Research Article

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Serum zinc associated with immunity and inflammatory markers in Covid-19

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Abstract: This study aimed to assess the association between serum zinc level with some inflammatory and immunity factors and the duration of hospitalization and mortality rate in patients diagnosed with Covid-19. In this cross-sectional study, blood samples were taken from polymerase chain reaction (PCR) positive patients. New patients diagnosed with Covid-19, admitted to different public hospital wards, were considered eligible for entering the study. The study was done on 179 hospitalized patients diagnosed with Covid-19. Fourteen patients died during the hospitalization and the in-hospital mortality rate was 7.8%, with 9.1% (13 patients) of patients with serum zinc level less than 70 mcg/dL and 3.4% (1 patient) of patients with zinc levels more than 70 mcg/dL. Higher levels of zinc were significantly associated with a higher and lower level of interferon-gamma (IFN-γ) (p-value = 0.035) and interleukin (IL)-6 (p-value = 0.004), respectively. The level of serum zinc did not have a significant association with mortality even after adjusting for confounding factors. The relationship between zinc level and the duration of hospitalization was also not significant. In conclusion, serum zinc level had an association with IL-6 and IFN-γ level, but it did not have any significant association with hospital duration or mortality.

Keywords: serum zinc, interleukin-6, interferon-gamma, duration of hospitalization, mortality rate, Covid-19

1 Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the cause of coronavirus disease 2019 (Covid-19), was first reported in China in late 2019 from a zoonotic source [1]. The full spectrum of Covid-19 ranges from mild, self-limiting respiratory tract illness to severe progressive pneumonia, multi-organ failure, and death [2]. After an incubation period, the acute viral phase in patients with symptomatic Covid-19 usually manifests as influenza-like symptoms. In some persons, the illness progresses to hypoxemic respiratory failure [3]. Evidence suggests that the pathophysiological basis of this profound decline is a severe inflammatory response resembling cytokine release syndrome [4,5]. In this phase, patients have markedly abnormal inflammatory markers, including elevated serum interleukin (IL)-6, ferritin, and C-reactive protein (CRP) levels [6–8]. Zinc (Zn) is an essential micronutrient that is involved in the regulation of innate and adaptive immune responses [9]. Zn is involved in a variety of biological processes due to its function as a cofactor, signaling molecule, and structural element. The most critical role of Zn is demonstrated in the immune system. Zn regulates the proliferation, differentiation, maturation, and functioning of leukocytes and lymphocytes [9]. Zn also plays a signaling role involved

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in the modulation of inflammatory responses [9]. Having said the role of Zn in inflammatory responses, there must be an understanding of cytokines. Cytokines are one term for a group of protein cell regulators, variously called lymphokines, monokines, IL, and interferons (IFN), which are produced by a wide variety of cells in the body. They play an important role in many physiological responses, involved in the pathophysiology of a range of diseases, and have a therapeutic potential [10]. Evidence has shown the role of different types of cytokines in Covid-cytokine storm syndrome (COVID-CSS). In CSS, many inflammatory cytokines such as IL-1, IL-10, and tumor necrosis factor (TNF)-α are elevated, approximately 2–100 folds above normative values, whereas IL-6 demonstrates much larger increases, in some cases more than 1000 folds above normal [11]. Other cytokines such as interferon-gamma (IFN-γ) is capable of orchestrating numerous protective functions to heighten immune responses in infections and cancers [12]. Zn deficiency results in altered numbers and dysfunction of all immune cells, subjects with suboptimal Zn state have an increased risk of infectious diseases and autoimmune disorders [11,13–15]. Zn deficiency is responsible for 16% of all deep respiratory infections worldwide [16]. During chronic Zn deficiency, the production of pro-inflammatory cytokines increases, influencing the outcome of a large number of inflammatory, metabolic, neurodegenerative, and immune diseases [17]. Zn is essential to preserve natural tissue barriers such as the respiratory epithelium, preventing pathogen entry, for a balanced function of the immune and redox system. There are several data surrounding the association between Zn status and viral respiratory tract infections, but there is still more to know regarding its association with Covid-19. It has also been suggested that most Covid-19 symptoms are associated with altered Zn homeostasis and Zn might even prevent or attenuate those symptoms and thus should be regarded as a promising cost-effective, globally available therapeutic approach for Covid-19 patients [18]. Given all the data surrounding the role of minerals, especially Zn in the regulation of immune responses, especially against respiratory tract infections and the unprecedented situation we are living in, with a global pandemic affecting many lives and causing many more hospitalizations, without much effective prophylaxis or treatment against Covid-19, studying the concentration of Zn in individuals affected with this disease and its association with some immunological and inflammatory factors might help us develop more accurate treatments. Prophylaxis against this disease can help us get into a deeper understanding of the role of minerals, especially Zn in Covid-19 and other similar respiratory infections. This study aimed to assess the association between serum Zn levels and some inflammatory and immunity factors and also to evaluate the association between serum Zn level and the duration of hospitalization and mortality rate in patients diagnosed with Covid-19.

2 Methods

2.1 Participants

In this cross-sectional study blood samples were taken from 179 polymerase chain reaction (PCR)-positive patients. New patients diagnosed with Covid-19, admitted to different public hospital wards, were considered eligible for entering the study. Demographic and lab data were also collected at the time of admission. The duration of hospitalization and the mortality rate of these patients were also monitored. The patients were required to fill and sign in a consent form that explained the goal of the study. The information gathered from the patients included: name and address, telephone number, hospitalization document code, date and duration of hospital stay, date of death, sex and age, height and weight, educational status, job status, past medical history such as (hypertension, dyslipidemia, diabetes, underlying heart or vascular disease, chronic lung and airway diseases such as asthma, cancer, etc.), drug history (including the history of vitamin or mineral supplement intake), alcohol and smoking history, and hospital prescriptions (antibiotics, corticosteroids, respiratory drugs, etc.) were gathered by interviewing and using hospital documents. Biochemical parameters such as oxygen saturation (SpO₂), complete blood count (CBC), erythrocyte sedimentation rate (ESR), CRP, liver and kidney function tests, ferritin, and lactate dehydrogenase (LDH) were also gathered from hospital documents at the time of admission, and serum Zn, IL-6, and IFN-γ level were measured.

2.2 Measurements

The samples were taken from patients hospitalized at the internal ward and emergency room (ER). 3cc of blood was drawn from each individual and was put in a clot activator tube. The tubes were then put in a centrifuge with a rotational speed of 4,000 rpm for 5 min. The residual plasma for each patient was transferred to a micro-tube and stored at −70°C until the end of the study.
of Helsinki and all procedures involving research study participants were approved by the Shiraz University of Medical Sciences (SUMS) ethics board committee, reference number: IR.SUMS.REC.1399.836. Written informed consent was obtained from all participants and questionnaires were anonymous and encoded.

3 Results

In this study, 179 hospitalized patients diagnosed with Covid-19 participated. The mean age of the participants was $55.27 \pm 16.23$ in the total sample, with $54.30 \pm 15.78$ in survivor patients, and $66.79 \pm 17.51$ in non-survivor patients. This difference was statistically significant ($p = 0.001$). There were 108 (60.3%) male patients in the study. Among all the patients, 140 (81.9%) patients had Zn levels under 70 mcg/dL in which 83 (82.2%) of the male and 57 (81.4%) of the female population were Zn insufficient or deficient. Hypertension was the most common underlying disease in the participants (39.1% of patients reported a history of hypertension) and dyspnea was the most common presenting symptom in the patients diagnosed with Covid-19 (dyspnea has been reported in 78.2% of patients). About one-quarter of the patients had a history of vitamin use (50, 27.9%). Other demographic and clinical information of patients are reported in Table 1.

Fourteen patients died during the hospitalization and the in-hospital mortality rate was calculated as 7.8%, and 9.1% (13 patients) of patients had serum Zn level less than 70 mcg/dL and 3.4% (1 patient) of patients had serum Zn level more than 70 mcg/dL; however, this difference was not statistically significant ($p = 0.331$). The median duration of hospitalization was 3 days (2–5 days) which happened to be the same for patients with Zn levels lower or higher than 70 mcg/dL. According to the results, there was a significant association between serum Zn and IFN-γ ($p = 0.035$), a higher level of Zn was significantly associated with a higher level of IFN-γ. A significant association was also found between Zn level and IL-6 ($p = 0.004$). Higher levels of serum Zn were significantly associated with a lower level of IL-6. There was no significant association between Zn level and other inflammatory factors (Table 2). Zn did not have a significant association with death. Even after adjustment for confounding factors such as age as well as history of underlying disease, there still happened to be no significant association between Zn and mortality rate. The relationship between serum Zn level and the duration of hospitalization was not significant either.
Table 1: Characteristics of patients with Covid-19 by survival status

| Characteristics                              | Patients (n = 179) | Survived (n = 165) | Non-survived (n = 14) | p Value |
|----------------------------------------------|-------------------|--------------------|-----------------------|---------|
| Age mean value ± SD                           | 55.27 ± 16.23     | 54.30 ± 15.78      | 66.79 ± 17.31         | 0.001*  |
| BMI (kg/m²) mean value ± SD                  | 27.54 ± 5.32      | 27.63 ± 5.46       | 26.37 ± 2.63          | 0.444   |
| Sex N (%)                                     |                   |                    |                       |         |
| Male                                          | 108 (60.3)        | 97 (58.8)          | 11 (78.6)             | 0.159   |
| Female                                        | 71 (39.7)         | 68 (41.2)          | 3 (21.4)              |         |
| Education N (%)                               |                   |                    |                       |         |
| Illiterate                                    | 34 (19.0)         | 33 (19.4)          | 2 (14.3)              | 0.544   |
| Primary school                                | 38 (21.2)         | 35 (21.2)          | 3 (21.4)              |         |
| Guidance school                               | 13 (7.3)          | 10 (6.1)           | 3 (21.4)              |         |
| High school and diploma                       | 30 (16.8)         | 30 (18.2)          | —                     |         |
| Undergraduate                                 | 27 (15.1)         | 26 (15.8)          | 1 (7.1)               |         |
| Post graduate                                 | 13 (7.3)          | 12 (7.3)           | 1 (7.1)               |         |
| Occupation N (%)                              |                   |                    |                       |         |
| Unemployed                                    | 4 (2.2)           | 4 (2.4)            | —                     | 0.781   |
| House wife                                    | 59 (33.0)         | 56 (33.9)          | 3 (21.4)              |         |
| Worker                                        | 8 (4.5)           | 7 (4.2)            | 1 (7.1)               |         |
| Employed                                      | 28 (15.6)         | 26 (15.8)          | 2 (14.3)              |         |
| Self-employed                                 | 46 (25.7)         | 43 (26.1)          | 3 (21.4)              |         |
| Retired                                       | 19 (10.6)         | 16 (9.7)           | 3 (21.4)              |         |
| Student                                       | 1 (0.6)           | 1 (0.6)            | —                     |         |
| Current smoking N (%)                         | 39 (22.2)         | 38 (23.0)          | 1 (7.1)               | 0.190   |
| Alcohol consumer N (%)                        | 15 (8.5)          | 15 (9.1)           | —                     | 0.273   |
| Place of residence N (%)                      |                   |                    |                       |         |
| Urban                                         | 147 (82.1)        | 135 (82.3)         | 12 (85.7)             | 0.691   |
| Rural                                         | 30 (16.8)         | 28 (17.1)          | 2 (14.3)              |         |
| Vitamin supplement consumption N (%)          | 50 (27.9)         | 47 (28.8)          | 47 (28.8)             | 0.557   |
| Vitamin C intake N (%)                        | 16 (8.9)          | 15 (9.1)           | 15 (9.1)              | 0.807   |
| Vitamin D intake N (%)                        | 27 (15.1)         | 25 (15.2)          | 25 (15.2)             | 0.931   |
| Zinc <70 mg/dL N (%)                          | 142 (79.3)        | 130 (78.8)         | 12 (85.7)             | 0.316   |
| History of underlying disease N (%)           |                   |                    |                       |         |
| Diabetes                                      | 52 (29.2)         | 46 (28.0)          | 6 (42.9)              | 0.249   |
| Hypertension                                  | 70 (39.1)         | 62 (37.6)          | 8 (57.1)              | 0.158   |
| Cardiovascular disease                        | 56 (31.3)         | 49 (29.7)          | 7 (50.0)              | 0.125   |
| Asthma and respiratory disease                | 22 (12.5)         | 20 (12.3)          | 2 (14.3)              | 0.827   |
| Cancer                                        | 7 (3.9)           | 6 (3.6)            | 1 (7.1)               | 0.618   |
| Autoimmune disease                            | 16 (8.9)          | 9 (5.5)            | —                     | 0.472   |
| HIV                                           | 2 (1.1)           | 2 (1.2)            | —                     | 0.849   |
| Duration of hospitalization median (IQ)       | 3 (2–5)           | 3 (2–5)            | 2.50 (1.75–6.25)      | 0.838   |
| Laboratory examinations mean value ± SD       |                   |                    |                       |         |
| Zinc (mcg/dL) (n = 171)                       | 58.65 ± 13.18     | 58.98 ± 13.38      | 54.61 ± 9.96          | 0.251   |
| IFN-γ (ng/mL) (n = 171)                       | 19.04 ± 19.88     | 19.12 ± 20.4       | 18.11 ± 18.51         | 0.860   |
| IL-6 (pg/mL) (n = 170)                        | 33.68 ± 60.21     | 32.80 ± 40.77      | 44.26 ± 31.99         | 0.330   |
| LDH (IU/L) (n = 153)                          | 728.92 ± 397.74   | 720.15 ± 407.08    | 823.31 ± 271.67       | 0.376   |
| RBC (×10⁶/µL) (n = 179)                       | 4.73 ± 0.69       | 4.69 ± 0.69        | 5.14 ± 0.64           | 0.026*  |
| HB (g/dL) (n = 179)                           | 13.15 ± 2.06      | 13.01 ± 2.01       | 14.77 ± 2.13          | 0.003*  |
| HCT (%) (n = 179)                             | 40.73 ± 5.6       | 40.34 ± 5.48       | 45.32 ± 5.05          | 0.002*  |
| WBC (×1,000/µL) (n = 179)                     | 6.85 ± 3.39       | 6.77 ± 3.47        | 7.76 ± 2.07           | 0.302   |
| PLT (×1,000/µL) (n = 179)                     | 216.24 ± 118.72   | 218.21 ± 121.43    | 193.07 ± 79.73        | 0.437   |
| Neutrophils (%) (n = 176)                     | 76.23 ± 57.17     | 75.87 ± 59.54      | 80.37 ± 8.08          | 0.781   |
| Lymphocytes (%) (n = 177)                     | 20.74 ± 10.48     | 21.38 ± 10.47      | 13.22 ± 7.29          | 0.008*  |
| ESR (mm/h) (n = 128)                          | 49.26 ± 26.53     | 49.04 ± 26.20      | 51.43 ± 30.66         | 0.767   |
| CRP (mg/L) (n = 164)                          | 36.65 ± 32.97     | 35.64 ± 32.66      | 48.41 ± 35.57         | 0.186   |
| SpO₂ (%) (n = 176)                            | 86.48 ± 11.08     | 87.25 ± 10.19      | 77.64 ± 15.95         | 0.005*  |
| FBS (mg/dL) (n = 91)                          | 146.12 ± 68.81    | 143.77 ± 67.19     | 161.58 ± 80.17        | 0.406   |
| BUN (mg/dL) (n = 179)                         | 19.53 ± 10.96     | 19.29 ± 11.23      | 22.43 ± 6.84          | 0.309   |
| Creatinine (mg/dL) (n = 179)                  | 1.26 ± 0.67       | 1.26 ± 0.69        | 1.31 ± 0.26           | 0.739   |

(Continued)
Table 1: Continued

| Characteristics | Patients (n = 179) | Survived (n = 165) | Non-survived (n = 14) | p Value |
|-----------------|-------------------|--------------------|-----------------------|---------|
| Uric acid (mg/dL) (n = 80) | 5.49 ± 2.55 | 5.69 ± 2.57 | 4.24 ± 2.10 | 0.081 |
| S.G.O.T (IU/L) (n = 164) | 53.63 ± 54.74 | 53.43 ± 59.0 | 55.85 ± 21.04 | 0.874 |
| S.G.P.T (IU/L) (n = 164) | 43.35 ± 36.40 | 44.11 ± 37.76 | 35.21 ± 13.73 | 0.388 |
| PTT (s) (n = 166) | 37.94 ± 15.01 | 38.53 ± 15.50 | 31.57 ± 4.84 | 0.035* |
| INR (n = 13) | 1.22 ± 0.39 | 1.15 ± 0.15 | 1.14 ± 0.15 | 0.360 |
| D-dimer (ng/mL) (n = 79) | 1,679.02 ± 1,850.33 | 1,699.43 ± 1,924.89 | — | 0.770 |
| Ferritin (ng/mL) (n = 36) | 742.80 ± 694.65 | 731.74 ± 722.38 | — | 0.750 |

Treatments

- Covid-19 drug: 153 (85.5) 139 (84.2) 14 (100.0) 0.101
- Other antibiotics: 135 (85.5) 142 (86.1) 11 (78.6) 0.450
- Corticosteroids: 122 (68.2) 111 (67.3) 11 (78.6) 0.389
- Respiratory drugs: 100 (55.9) 90 (54.5) 10 (71.4) 0.231

*p < 0.05. # Covid-19 drugs include: favipiravir, efavirenz, zidovudine, lamivudine, lopinavir, ritonavir, atazanavir, kaletra, remdesivir, linezolid, IFN-beta, ivermectin, HCQ. Other antibiotics include: imipenem, meropenem, tavanex, ampicilbactam, vancomycin, azithromycin, clexane, ceftriaxone, clindamycin, metronidazole, cloxacillav, ampicilbactam, ampicillin, sulbactam. Corticosteroids include: dexa-methasone, prednisolone, methylprednisolone, hydrocortisone, triamcinolone, pulmicort neb. Respiratory drugs include: salbutamol, atrovent, serollo, guaifenesin, carnitine, bromhexine, dextromethorphan, theophylline, pirfenidone, tiova. BMI, body mass index; BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FBS, fasting blood sugar; HA, hemoglobin; HCT, hematocrit; HIV, human immunodeficiency virus, IFN-gamma, interferon-gamma; IL-6, interleukin-6; INR, international normalized ratio; IQ, interquartile; IU, international unit; LDH, lactate dehydrogenase; PLT, platelets; PTT, partial thromboplastin time; RBC, red blood cells; S.G.O.T, serum glutamic-oxaloacetic transaminase; S.G.P.T, serum glutamic-pyruvic transaminase; SpO2, oxygen saturation; WBC, white blood cells.

Even after adjusting for confounding factors (age and history of underlying disease), there was still no significant association between serum Zn level and duration of hospitalization (Table 3).

The patients were divided into two groups based on their Zn status (less and more than 70 mcg/dL). The inflammatory factors in the two subgroups are shown in Figure 1. According to the results, there was no significant difference in inflammatory factors between the two subgroups based on serum Zn (less and more than 70 mcg/dL) except for IL-6 (p-value = 0.014). The amount of IL-6 in patients with serum Zn levels less than 70 mcg/dL was significantly higher than patients with Zn levels more than 70 mcg/dL. Correlation between serum Zn level and duration of hospitalization is shown in Figure 2.

4 Discussion

Given the novelty of the SARS-CoV-2 disease, not many studies have been reported regarding the measurement of serum Zn level and comparing it with inflammatory factors such as IL-6 or IFN-gamma in patients diagnosed with Covid-19, but the role of Zn in inflammation and immunity has been presented in previous studies. Proliferation, differentiation, maturation, and functioning of leukocytes including lymphocytes are all regulated by Zn [7]. Chronic inflammation is characterized by an increased level of inflammatory cytokine production and Zn deficiency could cause altered production of cytokines which could lead to inflammation [20]. Lower circulating Zn...
level correlates with increased IL-6, IL-8, and TNF-α, in addition, cytokine signaling pathways are influenced by Zn status [21]. Cytokines are produced by different types of cells, primarily by T-lymphocytes and macrophages and the influence of Zn on these cells may explain the observed effect Zn has on cytokine production [22,23]. Zn deficiency is associated with downregulation of IFN-γ, resulting in severe impairment of cell-mediated immunity [15]. As mentioned, regarding the association between Zn and inflammatory factors in our study, 2 inflammatory factors had a significant association (p-value <0.05) with increased Zn level, higher level of Zn were significantly associated with a lower level of IL-6 (p-value = 0.004) and a higher level of IFN-γ (p-value = 0.035) which are in accordance with the previous studies. Other inflammatory factors that we studied were: ESR, CRP, WBC, neutrophils, lymphocytes, SpO₂, and LDH. The association of all these other factors with increased serum Zn level was not statistically significant (p > 0.05). We also divided the patients into two groups regarding their Zn status and set the Zn level of 70 mcg/dL [24] as the cutoff value. In this division, the only inflammatory factor which was different between Zn sufficient and deficient groups was IL-6 (p-value = 0.014). Other factors that were measured and compared in these two groups were: WBC, lymphocytes, ESR, CRP, SpO₂, and IFN-γ. Patients with Zn sufficient status (Zn > 70 mcg/dL) had a higher SpO₂, lymphocytes, and IFN-γ but lower CRP and lower ESR compared to the Zn-deficient group. However, none of these differences were statistically significant. Serum Zn level did not have a statistically significant effect on mortality and hospitalization duration (p = 0.251). The only factor that had an effect on hospitalization and mortality was age with a p-value of 0.010. Thomas et al. conducted a randomized clinical trial study published in JAMA which recently concluded that the initiation of high-dose Zn gluconate, ascorbic acid, or a combination of the two supplements did not significantly decrease the duration of the symptoms or mortality compared with standard of care. This study also indicated that there was no significant difference in any secondary outcome such as number of days to reach no presence of fever, cough, shortness of breath, or fatigue in patients who received high dose Zn and ascorbic acid [25]. Based on our findings and a previous article, it seems that Zn levels do not have an effect on mortality and duration of hospitalization. The percentage of patients who died in this study was 7.8% with 9.1% being the mortality rate of patients with serum Zn levels less than 70 mcg/dL and 3.4% being the mortality rate of the patients with serum Zn levels higher than 70 mcg/dL. Although the mortality rate was higher in patients with serum Zn level less than 70 mcg/dL, the results were not statistically significant and the reason could be because of the disproportionate number of patients with serum Zn level less than 70 mcg/dL compared to those with serum Zn level higher than 70 mcg/dL. A study conducted by Nasrollahzadeh and colleagues in 2020 showed that the mortality percentage in their study was 21.9% but the study was done on Covid-19 patients who had an underlying disease [26] and it can explain the higher mortality rate reported in their study compared to this one. Our study has shown that there is an association between serum inflammatory markers and Zn level especially cytokine level such as IL-6 in patients with Covid-19. This association has been seen in other studies as mentioned above. Whether serum Zn level can have a subsequent effect on conditions such as cytokine storm in patients with Covid-19 warrants for further investigation.

### Table 3: Factors associated with duration of hospitalization and survival

|                      | Duration of hospitalization | Death |
|----------------------|-----------------------------|-------|
|                      | B   | SE  | p value | OR  | 95% CI   | p value |
| Model 1 (simple model) |    |     |         |     |          |         |
| Zinc                 | −0.01 | 0.01 | 0.541  | 0.97 | 0.93–1.02 | 0.251  |
| Model 2 (multiple model) |    |     |         |     |          |         |
| Zinc                 | −0.01 | 0.01 | 0.845  | 0.97 | 0.93–1.03 | 0.406  |
| Age                  | 0.02 | 0.01 | 0.041* | 1.06 | 1.01–1.10 | 0.010* |
| History of underlying disease | | | | |
| No                   | —  | —   | —      | Ref. | —        | — |
| Yes                  | 0.61 | 0.41 | 0.132  | 1.71 | 0.19–14.86 | 0.626  |

*Significant at 0.05 level; CI: confidence interval. B, regression coefficient; OR, odds ratio; SE, standard error.
Figure 1: Comparison of inflammatory factors in two subgroups of serum zinc (less and more than 70 mcg/dL). (a) Serum zinc and IL-6 (pg/mL). (b) Serum zinc and neutrophils (%). (c) Serum zinc and lymphocytes (%). (d) Serum zinc and ESR (mm/h). (e) Serum zinc and WBC (×1,000/µL). (f) Serum zinc and IFN-γ (ng/mL). (g) Serum zinc and CRP (mg/L). (h) Serum zinc and SpO₂ (%). (i) Serum zinc and LDH (IU/L).
Covid patients compared to non-Covid sepsis but the results were not statistically significant. But the study showed a statistically significant association between RBC rheological properties in Covid-19 infected patients. A statistically significant association was found between RBC and HCT levels in this study [28]. We should also note that a correlation between serum Zn level and Covid-19 outcome has been demonstrated in a recent study by Vogel-González et al. There were 249 participants in this study and serum Zn levels lower than 50 µg/dL at admission correlated with worse clinical presentation, longer time to recovery, and higher mortality. This study also demonstrated a higher level of inflammatory markers, such as IL-6 and CRP, in patients with low serum Zn levels [29]. Relative to hospitalization duration and mortality rates, our study has shown otherwise, with no association between serum Zn level and these two factors in patients diagnosed with Covid-19. There were some limitations in the study. The number of patients who were considered Zn deficient was disproportionate compared to those regarded as Zn sufficient, thus this could have probably been the limitation of the study and the reasons for not finding statistically significant associations. The study also had its strengths, the hospital where our research was conducted is one of the main hospitals for admitting patients diagnosed with Covid-19 in a city with a population of roughly 2 million. The criteria for admission for all the patients were the same and the same guidelines were followed.

5 Conclusion

In summary, serum Zn level had an association with IL-6 and IFN-γ levels but no significant association between serum Zn level and hospital duration or mortality was found. Although higher mortality rates were reported among patients considered to have inadequate serum Zn levels, this result was not considered to be statistically significant. We believe that further studies still have to be conducted in order to bring us more solid evidence with regards to the association between serum Zn level and hospitalization duration and mortality. In measuring other factors in patients infected with Covid-19, our study demonstrated a significant association between RBC, HCT, lymphocytes, and SpO2 in the patients who lived and those who died. Although the association between Zn and inflammatory markers and its outcome on non-Covid sepsis and other infections has been demonstrated in numerous studies, the effect of Zn on these
factors and other factors in patients diagnosed with Covid-19 warrants for further investigation.

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