

## Serum Iron and Magnesium Levels among Sudanese Patients with Corona Virus Disease 19

MOHAMMED FOUAD MOHAMMED, M.Sc

*Department of Clinical Chemistry, FMLS, University of Al Zaiem Al Azhari*

ABDALLA ELTOUM ALI, PhD

*Department of Clinical Chemistry, FMLS, University of Al Zaiem Al Azhari*

OMAR W. A. MOHAMED, PhD

*Department of Molecular Biology, IEND, U of K*

### Abstract

*COVID-19 was emerged in China in December 2019, on January 2020, World Health Organization (WHO) named it as novel Corona virus, and later it was renamed as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). This study was aimed to determine serum iron and magnesium levels among patients with corona virus disease 19 (Covid-19). This was a descriptive cross-sectional study conducted in Khartoum state during the period from February to July 2021, included 50 patients with Covid-19 and 30 healthy controls. Covid-19 patients were classified into mild, moderate and severe according to disease severity. Iron and magnesium levels were measured by fully automated analyzer. The study showed that there was significant low levels of iron in Covid-19 patients compared to healthy controls ( $42.08 \pm 5.19 \mu\text{g}\backslash\text{dl}$ ) and ( $92.80 \pm 8.60 \mu\text{g}\backslash\text{dl}$ ) respectively and *P*.value (0.0001) , while magnesium levels showed insignificant difference in Covid-19 patients compared to healthy controls ( $2.15 \pm 0.47 \text{mg}\backslash\text{dl}$ ) and ( $2.173 \pm 0.19 \text{mg}\backslash\text{dl}$ ) respectively and *P*. value (0.8000) .In addition, there was significant correlation between iron levels and disease severity ( $R= - 0.337$ ), while no association founded between magnesium levels and disease severity ( $R= - 0.137$ ). Also there was no correlation between iron and magnesium levels with the age ( $R= -0.07$ ) and ( $R= 0.08$ ) respectively. This study concluded that there was significant decrease in level of iron in Covid-19 patients. Also there was significant correlation between the iron levels and disease severity. In addition there was no correlation between iron and magnesium levels with the age among Covid-19 patients.*

**Keywords:** Covid-19, Iron, Magnesium, RT-PCR, Trace element

## **1. INTRODUCTION:**

COVID-19 was emerged in China in December 2019, on January 2020, World Health Organization (WHO) named it as novel Corona virus, and later on February 2020 it was renamed as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2).<sup>(1)</sup> It is caused by a strain of corona virus which is a member of the genus Betacoronavirus and has become a global health problem that affected the lives of billions of people worldwide.<sup>(2)</sup> Scientists have noted that SARS-CoV-2 enters the human body through angiotensin-converting enzyme 2 (ACE2) receptors which found in type II alveolar epithelial cells of the human lungs, and thus the lungs became the main target of SARS-CoV-2 in Covid-19.<sup>(3)</sup> The clinical spectrum of SARS-CoV-2 infection appears to be wide, encompassing asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death, with many patients being hospitalized.<sup>(4)</sup> Because of anti-inflammatory and antioxidant attributes of some nutrients, they may be beneficial for the infected patients with Covid-19; trace elements have important roles in supporting the innate and adaptive immune systems.<sup>(5)</sup> Trace elements are chemical element whose concentration is very low, they serve as catalysts to engage in oxidation and reduction mechanisms.<sup>(6)</sup> Iron is an essential element for all living cells as it is key to establishing many functioning metabolic processes.<sup>(7)</sup> The activity of the enzyme helicase that guide DNA replication, in both SARS-CoV and human, needs iron for ATP synthesis providing its role in both the pathogenicity of the virus and the immunity of the host.<sup>(8)</sup> It has been reported that iron leakage is a risk factor for the development of Covid-19 disease.<sup>(9)</sup> Magnesium is one of the important ion which is required as a cofactor for ATP enzyme that is involved in many essential enzymatic reactions.<sup>(10)</sup> A recent study has shown that serum magnesium level might have a protective effect against lung function loss in chronic obstructive pulmonary disease, which is an important result to understand the potential relationship between magnesium and pulmonary outcomes of Covid-19 disease.<sup>(11)</sup>

## **2. MATERIALS AND METHODS:**

### **2.1 Study design:**

It is a descriptive cross-sectional study.

### **2.2 Study area:**

This study was conducted in Khartoum state, Sudan.

### **2.3 Study population:**

Patients who diagnosed with Covid-19 during the study period were enrolled to participate in this study. The confirmation of Covid-19 will be based on CT scan and/or RT-PCR. Apparently healthy individuals were enrolled as controls.

### **2.4 Sample size:**

Fifty patients with Covid-19 and 30 apparently healthy subjects were included in this study.

### **2.5 Study duration:**

Approximately 6 months, from February to July 2021.

### **2.6 Ethical considerations:**

The study was revised and ethically approved by the ethical and scientific committee of the Medical laboratory sciences colleague, University of Alzaiem Alazhari. Samples were taken with verbal consent from patients or their relatives.

### **2.7 Data collection:**

A coded enrollment number was given for each enrolled patient. The data were collected by using a direct interviewing questionnaire. Medical information's was collected from the patient file with help of the treating physician.

### **2.8 Collection of specimens:**

From all selected subjects under aseptic condition 3 ml of venous blood was collected using sterile disposable syringes and poured into heparin anti-coagulated container. The plasma was separated by centrifuged the whole blood at 3000 rpm for 5 minutes. The sample was analyzed immediately after centrifugation.

### **2.9 Investigations Applied:**

Serum iron and magnesium levels were measured by Cobas 6000 fully automated analyzer (Roche -Germany).

### **2.10 Data analysis:**

The statistical analysis of the results was performed by using the Statistical Package for Social Sciences (SPSS) version 15.0 for windows version 10 using T-test for testing difference significance and Pearson correlation test ( r value as the coefficient ) . A P value < 0.05 was considered statistically significant.

The results were formulated into figures using the Microsoft Excel computer program.

### 3. RESULTS:

This study consisted of 80 subjects. The case group was consisted of 50 subjects (26 males (52%) and 24 femals (48%) ), while the control group was included 30 subjects (17 males (56%) and 13 femals (44%) ). Fig 3.1, Fig 3.2

The mean values of age of case group was (50.7 ± 15.6 years) while the control group was (54.0 ± 15.6 years) . Fig 3.3

The case group is classified into mild (n=18), moderate (n=9) and severe (n=23) according to disease severity. Fig 3.4

The mean values of plasma Fe among case group was lower than in the control group, (42.08 ± 5.19 µg\dl) and (92.80 ± 8.60 µg/dl) repectively, this diffrence was statistically significant , *P*. value (0.0001). Fig 3.5

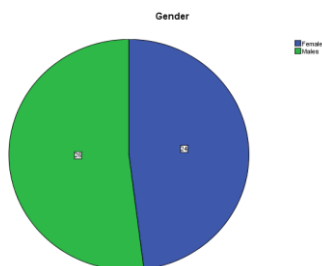
The mean values of plasma Mg in case group was (2.15 ± 0.47 mg\dl) while in the control group was (2.173 ± 0.19 mg/dl), this diffrence was staistically insgnificant, *P*. value (0.8000). Fig 3.6

Pearson correlation founded that plasma levels of Fe were negatively correlated with the disease severity, this was statically significant (R= - 0.337, *P*.value = 0.0170). Fig 3.7

Pearson correlation founded that there is no significant correlation between plasma levels of Mg and the disease severity, (R= - 0.137, *P*.value = 0.3440). Fig 3.8

Although older individuals tend to have lower levels of serum Fe, Pearson correlation showed that the corelation between serum Fe and the age were statstically insignificant, (R= -0.07, *P*. value = 0.6000). Fig 3.9

Although the plasma levels of Mg tend to be directly correlated with age, however Pearson correlation demonsatrated that assoication was statistically insignificant, (R= 0.08, *P*. value = 0.5000). Fig 3.9



**Fig 3.1: The frequency distribution of gender among case group**

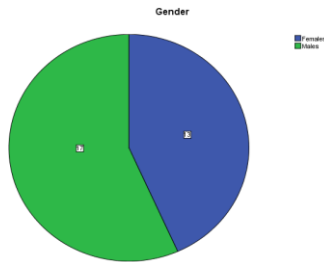


Fig 3.2 the frequency distribution of gender among control group

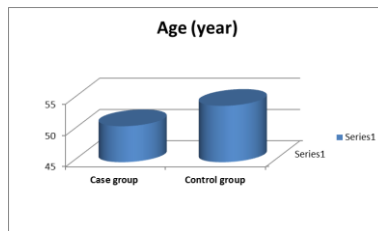


Fig 3.3 the frequency distribution of age among study groups

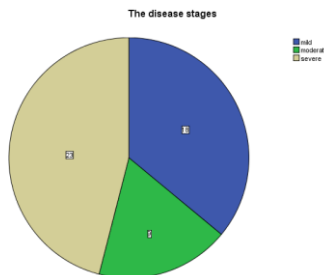


Fig 3.4: The frequency distribution of case group according to disease severity

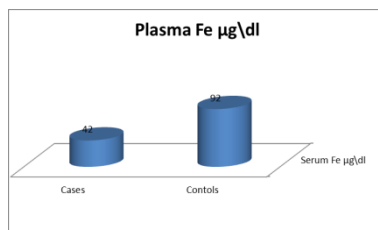


Fig 3.5 plasma Fe levels in case versus control groups

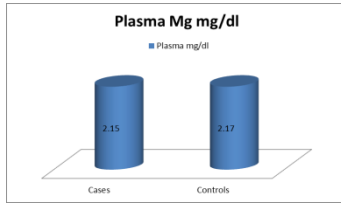


Fig 3.6 plasma Mg levels in case versus control groups

On x axis , 1 ≡ mild , 2≡ moderate and 3 ≡ severe

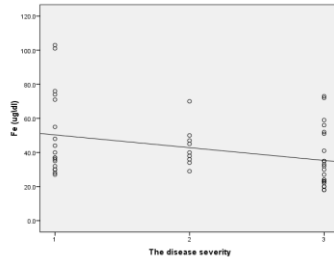


Fig 3.7 Correlation of plasma Fe levels to the disease severity ( R = - 0.337, P.value = 0.0170 )

On x axis , 1 ≡ mild , 2≡ moderate and 3 ≡ severe

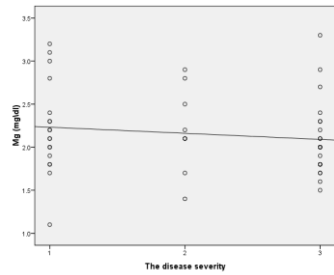


Fig 3.8 Correlation of plasma Mg levels to the disease severity (R = - 0.137, P.value = 0.3440)

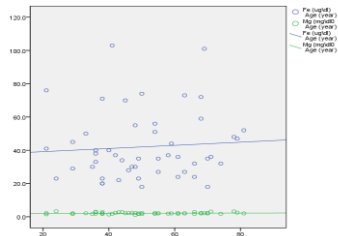


Fig 3.9 Correlation of plasma Fe and Mg levels to the age in case group (R= -0.07, P.value = 0.6 for Fe) , ( R=0.08 ,P.value = 0.5 for Mg )

#### 4. DISCUSSION:

COVID-19 caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV2), and has become a global health problem that affected the lives of billions of people worldwide. <sup>(12)</sup> Since its appearance and till now, it changes the entire world tract, not only on the health domain, but the entire disciplines.

On a very short time relatively, there is no previous health problem occupied the all research like Covid-19. No universal treatment protocol described for the management of Covid-19 yet and thus the most health advice address the prevention by several measures like social distance, health hygiene and others.

Trace elements tend to play an important role in immunity as constituent or as cofactors for reaction. Several previous studies tried to found the role of trace elements in Covid-19 infection and/or its disease course.

This cross-sectional study was conducted on the period from February to July 2021 in Khartoum, with study population of 50 patients with Covid-19 and 30 healthy controls. The study aimed to compare serum levels of iron and magnesium between Covid-19 patients and control group, as well as to correlate their levels with the severity of the disease that is classified into mild, moderate and severe according WHO guidelines. Furthermore, to evaluate the association of serum Fe and Mg levels with the age. This study showed that there was significant decrease in the mean levels of iron in Covid-19 patients compared to healthy controls ( $P$ . value =  $0.0001$ ). This in agreement with previous finding of Sema Yağcı et al <sup>(13)</sup>.

This can be attributed to tissue damage, impaired host-immune function and/or cytokine storms. Also the study showed that there was no significant difference in the mean levels of magnesium in Covid-19 patients compared with healthy controls ( $P$ . value =  $0.8000$ ). No previous publications address the association of Mg with covid-19 comparing to control group. This study showed a significant negative correlation between serum iron levels and disease severity ( $R= - 0.337$ ).

This in agree with study of Kang Zhaon et al <sup>(14)</sup> and Sema Yağcı et al <sup>(13)</sup> who founded relationship between decreased iron levels and disease severity. Although serum levels of Mg tend to be lower in those with advanced disease, this study showed an insignificant correlation between serum magnesium levels and disease severity ( $R= - 0.137$ ). The correlation analysis showed insignificant correlation of iron and magnesium levels to the age among case group ( $R= - 0.07$  for Fe, and  $R= 0.08$  for Mg).

## **5. CONCLUSION:**

This study concluded that there was significant decrease in levels of iron in Covid-19 patients. Also there was significant correlation between the iron levels and disease severity. In addition there was no correlation between iron and magnesium levels with the age among covid-19 patients.

## **REFERENCES:**

1. Moynihan AB, Van Tilburg WA, et al .Eaten up by boredom: consuming food to escape awareness of the bored self. *Front Psychol.* 2015;6:369.
2. Nishiga M,WangDW, HanY,Lewis DB,Wu JC.COVID19 and cardiovascular disease: from basic mechanisms to clinical perspectives. *Nat Rev Cardiol* 2020:116
3. Reyfman PA, Walter JM, Joshi N, et al. Single-cell transcriptomic analysis of human lung provides insights into the pathobiology of pulmonary fibrosis. *Am J Respir Crit Care Med* 2019; 199:1517–36.
4. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395: 497–506.
5. Chandra RK. Nutrition and the immune system: an introduction. *Am J Clin Nutr.* 1997;66(2):460s–463s.
6. Cernari, X., Qiu, L., et al . Sensitive and Specific Monoclonal Antibody-Based Capture Enzyme Immunoassay for Detection of Nucleocapsid Antigen in Sera from Patients with Severe Acute Respiratory Syndrome. *Journal of Clinical Microbiology*, 2004; 42(6), pp.2629-2635.
7. Belouzard S, Millet JK, Licitra BN, Whittaker GR. Mechanisms of coronavirus cell entry mediated by the viral spike protein. *Viruses.* 2012;4(6):1011–33.
8. Wessling-Resnick M .Crossing the Iron gate: why and how transferrin receptors mediate viral entry. *Annu Rev Nutr* 2018 ;38:431– 458
9. Jayaweera J, Reyes M,Joseph A .Childhood iron deficiency anemia leads to recurrent respiratory tract infections and gastroenteritis. *Sci Rep* 2019; 9(1):12637.
10. Kanellopoulou C, George AB, et al. Mg<sup>2+</sup> regulation of kinase signaling and immune function. *J Exp Med* 2019;216(8):1828–1842.
11. Ye M, Li Q, Xiao L, Zheng Z . Serum magnesium and fractional exhaled nitric oxide in relation to the severity in asthma-chronic obstructive pulmonary disease overlap. *Biol Trace Elem Res* ,2020.
12. Nishiga M,WangDW, HanY,Lewis DB,Wu JC(2020) COVID19 and cardiovascular disease: from basic mechanisms to clinical perspectives. *Nat Rev Cardiol*:1–16.
13. Yağcı S, Serin E, Acicbe Ö, Zeren Mİ, Odabaşı MS. The relationship between serum erythropoietin, hepcidin, and haptoglobin levels with disease severity and other biochemical values in patients with COVID-19. *Int J Lab Hematol.* 2021 Jul;43 Suppl 1:142-151.
14. Kang Zhao,1 Jucun Huang et al . Serum Iron Level as a Potential Predictor of Coronavirus Disease 2019 Severity and Mortality: A Retrospective Study , *Infectious Diseases society of America* (2020).