, according to the literature, and the highest %NEU and lowest %LYM levels have been found in the deceased dementia patients in our clinical data (Figure 6, Table 2) [36].

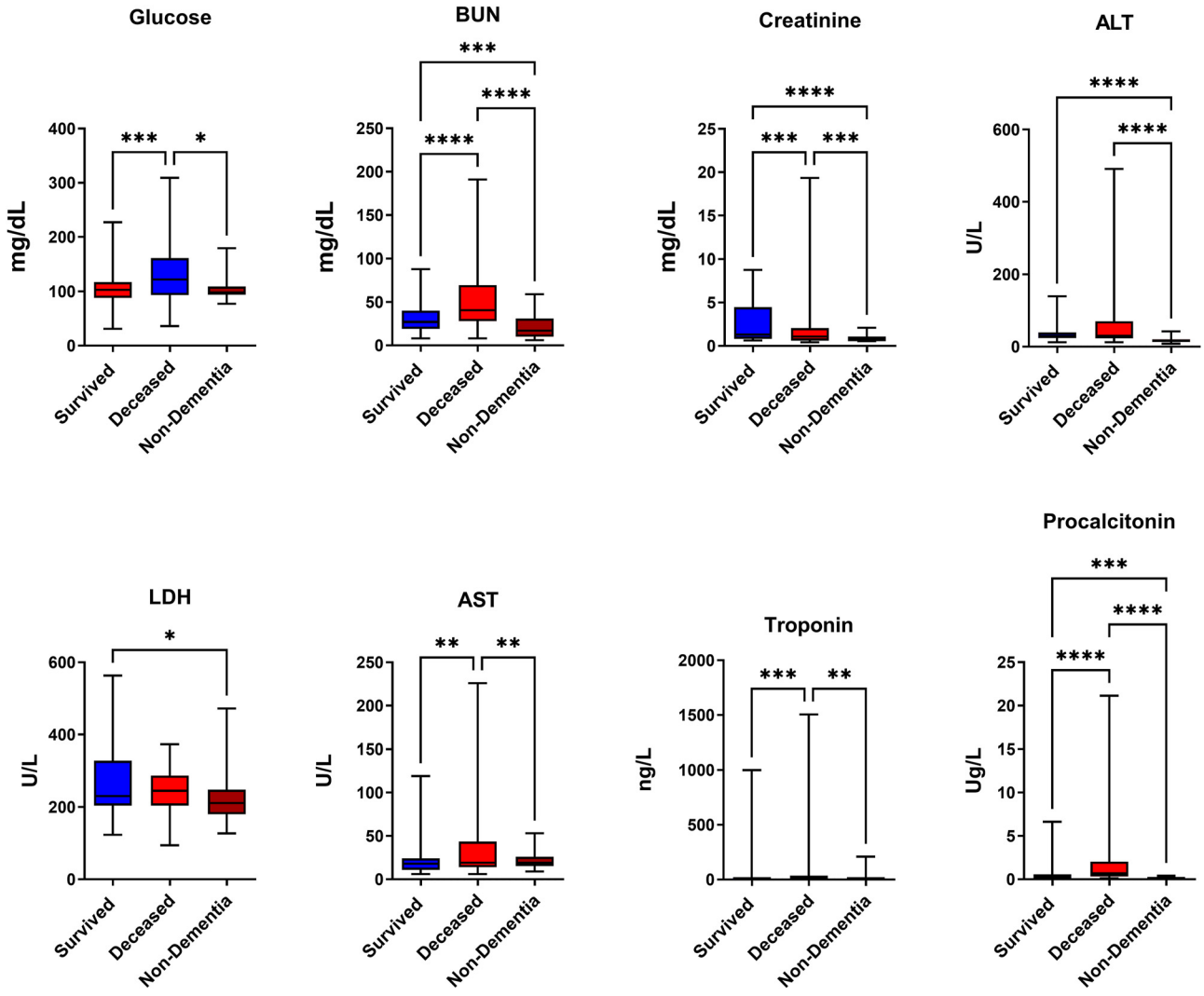

Figure 3: Serum biochemistry parameters in deceased dementia, survived dementia, and non-dementia patients infected by COVID-19. All data were analyzed by GraphPad Prism (9.0) via the Kruskal Wallis test with Dunn's multiple comparisons. Data are presented as box and whisker plots showing the median, 25–75th percentiles (box), and the minimum-maximum values (bars). Statistically significant differences between groups are labeled with an asterisk (*), and a p-value ≤0.05 was considered significant. BUN, blood urea nitrogen; ALT, alanine transaminase; LDH, lactate dehydrogenase; AST, aspartate aminotransferase. *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001.

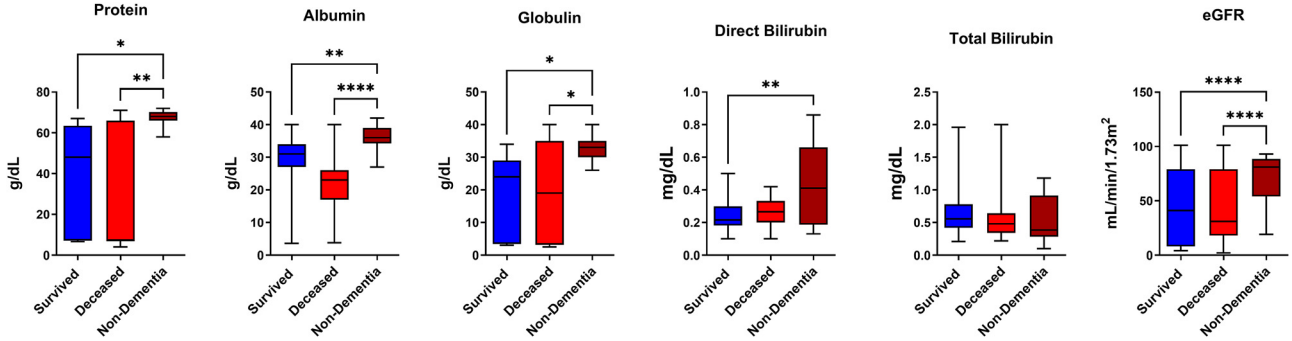

Figure 4: Serum biochemistry parameters in deceased dementia, survived dementia, and non-dementia patients infected by COVID-19. All data were analyzed by GraphPad Prism (9.0) via the Kruskal Wallis test with Dunn's multiple comparisons. Data are presented as box and whisker plots showing the median, 25–75th percentiles (box), and the minimum-maximum values (bars). Statistically significant differences between groups are labeled with an asterisk (*), and a p-value ≤0.05 was considered significant. *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001.

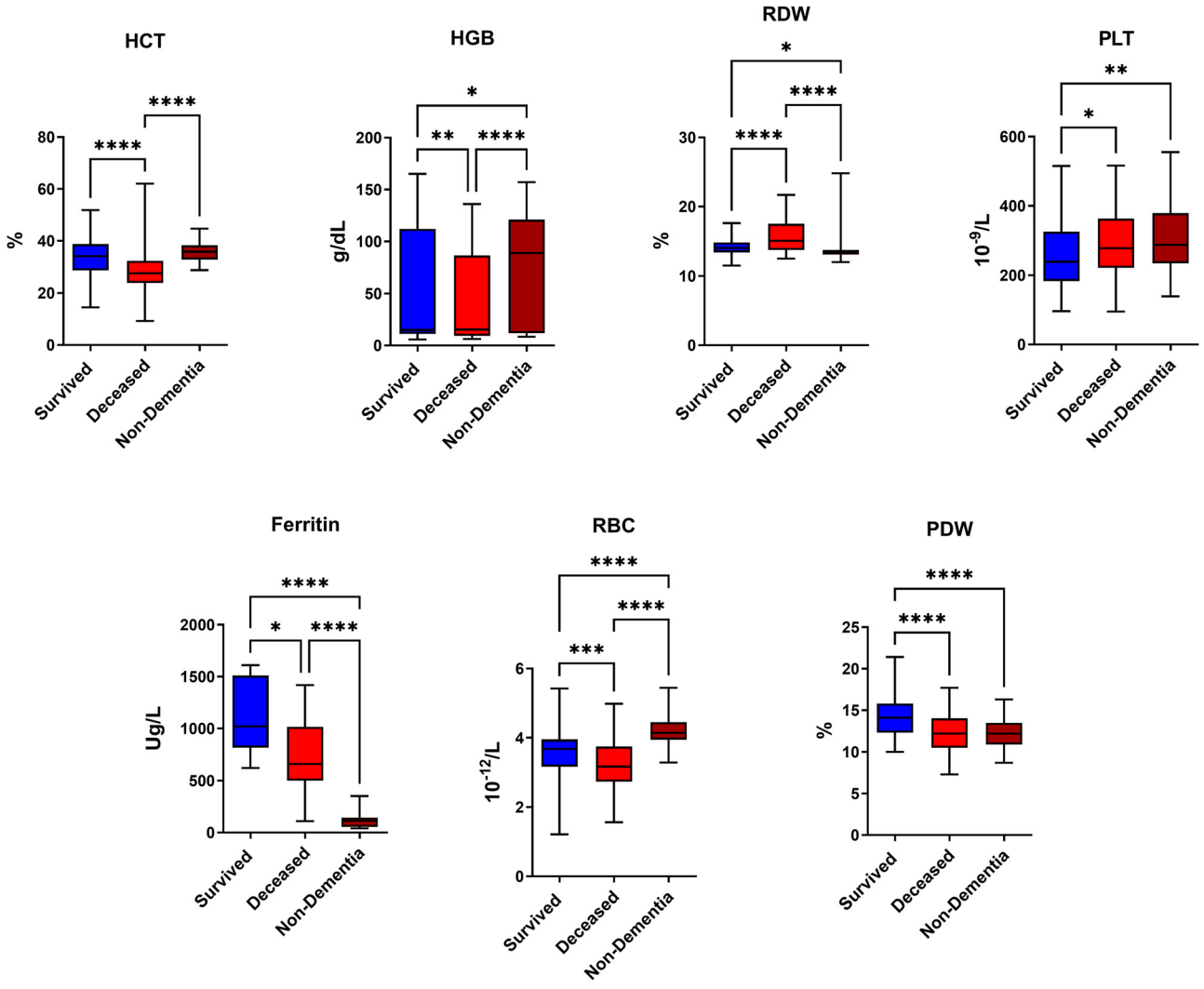

Figure 5: Hematological parameters in deceased dementia survived dementia, and non-dementia patients infected by COVID-19. All data were analyzed by GraphPad Prism (9.0) via the Kruskal Wallis test with Dunn's multiple comparisons. Data are presented as box and whisker plots showing the median, 25–75th percentiles (box), and the minimum-maximum values (bars). Statistically significant differences between groups are labeled with an asterisk (*), and a p-value ≤0.05 was considered significant. HCT, hematocrit; HGB, hemoglobin; RDW, red cell distribution width; PLT, platelet; RBC, red blood cell; PDW, platelet distribution width. *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001.

In conclusion, individuals with dementia are reported to be more vulnerable to viral and bacterial infections, including COVID-19, because of poor anatomy, altered immune system, aging, and chronic disorders. Thus, according to the literature, these patients should be tightly controlled because of the disease severity and mortality during COVID-19 infection [6, 8]. In this context, we evaluated serum biochemistry and hematological biomarkers, including D-dimer, CRP, glucose, ALT, AST, BUN, troponin, procalcitonin, RDW, RBC, WBC, NEU, %NEU, Ca, HCT, %LYM, %MONO, and %BASO in patients infected by COVID-19 and according to our data indicated parameters significantly altered in dementia patients infected by COVID-19 compared to the survived dementia and non-dementia patients.

Limitations of the study

We have tried to explain our data in detail with various biochemical and hematological parameters; however, this study has potential limitations, including sample size and time constraints. We collected our data during the first wave of the COVID-19 pandemic following a lockdown in Turkey. We have access to a few patients due to restrictions and limitations in the data-sharing policies. Since we collected our data at the beginning of the pandemic, called the first wave, there was a limited number of patients, especially the ones with dementia. Our study can give an idea of further studies containing a massive number of patients to reveal a depth of knowledge about the impact of COVID-19 on dementia patients.

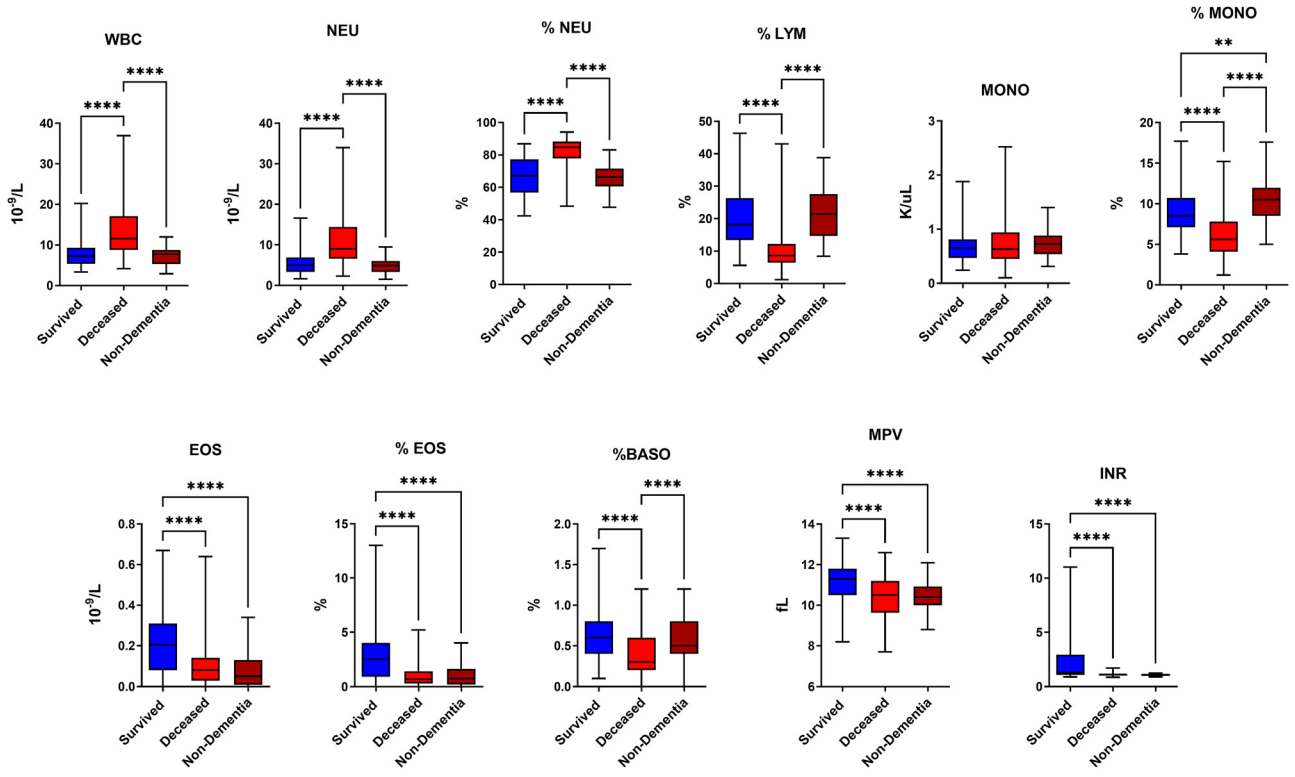

Figure 6: Hematological parameters in deceased dementia, survived dementia, and non-dementia patients infected by COVID-19. All data were analyzed by GraphPad Prism (9.0) via the Kruskal Wallis test with Dunn's multiple comparisons. Data are presented as box and whisker plots showing the median, 25–75th percentiles (box), and the minimum-maximum values (bars). Statistically significant differences between groups are labeled with an asterisk (*), and a p-value ≤0.05 was considered significant. WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; MONO, monocyte; EOS, eosinophil; BASO, basophil; MPV, mean platelet volume; INR, international normalized ratio. *p≤0.05, **p≤0.01, *** p≤0.001, **** p≤0.0001.

Acknowledgments: The authors gratefully acknowledge the use of the services and facilities of the Koç University Research Center for Translational Medicine (KUTTAM), funded by the Presidency of Turkey, Head of Strategy and Budget.

Research ethics: The Ethics Committee (Non-interventional Clinical Studies, Institutional Review Board) of the Medical School of Katip Celebi University approved this study with the number of IRB#179 on 18.06.2020.

Informed consent: Informed consent was obtained from all individuals included in this study, or their legal guardians or wards.

Author contributions: D.A. is responsible for the writing the original draft, revision, conceptualization, visualization and data analysis. M.Y. is responsible for the revisions, conceptualization, supervision, sources and data analysis. M.K. is responsible for the conceptualization and sources. N.N.U is responsible for the supervision, sources and conceptualization. The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: Authors state no conflict of interest.

Research funding: None declared.

Data availability: The raw data can be obtained on request from the corresponding author.

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Supplementary Material: This article contains supplementary material (https://doi.org/10.1515/tjb-2022-0206).