Original Article

The Relationship Between Serum Level Of C-Reactive Protein And Zinc In Covid-19 Patients

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Abstract

Introduction: COVID-19 is a novel coronavirus which has varies from mild to severe symptoms. This study aimed to determine serum zinc level in COVID-19 patients and find out it's correlation with c-reactive protein. Method: 150 Covid-19 patients, with certain RT-PCR positive result and CT-scan for percentage of lung involvement, were enrolled in the study. Blood samples were collect from the patients for biochemical assessment. Results: The results showed a significant negative correlation between serum zinc with c-reactive protein, percentage of lung involvement and recovery days. Conclusion: zinc is trace element with important body functions and need further studies to enforced its role on COVID-19 inflammatory status.

Keyword: SARS-Co-2, Inflammation, Zinc

Introduction

The new RNA virus that causes severe acute respiratory syndrome coronavirus 2 is the cause of the coronavirus disease 2019 (COVID-19), an acute respiratory disease. Since the initial COVID-19 patient report in Wuhan, China, in December 2019, there have been a significant surge in COVID-19 cases globally[1][2]. As 2022 approaches, there is a significant COVID-19 wave brought on by SARS-CoV-2 mutations (i.e., delta, lambda, mu, and omiclone). About 80% of SARS-CoV-2-infected individuals had mild to moderate disease (stage I) (Fig. 1). Within a week, the remaining 20% may reach severe clinical stages (stage II). A portion of stage II (about 5% of the total) may then transition to stage III, which could ultimately lead to intubation or death[3].

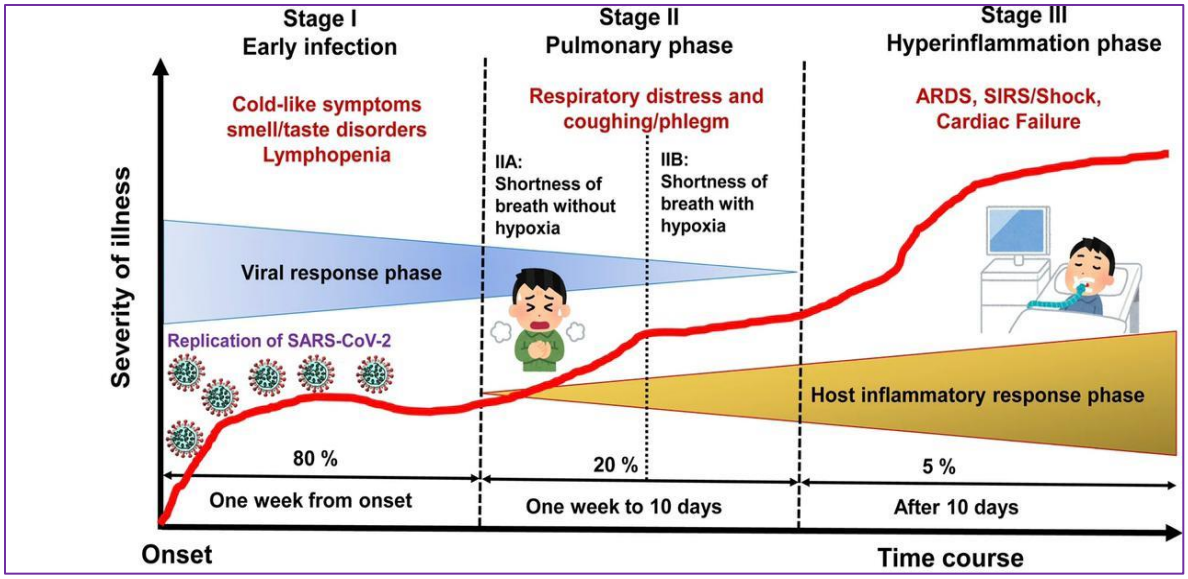

Figure 1[4]: The three stages of COVID-19 progression, together with the symptoms they bring.

At the beginning of the illness, common symptoms included myalgia, fatigue, fever, and cough. Acute respiratory distress syndrome (ARDS), acute heart injury, liver injury, renal impairment, and even death can result from the condition in extreme situations[5]. One of the hallmarks of COVID-19 is the systemic inflammatory response to the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection, and the majority of hospitalized COVID-19 patients exhibit aberrant inflammatory biomarkers[6]. C-reactive protein (CRP), an acute-phase protein first described by Tillet and Francis[7], one of the most common biomarkers of inflammation which the liver produces in response to interleukin-6 (IL-6). Additionally, C-reactive protein has been linked to serious illness in people with H1N1 influenza pneumonia [8] and in several recent studies, it has been shown that COVID-19 disease severity and CRP concentrations are correlated[9]. The fact that zinc is involved in so many biological processes and is able to bind to more than 300 enzymes and 2,000 transcriptional factors makes it one of the most significant necessary minerals[10]. It plays a significant role in both gene transcription and the metabolism of proteins, fats, and nucleic acids. It plays a significant part in the human body's immune system, wound healing, reproduction, and microcellular processes like macrophage, neutrophil, natural killer cell, and complement activity[11]. Low zinc levels have been linked to increased vulnerability to infectious illnesses, including viral infections, reduced lymphocyte activation, and weakened innate host defense via disruption of intercellular communication via cytokines[12][13]. Because zinc has a broad impact on the immune system, which includes both the adaptive and innate immune systems, this is one of the most important functions of zinc in our bodies. Zinc functions as an anti-inflammatory in innate immunity[14].

Material and method

Study design and participants

From November 2021 to March 2022, this a prospective study was conducted in Al-Basra city of Iraq. 150 participants in total, both male and female, were included in the study. Real-time polymerase chain reaction (RT-PCR), which looks for SARS-CoV-2 positive, was used to confirm the diagnosis of COVID-19 infection that made by specialized doctors. All patients with covid-19 infection were chosen from private clinics or Al-Basra Teaching Hospital patients who agreed to participate in the study.

Ethical consideration

Both the continuing Education section in the Basra Health Department and the Scientific Committee at the University of Basra's College of Pharmacy gave their approval to the project. All subject who participated in the study gave their consent.

Inclusion and exclusion criteria

This study included both male and female infected with Covid-19 who are older than 18 with positive RT-PC and either go to an outpatient clinic or are admitted to the hospital. while infected patients with age younger than 18, pregnancy, lactation mother, patients who refused to participate and patient with anemia disorders were excluded from this study

Measurement and analysis

Demographic information: A well-designed patient information sheet was used to obtain all demographic information from patients and their relatives. CT scan demonstrated the percentage of lung involvement, Spo2 and heart rate by Fingertip Pulse Oximeter, body mass index was calculated by the equation (weight/height^2) and body temperature by Digital Thermometer.

Biochemical analysis: 5ml blood samples were drawn from COVID-infected patients and were put in serum-separating tubes(SSTs). Then the samples centrifuged to getting fully separation of serum from whole blood and the serum samples refrigerated at -40º for keeping.

Serum zinc level measured by atomic absorption spectroscopy (AA-7000 ATOMIC ABSORPTION SPECTROSCOPY) and serum C-reactive protein measured by The Finecare CRP Rapid Quantitative Test.

Statistical analysis

IBM SPSS Statistics 26 software was used for statistical analysis and the data was expressed as number and percentage and Pearson correlation was used for correlation between data. $P<0.05$ was accepted as statistically significant.

The results

Totally 150 patients included in this study (72 (48%) male and 78 (52%) female p-value = 0.624). The median age of participants was 41 (18-84) years. 68% of enrolled patients in study had body mass index above the normal range where 56.57% overweight and 11.33% obese. Table 1 shows the demographic data that obtained from patients participated in this study.

Table 1: Demographic data of patients participated in this study

Parameters	Number(N)	Percentage (%)	P-value
Gender			
Male	72	48%	0.6242
Female	78	52%	
Age distribution			
18-28	28	18.67%	
29-39	40	26.67%	
40-50	39	26%	<0.0001
51-61	31	20.67%	
62-72	7	4.67%	
>72	5	3.33%	
Average	42.4 ± 14.8		

Range	18-84		
CI95%	42.4 ± 2.37		
Weight 45-55 56-65 66-75 76-85 86-95 >95	 9 42 49 38 10 2	 6% 28% 32.67% 25.33% 6.67% 1.33%	 <0.0001
Average	71.6 ± 10.5		
Range	45-96		
CI95%	71.6 ± 1.68		
Body mass index (MBI) 18-21 21-25 25-29 29-33 >33	 5 43 85 14 3	 3.33% 28.67% 56.67% 9.33% 2%	 <0.0001
Average	26 ± 2.7		
Range	18.97-35.75		
CI95%	26 ± 0.43		
SpO2			
<86	14	9.33%	<0.0001
86-95	52	34.67%	
>95	84	56%	
Average	93.9 ± 7.7		
Range	45-99		
CI95%	93.9 ± 1.23		
Patients who Required hospital admission Required steroid Required oxygen supply With Co-morbid disease	 47 42 48 52	 31.33% 28% 32% 34.67%	 <0.0001 <0.0001 <0.0001 0.0002

P value < 0.05 considered significant, CI95% =confidence interval at α=0.05

47(31.33%) of patients required hospital admission, while 42(28%) required steroids, 48(32%) required O2 supply, 52(34.67%) presented with co-morbid diseases. Table 2 showed the clinical and biochemical parameters of COVID-19 patients who enrolled in the present study where mean ± SD of SpO2 93.9 ± 7.734, CRP 49.8379 ± 69.53, serum zinc 0.8768 ± 0.65, % of lung involvement 26.2867% ± 21.9% and recovery days 9.02 ± 7.993.

Table 2: Clinical and biochemical parameters of COVID-19 patients who participated in this study

Parameters N = 150	Mean ± SD
Spo2	93.9 ± 7.734
CRP mg/l	49.8379 ± 69.53
Serum zinc mg/l	0.8768 ± 0.65
% of lung involvement	26.2867% ± 21.9%
Recovery days	9.02 ± 7.993

Spo2= oxygen of saturation, CRP= c-reactive protein, %= percentage

Results from table 3 showed a significant negative correlation of serum zinc with age (r = -0.186, p-value=0.022) (table 3), C-reactive protein (r = -0.289, p-value < 0.0001), recovery days (r = -0.281, p-value < 0.0001)and % of lung involvement (r = -0.204, p-value=0.012) and no significant correlation of serum zinc with gender (r = 0.022, p-value = 0.787), Spo2 (r = 0.138, p-value = 0.091). Also current study observed a significant positive correlation between C-reactive protein with age (r = 0.462, p-value < 0.0001), percentage of lung involvement(r= 0.525, p-value < 0.0001) and recovery days (r = 0.448, p-value < 0.0001) while a significant negative correlation of C-reactive protein with Spo2 (r=-0.462, p-value < 0.0001) and serum zinc (r=-0.289, p-value < 0.0001) and no significant correlation between C-reactive protein and gender.

Table 3: Correlation coefficient of study parameters

Parameters	CRP		Serum zinc	
	r	p-value	r	p-value
Age	0.462	<0.0001	-0.186	0.022
Gender	-0.033	0.686	0.022	o.787
BMI	0.061	0.461	-0.014	0.866
Spo2	-0.462	<0.0001	0.138	0.091
CRP	1.000	1.000	-0.289	<0.0001
Serum zinc	-0.289	<0.0001	1.000	1.000
% of lung involvement	0.525	<0.0001	-0.204	0.012
Recovery days	0.448	<0.0001	-0.281	<0.0001

Spo2= oxygen saturation, CRP= c-reactive protein, %= percentage

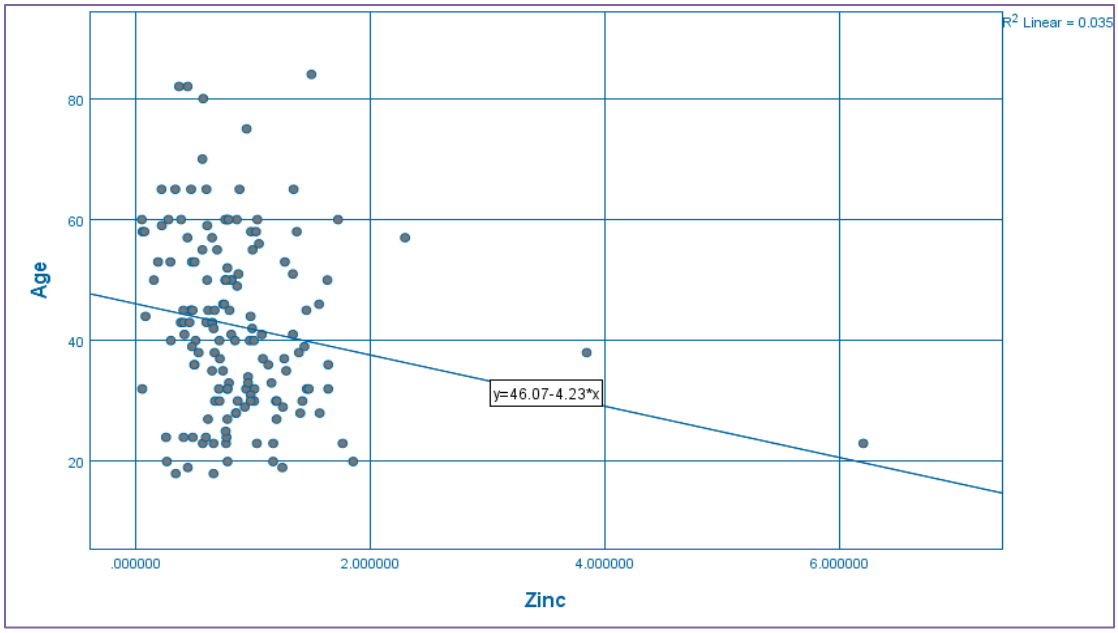

Figure 2: correlation between serum zinc and age.

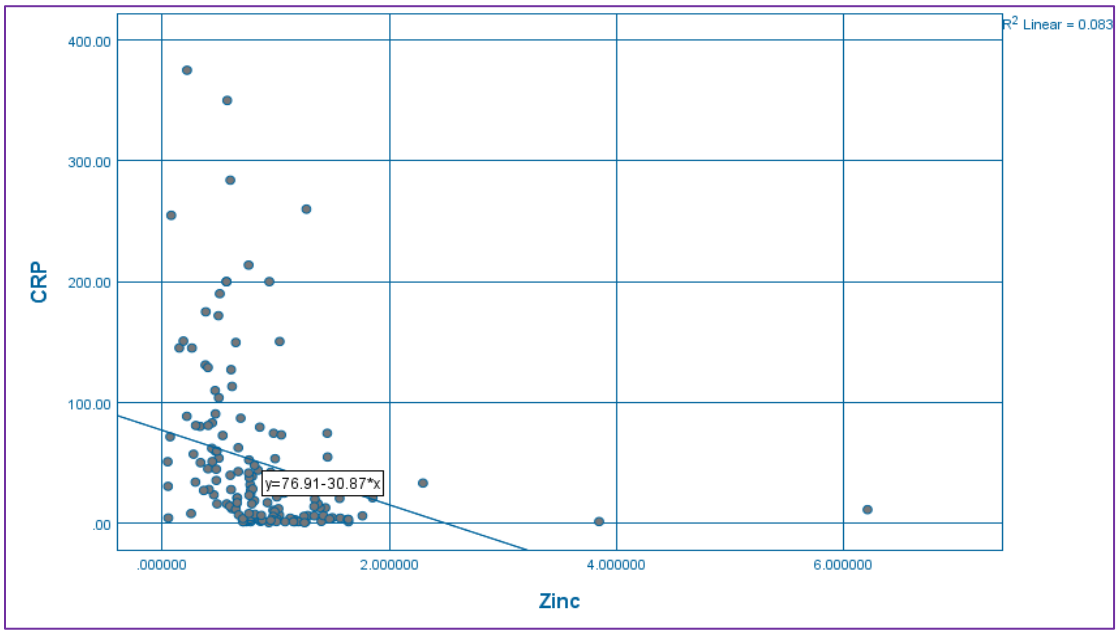

Figure 3: correlation between serum zinc and c-reactive protein.

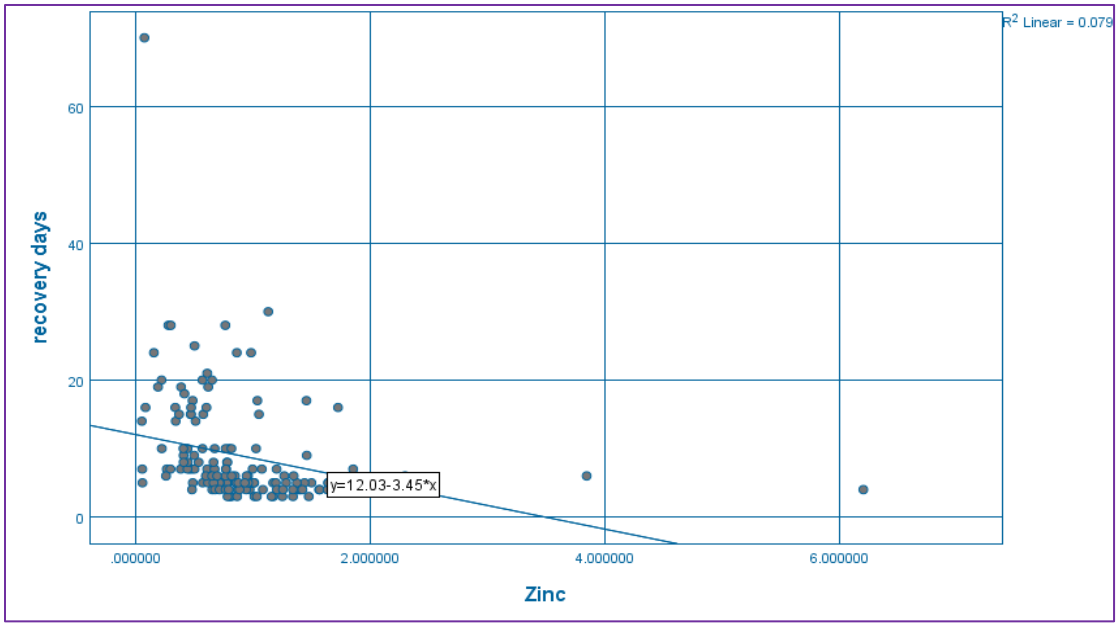

Figure 4: The correlation between serum zinc and recovery days.

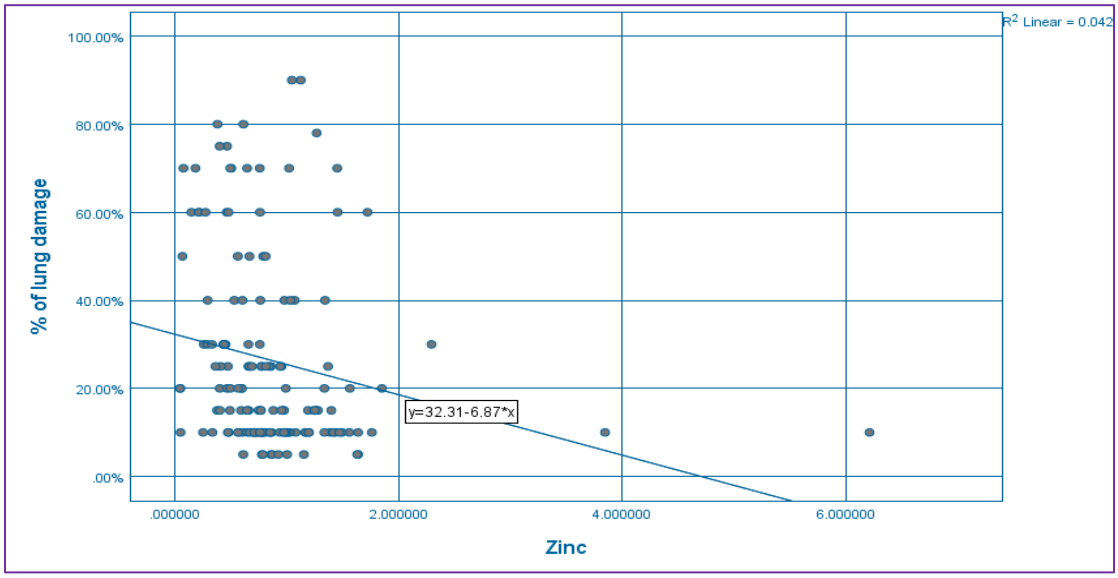

Figure 5: The correlation between serum zinc and percentage of lung damage.

Discussion

This study demonstrated a relation between serum zinc levels and infection and inflammatory status. Zinc has demonstrated antiviral effects via inhibiting RNA synthesis, viral application, DNA polymerase, and reverse transcriptase status[10][15][16]. As mentioned in results that the study found a negative correlation between c-reactive protein and zinc serum level ($r=-0.289$, $p<0.0001$), the zinc is well known for its ability to regulate inflammatory responses via the Nuclear Factor Kappa B (NF-B) signaling pathway to modulate oxidative stress as well as inflammatory cytokines [17]. However, zinc uptake into cells increases and zinc is incorporated into organelles or zincosomes during the acute phase of infection, which may cause serum zinc levels to fall. Additionally, it was

discovered that higher urine zinc excretion during the acute phase response was correlated with elevated CRP [17]. There were studies [14][18][19][20] that found the same negative correlation between c-reactive protein and serum zinc level. The present study showed that there was a significant positive correlation between c-reactive protein and percentage of lung involvement (r=0.448 and p-value<0.0001) and significant negative correlation between serum zinc and percentage of lung involvement(r=-0.204,p<0.012). Lung injury and the chance of developing ARDS(acute respiratory distress syndrome) increase in proportion to early CRP levels. Therefore patients with COVID-19 who have elevated CRP should regulate their lung condition to prevent serious illness as elevated CRP in COVID-19 patients may indicate lung deterioration [21][22]. There was a study that found c-reactive protein levels were positively correlated with lung lesions and severe presentation (P < 0.001)[23]. Because a rise in CRP is associated with pulmonary lesions, it is possible to use alongside radiological data to track progression of the disease, making it an ideal serological test to monitor disease development in an outbreak area with a lot of COVID-19 patients but few medical resources for radiographic testing [24][25]. Because changes in CRP occur before the appearance of respiratory damage, clinical outcomes can often be identified even before the severity of health manifestations [22]. In a recent research of COVID-19 patients, it was discovered that individuals with low zinc levels had greater complication rates (p=0.009), including longer hospital stays (p=0.05), the need for corticosteroid medication (p=0.02), and higher mortality rates (18.5% vs. 0%). The odds ratio of complications linked with low level serum zinc was discovered to be 5.54 [26]. In this current study we observed significant negative correlation between serum zinc level and recovery time. Increased ROS and pro-inflammatory markers have been linked to low serum zinc levels [27]. By increasing the formation of ROS in platelets, zinc deficiency may facilitate thrombocyte aggregation and coagulation [19]. The primary causes of COVID-19 patients death are those diseases that induced coagulopathy, which is brought on by microangiopathic organ failure, venous thromboembolism, and the development of atherosclerosis [28][29].A poor prognosis for COVID-19 has been linked to leukocytosis and neutrophilia. Clinical recovery can be enhanced by lymphopenia recovery [30]. Innate immune cells with lymphopenia may respond favorably to zinc supplementation. Additionally, zinc is a crucial modulator of the signaling pathways generated by TLR-3 and TLR-4. [31].

6-Conclusion

The goal of this study is to bring clinical attention to the relationship between c-reactive protein and serum zinc levels in COVID-19 patients (as a non-specific inflammatory marker). Zinc is a trace element having significant physiological effects. The study's findings revealed a negative link between the serum zinc levels and the levels of c-reactive protein, lung involvement percentage, and recovery days. More research that are slated to be conducted in the future will help to better understand this relationship.

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