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Estimation of oxidative stress, antioxidants and trace elements for COVID-19 patients: a cross-sectional study

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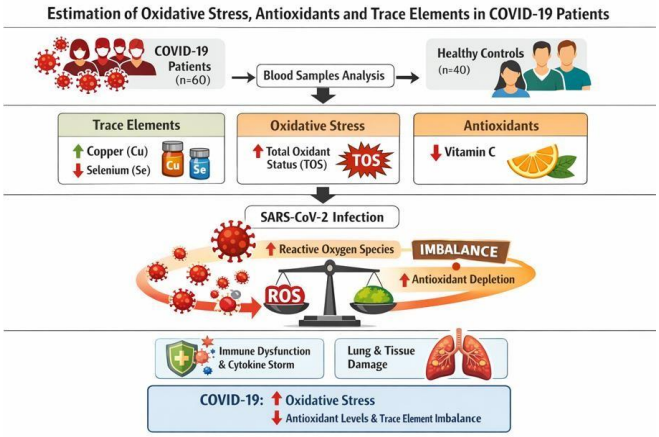
Abstract

Introduction: The World Health Organization announced coronavirus-disease 2019 (COVID-19) to be a global pandemic. Recently oxidative stress has implicated in the pathogenesis of COVID-19. The buildup of free radicals together with the inability of the antioxidant system to counterbalance the free radicals produces oxidative stress which ultimately exacerbate respiratory diseases including COVID-19**.** **Objective:** This was a study to explore the impact of corona virus 2019 (COVID-19) on blood oxidants and antioxidants. **Methods:** A total of blood samples were taken from (60) patients infected with COVID-19 and 40 volunteers as a control group. **Results:** The Copper levels that show a significant increase of Copper levels in the COVID-19 patients compared to the healthy subjects, and Selenium levels show a significant decrease of Selenium levels for the COVID-19 patients compared to the healthy subjects, and total oxidant levels show a very high significant increase of COVID-19 patients compared to the healthy subjects, and Vitamin C levels show a significant decrease of Vitamin C levels for the COVID-19 patients compared to the healthy subjects. **Conclusion**, in COVID-19 positive patients, the levels of the antioxidant substances are decreased as they are progressively consumed to balance the injurious effect of the free radicals.

Keywords: COVID-19. Trace elements. Oxidative stress. Vitamin C.

Graphical Abstract



Source: Own authorship.

Introduction

A new corona virus 2019 (COVID-19) infection has recently emerged that can cause life-threatening complications and deaths, first appeared late in 2019 in Wuhan, China [1]. COVID-19 is often followed by aberrant host immune response, resulting in excessive inflammatory responses (or cytokine storm), i.e., high blood levels of chemokines, cytokines and C-reactive protein, and is connected with severe damage of the respiratory and failure of any organ resulting in fatality of the infected individual [2]. The air spaces of COVID-19 lungs at post-mortem were also filled with inflammatory mononuclear cells and macrophages, which affect diffuse remodeling of the alveolar wall [3].

There is growing evidence that high levels of inflammation, oxidative stress, and immune imbalance may play a role in the pathogenesis and sequelae of COVID-19 infection. These factors evoke an overproduction of pro-inflammatory cytokines, also known as cytokine storm, which can lead to serious complications like acute lung injury, ARDS, shock, and even death **[4]**.

It has a pandemic nature around the world and being announced as a global pandemic by WHO **[5,6]**. SARS-CoV-2 presentation can be asymptomatic or mild to moderate to severe with cough, fever, and dyspnea **[6]**. In these cases, it can result in acute-respiratory-distress-syndrome, acute-cardiac-complications, MODS, septic-shock, and death **[7]**. These sequelae are thought to be due to the so-called cytokine storm, in which viral replication induces an appropriately excessive response of cytokines and other immune-stimulating agents, creating a state of hyper-inflammation **[8]**.

The evolution of this outbreak of new emerging infectious disease has occurred in the rapid time frame. National policies based more or less strictly on the containment of the disease have been established, i.e., social measures of distance or encouragement, if not coercion, to remain at home have been dictated. During this self-isolation, often considered as stressful, many people are stuck on what to eat in order to be healthy and how to maintain nutrient status to be healthy. To avoid infection, a functional immune system is the most foremost key, and a well-balanced and enough diet is an essential basis for an effective immune response **[9,10]**.

Reactive oxygen (ROS) and reactive nitrogen species (RNS) dominate oxidative stress imbalance, including typical ROS species such as singlet oxygen, lipid peroxides, or nitric oxide to which the effect of antioxidant activity or compounds (e.g., albumin, urea, reduced glutathione, vitamin E, vitamin C, polyphenols, carotenoids, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), etc.) are decreased **[11]**. Oxidative stress during infection is poorly defined, but free-radicals have been reported as protectors from invading microbes **[12]**. Chronic oxidativecompromise occurs in persistent viral infections, such as those with Epstein–Barr virus (EBV) and human immunodeficiency virus (HIV) **[13]**, and both have also been associated with diminished immune responses **[14]**. It has been reported that there is an association between NO and other ROS, the superoxide-radical, and peroxynitrites which leads to endothelial damage and inflammation **[15]**. Endothelial damage as well as inflammation seems critical in COVID-19 (Varga et al., 2020). Although the recent papers have revealed that the duet of oxidative stress and inflammation is of paramount importance in the mechanisms of COVID-19 **[16]**.

They stop or slow down the cellular damage caused by reactions with free radicals. Antioxidants neutralize the activity of radical molecules through the ability to scavenge them by breaking the chain reactions, decomposing the peroxides, dithering the metals, and inducting the antioxidant enzymes **[17]**. There is now considerable interest in the notion that ROS is a contributing factor to the etiology of a great many human diseases. Consequently, they can lead to the production of ROS and/or a lack of antioxidant defenses, which in combination with a high concentration of free radicals, has aggravated respiratory diseases (including COVID-19) **[17]**. Normal cell metabolism creates free radicals, and the body can cope with these radicals, however, once there is a secondary condition like COVID-19, the abnormal high levels of these radicals can contribute to the pathogenesis and progression of the disease through depletion of antioxidants **[18,19]**.

As a broad discussion regarding the potential role and deficient antioxidants in COVID-19 problems (see Tables 1-3). Areas in where the relationship is reported between some important elements such as TEs, Zn, Se, Mn and Cu against COVID- 19, as supplementation in COVID-19 parenteral nutrition should be further investigated **[20]**. Various trace elements involved to support the immune systems directly or indirectly by acting as cofactors of antioxidant enzymes to protect the body from Os, by being the components of many viral enzymes, proteases and polymerases that help in preventing viral infections **[20]**.

Copper is a more specific trace element essential to immune function and free-radical defense. In viral infections, this metal is important for its both, for the pathogens and the hosts. As a result, copper has been successfully used clinically to minimize bacterial and viral contamination. Copper, like some of the other transition metals, is an attractive metal because of its high biological ligand binding and redox properties. – International Union of Pure and Applied Chemistry This renders it perfect to drive redox and oxygen chemistry mediated biochemical reactions. Good as these chemical properties are to make copper an excellent cofactor for many enzymes, the metal can also be toxic and is especially so for unicellular microbes. Hence, due to the antimicrobial properties of copper, it serves as efficient biocides for pathogens from COVID-19 to eukaryotic pathogens **[21]**.

The more-semi-metal selenium is an essential micronutrient for humans and is also particularly important for maintaining a balanced immune

response. But the selenoprotein status that is sub-optimal is anything but rare in the world, throughout many areas/regions of China and Europe. This is largely because of the inclusion of this element into selenoproteins, which have diverse and protective roles in human health. These included the demonstration of the advantages of selenium supplementation in viral infections like HIV-1 **[22]**.

In February 2020, an ecological investigation in China reported the determination of selenium levels in hair samples of residents of the Chinese province of Hubei **[23]**. The aim of this study was to examine regional selenium status and the reported incidence of COVID-19 cases. Among several nutrients, selenium deficiencies were associated with an increase virulence of COVID-19.

Even there are metabolomic wide thousands of antioxidant and oxidant molecules depicting the involvement of oxidative stress state in the respective organism, it is incompatible and costly to measure their levels independently. Hence, TOS and TAS are measured practically **[24]**, and the Oxidative Stress index (OSI), which is an index reflecting the severity of oxidative stress, is calculated by the ratio of TOS to TAS **[25]**. The current investigation was designed to determine the levels of oxidative stress markers, antioxidant substances and trace elements in specimens from the patients with COVID-19.

Materials and methods

Study design

This study followed the STROBE checklist for a cross-sectional study (https://share.google/I6JChcAHKcn6KbWYY). Accessed on: March 10, 2026.

Study subjects

60 consecutive patients who were diagnosed were used for study population comprises and admitted due to COVID-19 with or without comorbidity and 40 apparently healthy individuals.

Collection of Blood Preparation

Blood samples were obtained from both patients and healthy volunteers. A vein puncture was used to extract 5ml of blood from each volunteer, whereas blood , with in containing of gel tubes were centrifuged at 4000 g to about (15 min), and sera was collected , stored at (-15°C). This study included (60) subjects with COVID-19 and (40) volunteers.

Determination of trace elements

Serum selenium was determined colorimetrically, while the biochemical used Randox colorimetry (Randox Laboratories, Sadat et al., 1996).

Total oxidative status (TOS) analysis

TOS of serum was assayed according to a new method based on the method described by Erel **[26]**. Oxidants present in the sample oxidize the ferrous ion–o-dianisidine complex to ferric ions – O-dianisidine. Each glycerol molecule serves to amplify the oxidation reaction that is abundant in the reaction milieu. In an acid medium, the unbound forms of ferric ion react with xylenol orange and form a colored complex. The color intensity was spectrophotometrically measured at 570 nm and is related to the total number of molecules of the oxidant present in the sample (10-13). A standard curve was plotted using hydrogen peroxide (H_2O_2; Gaussian, 2012) and the results are presented as micromoles of equivalent hydrogen peroxide per liter (µmol H_2SO_4 Eq/L).

Assay Reagents

Reagent 1: was prepared by dissolving 3.17 g of O-dianisidine dihydrochloride and 1.96 g of the ferrous ammonium sulfate in (1000 mL H_2SO_4 solution, 25 mM). The final reactant included 10 mM O-dianisidine dihydrochloride and 5 mM ferrous ammonium sulfate. Reagent is stable at 4°C for minimum six months.

For reagent 2: 8.18 g of NaCl and 114 mg of xylenol orange were dissolved in 900 mL 25 mM H_2SO_4 solution. The glycerol was added up to 100ml and then the solution was made to 1L by adding Glycerol. The reagent contains a final concentration of 150µM xylenol orange, 140 mM NaCl and 1.35 M glycerol. The equilibrium reagent had a pH of 1.75. The stability of this reagent reaches to 6 months at 4°C.

An amount of H_2SO_4 (100 µmol/L) was standardized daily and freshly diluted depending upon a molar extinction coefficient at 240 nm, which equal to 43.6 M^{-1} cm^1 (Table 1).

Table 1. Procedure.

	Blank	Standard	Sample
D.W.	50 µL	-----	------
Serum	------	-----	50 µL
H_2SO_4	------	50 µL	------
R1	2 mL	2 mL	2 mL
Test tubes were mixed by vortex, and then add:			
R2	2 mL	2 mL	2 mL

Source: Own authorship.

Quietly mix the content of each tube after addition, that allow standing at room temperature for 3 mins., then the results read by using spectrophotometric deviceat 560 nm.

$$\text{Total oxidants status} = \frac{\text{A.test}}{\text{A.STD}} * \textit{Conc.of STD}$$

Determination of ascorbic acid (vitamin C)

Pharmacokinetic methods for determining ascorbic acid are based on cogeneration of dehydroascorbic acid, colorimetric detection of 1,2-enediol group-dependent absorbance changes of indicator dyes, and 2,4-dinitrophenyl hydrazine (DNPH) methods (AA) is oxidized by copper ions to produce dehydroascorbic acid (DHA) and diketogulonic acid .

The 2,4-dehydrophenyl osazon product formed in the presence of DNPH, react with sulfuric acid **[27]**, to give an orange red complex that gave rise to absorbance at 520 nm as illustrated in Figure 1.

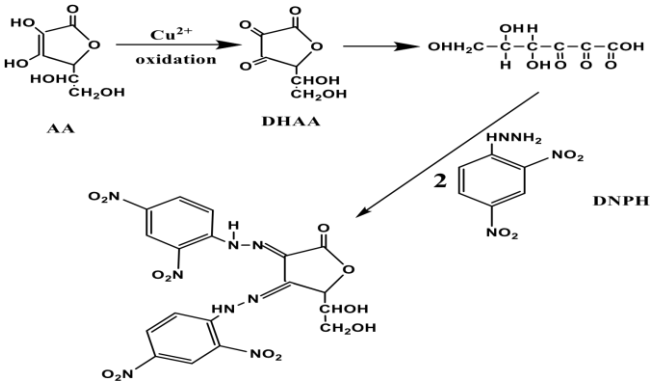


Figure 1. Reaction between ascorbic acid and 2,4 dinitro phenylhydrazine **[27]**.

Reagents

1-Meta phosphoric acid m-HPO_3 (0.75 M): dissolve 3 gm of m- HPO_3 in 50 ml DDW. 2-Sulfuric acid (4.5 M): 25 ml of H_2SO_4 concentrated was added to 30 ml DDW then brought to final volume of 100mL.

3-Sulfuric acid (12M): 65mL of H_2So_4 Conc. Was added to 30mL of cold DDW then brings to a final volume of 100mL.

4-Thiourea (0.66M): 2.5 gm of thiourea was dissolved in 50ml DDW.

5-2,4 dinitrophenyl hydrazine (0.01 M): dissolve 5.0gm of 2,4 DNPH in 200mL 0f (4.5 M) of H_2SO_4 and brought to a final volume of 250 ml with 4.5M of H_2SO_4 then refrigerated overnight and filtrated.

6-Copper sulfate (0.027 M): dissolve 0.6mg of anhydrous copper sulfate in 100ml DDW.

7-DTCS reagent contain the following:-

5mL of thiourea, 5mL copper sulfate and 100 mL of 2,4-DNPH reagent.

8-Ascorbic acid standard stock standard solution (2.8 mM) is prepared by taken a 50 mg of (AA) in a 100 ml of m-HPO_3 dilutions are made in m-HPO_3 to 2.5, 5, 10, 15 and 20 mg/L that equal (0.014, 0.028, 0.056, 0.084 and 0.12mM) respectively (Table 2).

Table 2. Procedure.

Reagent	Sample µL	Standard µL	Blank
m-HPO_3	800		
D.W		1000	1000
Serum	200		
Mixed in vortex mixture, then centrifuged at 2500Xg for 10 minutes			
Supernat Standard	600	600	
m-HPO_3			600
DTCS reagent	200	200	200

Source: Own authorship.

The sample and standard test tubes are prepared, then pipetted into test tubes.

Mixed and vortex mixture, then incubate in water bath at 37C^0 for 3 hrs, then the tubes arising from water bath and chilled for 10 minutes in an ice water bath with gradually mixing (Table 3).

Table 3. Reagent and samples - H_2SO_4 (12 mol/L).

Reagent	Sample µL	Standard µL	Blank µL
H_2SO_4 (12 mole/L)	1000	1000	1000

Source: Own authorship.

The mixture was motley by vortex and returned immediately to the icy water bath. The spectrophotometer was adjusted with blank reagent and the measure absorbance for sample and standard was read at 520nm.

Calculation

The concentration of AA can be determined directly by a comparator standard as follow:

$$\text{Concentration of sample} = \frac{A_{sample}}{A_{standard}} \; x\, Conc.of\ standard$$

Where: A=absorbance at 520 nm for sample and standard.

C= concentration (mg/dL) of ascorbic acid in the sample and standard.

Ethical Approval and Safety Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of Al-Mustaqbal University, Hilla City, Babylon Governorate, Iraq. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Blood samples were collected from confirmed COVID-19 patients and healthy volunteers following standard clinical procedures. All procedures involving biological samples were carried out under strict biosafety conditions in accordance with institutional and international guidelines for handling infectious materials. Appropriate personal protective equipment (PPE) was used to minimize the risk of infection to laboratory personnel. All biological waste was disposed of safely following approved biosafety protocols.

Data Availability

The datasets generated and analyzed during this study, including measurements of oxidative stress markers, antioxidant levels, and trace elements, are available from the corresponding author upon reasonable request. Data will be shared for research purposes in accordance with institutional ethical guidelines and data protection regulations

Results and Discussion

Biochemical and clinical characteristics of the study subjects

The present study includes of 60 COVID-19 patients and 40 control subjects.

G1: Healthy subjects

G2: COVID-19 patients

Copper levels in sera of COVID-19 patients and control

This study of plasma Cu level observed the decrease in COVID-19 patients compared to controls, as shown in (Table 4).

Table 4. Copper (µmol/L) in sera of healthy subject and COVID-19 patients.

	NO.	Mean	STD	SE	95% C.I.	
					Lower Bound	Upper Bound
G1	40	9.12	0.341	0.09	4.31	11.32
G2	60	15.82	0.475	0.106	10.12	18.35

Source: Own authorship.

The serum concentration of Cu is unknown in COVID-19 patients **[28]**. But Cu is an important micronutrient in the body, and it is necessary for DNA protection from Os. Cu is extremely necessary for a great part of the antioxidant defense system (inclination of CuZn-SOD) **[29]**, hence independently on the fact that COVID-19 is known to change and suppress the internal antioxidant defense system, one may suppose the existing relation in Os impacts the serum Cu concentration. Kardos et al. 2018 reported that when Cu is deficient, human immune system response is weak **[30]**. Based on the finding of the present study, low serum Cu has also been linked to poor immune response and a higher incidence of infections along with greater Os Mechanistically, Zabetakis et al. Chronic TNF-α-mediated lung inflammation develops in response to prolonged Cu deficiency. Due to the relationship between COVID-19 and the action of inflammatory cytokines, the level of Cu will decrease due to the inflammatory process in the lungs **[31]**.

Selenium levels in sera of COVID-19

It is an important component in the regulation of redox reactions, mainly to reduce the ROS generated in oxidative stress conditions. Low selenium dietary condition, associated with high oxidative stress on host tissue, could be responsible for the change of viral genome.

Results and discussion

These studies (Table 5) report that selenium is meaningfully lower in COVID-19 patients than in control groups.

Table 5. Selenium (ng/dL) in sera of healthy subject and COVID-19 patients.

	NO.	Mean	STD	SE	95% C.I.	
					Lower Bound	Upper Bound
G1	40	28.11	1.74	0.054	23.21	30.04
G2	60	24.33	2.01	0.091	19.83	25.11

Source: Own authorship.

In particular, the role of selenoproteins in providing antioxidant defense, modulate systemic functions of host leukocytes and natural killer (NK) cells **[32]**, whereas selenium deficiency alters immune response via diminishing T cell proliferation, the lytic effector functions of lymphocytes and NK cell activity **[33]**. Besides being highlighted as a potential treatment for COVID-19 (Zhang et al., 2020), selenium suggested to play an important role in the emergence and dissemination of SARS-CoV-2. Selenium decreased host status **[34]** and virulent virus **[35]** Selenium supplementation (dietary) can prompt the cytotoxic effector cells activity in COVID-19 **[36]**.

Total oxidants in sera of COVID-19 patients and control

Oxidative stress is defined as the state in which the systems of neutralization and removal of free radicals are overcome. Plasma level Measuring of total oxidant in Between COVID-19 patients and control cohort: Also measures the level of total oxidant in plasma between COVID-19 patients and control. As Table 6 shows total oxidant concentration in plasma of patients with COVID-19 disease was much higher than control group.

Table 6. Total oxidant levels (µmol/L) in sera of healthy subject and COVID-19 patients.

	NO.	Mean	STD	SE	95% C.I.	
					Lower Bound	Upper Bound
G1	40	2.77	0.451	0.041	1.302	3.43
G2	60	3.71	0.661	0.031	1.92	3.54

Source: Own authorship.

Oxidative stress due to decreased antioxidant defense system and/or increased production of reactive oxygen species (ROS) is believed to be critically important in viral multiplication and the development of virus-related diseases **[37]**. The present study reports an enhanced oxidative process associated with COVID-19 disease. The total oxidant is increased, which leads to an increase in lipid peroxidation with the subsequent release of free lipid peroxidation intermediates, 8-iso-PGF2α **[38]**.

Ascorbic acid) concentrations in sera of patients with COVID-19 and control

The Vitamin C acts as an antioxidant directly, by reacting with extraneous ROS or by recycling the vitamin E (α-tocopheroxyl radical). Apart from vitamin C which a little bit lower level in COVID 19 patients as compared to controls (Table 7). These results are in line with that of Care who reported highest depletion of vitamin C in COVID-19 patients **[39]**.

Table 7. Vitamin C (mg/dL) in sera of healthy subject and COVID-19 patients .

	NO.	Mean	STD	SE	95% C.I.	
					Lower Bound	Upper Bound
G1	40	0.904	0.370	0.057	0.640	1.821
G2	60	0.210	0.023	0.006	0.085	0.186

Source: Own authorship.

The finding from this study is also in accordance with report of Chris explaining that antioxidant vitamins levels are effective to their scavenging effect on ROS reduced in SARS-COV-2 infection **[40]**, further low level of antioxidant vitamins have also been reported in COVID 19 patients, hence proposed that strategies to enhance level of these vitamins may beneficial in these patients **[41]**. The lower values of antioxidant vitamins observed in the COVID 19 subjects could be due to an overproduction of ROS and a depleted antioxidant system. This role of phagocytes, producing ROS, is a well-established pathway through which infections elevate. As powerful antioxidants, Vitamins C and E and to some extent vitamin A scavenge these ROS and alleviate their impacts **[42]**.

This scavenging lowers plasma concentrations of these vitamins. These two vitamins are taken to be obliging in cytokine storms and cell wound, both the outcomes of SARS-COV-2 and other viral diseases **[4]**. Accordingly, Jan et al. **[43]** considered these vitamins for example vitamins E and C to be protective effects against SARS-Cov-2 and other viral infections due to their potent antioxidant and reactive oxygen species scavenging effects. Due to their ability in scavenging the ROS these vitamins along with the pollution factors are consumed in the process so the low level of these vitamins noted in this study.

Conclusion

Deficits in some antioxidants (vitamin C) but also in trace elements (selenium) were also found, strengthened in COVID-19 patients by increased systemic oxidative stress, as expressed in elevated concentrations of copper. These results proved the role of copper in ROS changes in COVID-19 patients.

CRediT

Conceptualization; Data Curating; Formal Analysis; and Investigation: **Thulfeqar A. Hamza,** Project Administration; Supervision; Writing - Original Draft: **Rafal Fawze Kaream**.

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Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of Al-Mustaqbal University, Hilla City, Babylon Governorate, Iraq. Prior to inclusion in the study, written informed consent was obtained from all participants.

Informed Consent

Informed consent was obtained from all participants, and all study procedures were fully explained prior to participation.

Funding

Not applicable.

Data Sharing Statement

Data used and analyzed during the current study are available from corresponding author upon reasonable request, and all data is stored in accordance with privacy and ethical guidelines.

Conflict of Interest

The authors declare no competing interests.

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It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

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References

1. Huang C, Wang Y, Li X et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (London, England) 2020, 395(10223):497–506. https:// doi. org/ 10. 1016/ S0140- 6736(20) 30183-5.
2. Coperchinia F, Chiovatoa L, Crocea L, Magria F, Rotondia M. The cytokine storm in COVID-19: An overview of the involvement of the chemokine/chemokine-receptor system. Cytokine Growth Factor Rev. 2020, 53, 25–32.
3. Carsana L, Sonzogni A, Nasr A, Rossi RS, Pellegrinelli A, Zerbi P, Rech R, Colombo R, Antinori S, Corbellino M et al. Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: A two-centre descriptive study. Lancet Infect. Dis. 2020, 20, 1135–1140.
4. Delgado-Roche L, Mesta F. Oxidative stress as key player in severe acute respiratory syndrome coronavirus (SARS-CoV) infection. Arc Med Res. 2020, 51(5):384–387. https://d oi.o rg/ 10.1 016/j. arcmed. 2020. 04. 019
5. Lake MA. What we know so far: COVID-19 current clinical knowledge and research. Clin. Med. (Lond.) 2020, 20, 124–127.
6. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, Mehra MR, Schuepbach RA, Ruschitzka F, Moch H. Endothelial cell infection and endotheliitis in COVID-19. Lancet 2020, 395, 1417–1418.
7. Bansal M. Cardiovascular disease and COVID-19. Diabetes Metab. Syndr. 2020, 14, 247–250.
8. Xie P, Ma W, Tang H, Liu D. Severe COVID-19: A Review of Recent ProgressWith a Look Toward the Future. Front. Public Health 2020, 8, 189.
9. Chacko SA, Song Y, Nathan L, Tinker L, de Boer IH, Tylavsky F, Wallace R, Liu S. Relations of dietary magnesium intake to biomarkers of inflammation and endothelial dysfunction in an ethnically diverse cohort of postmenopausal women. Diabetes Care 2010, 33, 304–310.
10. George SM, Neuhouser ML, Mayne ST, Irwin ML, Albanes D, Gail MH, Alfano CM, Bernstein L, McTiernan A, Reedy J et al. Postdiagnosis diet quality is inversely related to a biomarker of inflammation among breast cancer survivors. Cancer Epidemiol. Biomark. Prev. 2010, 19, 2220–2228.
11. Bouayed J, Bohn T. Exogenous antioxidants—Double-edged swords in cellular redox state: Health beneficiale_ects at physiologic doses versus deleterious e_ects at high doses. Oxid. Med. Cell Longev. 2010, 3, 228–237.
12. Pohanka M. Role of oxidative stress in infectious diseases. A review. Folia Microbiol. 2013, 58, 503–513. [CrossRef] [PubMed]
13. Ivanov AV, Bartosch B, Isaguliants MG. Oxidative Stress in Infection and Consequent Disease. Oxid. Med. Cell Longev. 2017, 2017, 3496043.
14. Rahman I, Adcock IM. Oxidative stress and redox regulation of lung inflammation in COPD. Eur. Respir. J. 2006, 28, 219–242.
15. Radi R. Oxygen radicals, nitric oxide, and peroxynitrite: Redox pathways in molecular medicine. Proc. Natl. Acad. Sci. USA 2018, 115, 5839–5848.
16. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J. Autoimmun. 2020, 109, 102433.
17. Ntyonga-Pono MP. COVID-19 infection and oxidative stress: an underexplored approach for prevention and treatment? Pan African Med J 2020; 35(Suppl. 2): 12.
18. Arvinte C, Singh M and Marik PE. Serum levels of Vitamin C and Vitamin D in a cohort of critically Ill COVID-19 patients of a North American community hospital intensive care unit in May 2020: a pilot study. Med Drug Discov 2020; 8: 100064.
19. Weir EK, Thenappan T, Bhargava M, et al. Does vitamin D deficiency increase the severity of COVID-19. Clin Med 2020; 20(4): e107–e108.
20. Te Velthuis AJ, van den Worm SH, Sims AC, et al. Zn2+ inhibits coronavirus and arterivirus RNA polymerase activity in vitro and zinc ionophores block the replication of these viruses in cell culture. PLoS Pathog 2010; 6: e1001176.
21. Culbertson EM, Culotta VC. Copper in infectious disease: using both sides of the penny. Semin. Cell Dev. Biol. https://doi.org/10.1016/ j.semcdb.2020.12.003R (in press), 2021, S1084-9521(20)30187-7.
22. Guillin OM, Vindry C, Ohlmann T, Chavatte L. Selenium, selenoproteins and viral infection.

Nutrients, 2019, 11, 2101.

23. Zhang J, Saad R, Taylor EW, Rayman MP. Selenium and selenoproteins in viral infection with potential relevance to COVID-19. Redox Biol. 2020, 37, 101715.
24. Erel O. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clin Biochem. 2004, 37(4):277–285. https:// doi. org/ 10. 1016/j. clinb iochem. 2003. 11. 015
25. Cakirca G, Manav V, Celik H et al. Effects of anxiety and depression symptoms on oxidative stress in patients with alopecia areata. Postepy dermatologii i alergologii. 2020, 37(3):412–416.
26. Erel O. A new automated colorimetric method for measuring total oxidant status. Clinical biochemistry. 2005;38(12):1103-11.
27. Burtis CA, Ashood ER. "Tietz textbook of clinical chemistry" 3rd ed. W.B. Saunders Company, Tokyo 1999; 1034-54.
28. Taheri M, Bahrami A, Habibi P, et al. A review on the serum electrolytes and trace elements role in the pathophysiology of COVID-19. Biol Trace Elem Res 2020; 8: 1–7.
29. Fooladi S, Matin S and Mahmoodpoor A. Copper as a potential adjunct therapy for critically ill COVID-19 patients. Clin Nutr ESPEN 2020; 40: 90–91.
30. Kardos J, Héja L, Simon ء, et al. Copper signalling: causes and consequences. Cell Commun Signal 2018; 16(1): 71.
31. Zabetakis I, Lordan R and Norton C. COVID-19: the inflammation link and the role of nutrition in potential mitigation. Nutrients 2020; 12: 1466.
32. Sahin E, Orhan C, Uckun FM, Sahin K. Clinical Impact Potential of Supplemental Nutrients as Adjuncts of Therapy in High-Risk COVID-19 for Obese Patients. Front Nutr 2020; 7: 580504.
33. Ivory K, Prieto E, Spinks C, Armah CN, Goldson AJ, Dainty JR, Nicoletti C. Selenium supplementation has beneficial and detrimental effects on immunity to influenza vaccine in older adults. Clin Nutr 2017; 36: 407-415.
34. Bae M, Kim H. Mini-Review on the Roles of Vitamin C, Vitamin D, and Selenium in the Immune System against COVID-19. Molecules 2020; 25: 5346.
35. Zhang R, Wang X, Ni L et al (2020) COVID-19: Melatonin as a potential adjuvant treatment. Life Sci. 2020, 250:117583. https:// doi. org/ 10. 1016/j. lfs. 2020. 117583
36. Kieliszek M, Lipinski B. Selenium supplementation in the prevention of coronavirus infections (COVID-19). Med Hypotheses 2020; 143: 109878.
37. Camini FC, da Silva Caetano CC, Almeida LT et al (2017) Implications of oxidative stress on viral pathogenesis. Arch Virol 162(4):907–917.
38. Derouiche S. Oxidative stress associated with SARS-Cov-2 (COVID-19) increases the severity of the lung disease—a systematic review. J Infect Dis Epidemol 2020; 6(3): 1–6.
39. Care C, Chiscano-Cam ó n L, Ruiz-Rodriguez JC, et al. Vitamin C levels in patients with SARS-CoV-2-associated acute respiratory distress syndrome. Crit Care 2020; 24: 522.
40. Derbyshire E and Delange J. COVID-19: is there a role for immunonutrition, particularly in the over 65s? BMJ Nutr Prevent Health 2020; 3: 071.
41. Shakoor H, Feehan J, Al AS, et al. Immune-boosting role of vitamins D, C, E, zinc, selenium and omega-3 fatty acids: Could they help against COVID-19? Maturitas 2020; 143: 1–9.
42. Zhang J, Taylor EW, Bennett K, Saad R, Rayman MP. Association between regional selenium status and reported outcome of COVID-19 cases in China. Am J Clin Nutr 2020; 111: 1297-1299.
43. Jan H, Usman H and Zainab R. COVID-19: a brief overview on the role of vitamins specifically vitamin C as immune modulators and in prevention and treatment of SARS-Cov-2 infections. Biomed J Sci Tech Res 2020; 28(3): 21580–21586