

Case Report

Serum iron level in patients with COVID-19: a case report study

Rasoul Alipour^{1*}, Seyed Hasan Hashemi², Fariba Mikaeili³

¹Department of Emergency Medicine, Emergency Unit of Alinasab Hospital, Social Security Organisation, Treatment Management of East Azerbaijan, Tabriz, Iran

²Department of Gastroenterology, Gastroenterology unit of Alinasab Hospital, Social Security Organisation, Treatment Management of East Azerbaijan, Tabriz, Iran

³Department of Midwifery, Islamic Azad University, Tabriz, Iran

Received: 15 May 2020

Accepted: 08 June 2020

*Correspondence:

Dr. Rasoul Alipour,

E-mail: Dr.Rasoul.Alipour@gmail.com

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ABSTRACT

Coronavirus disease emerged in Wuhan, China in December 2019 and led to worldwide pandemic in March 2020. Due to early diagnose, treatment and prevent transmission of COVID-19 disease, we need rapid laboratory tests and develop them. This paper focuses on serum Iron level in patients with COVID-19. We assess the serum Iron level due to the following reasons: I. Iron is a key part of hemoglobin structure in which is essential for providing Oxygen to the body organs, particularly for the patients with pulmonary involvement such as COVID-19. II. Iron deficiency can contribute to muscle weakness and reduction of respiratory capacity, at which increases the risk of deterioration of COVID-19 patients. III. Elevation in Hcpidin level (due to the increase in IL-6 level) in COVID-19 patients inhibits Iron absorption from intestinal lumen and blocks the Iron release from macrophages. IV. Iron is an essential element in infectious suppress and inflammatory process. We noticed that most of the patients, especially admitted to hospital due to the respiratory symptoms, have lower serum Iron level.

Keywords: Coronavirus, COVID-19, Ferritin, Hcpidin, Serum iron level

INTRODUCTION

Coronavirus and COVID-19

The Coronavirus disease, also known as COVID-19, first emerged in Wuhan, China in December 2019.¹ with severe lung diseases and the corresponding virus was named as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in January 2020.² The primary source of COVID-19 is reported to be Rhinolophus bats while the intermediate source is not known.^{3,4} However, the human to human transmission is very fast, which led to worldwide pandemic announcement by WHO in March 2020.⁵ COVID-19 is mostly similar to SARS and MERS, but with more

spreading capabilities and severe/deadly forms that exhibits lung injuries in varying stages, such as acute fibrinous, diffuse alveolar damage and pneumonia.^{4,6,7} It has many symptoms including sore throat, nasal congestion, rhinorrhea, fever, cough, fatigue, pneumonia, shortness of breath, myalgia, anorexia, headache, diarrhea, hemoptysis and dyspnea.^{1,8,9}

However, patients with COVID-19 are generally asymptomatic and usually have mild disease but it may progress to multi organ dysfunction, particularly in elder patients and those with comorbidities such as Diabetes, Hepatitis, Hypertension, Ischemic Heart Disease and Chronic Renal Disease.^{3,5,9,10} Children appear to have less severe disease in comparison to adults and almost 90% of

pediatric patients are recognized asymptomatic or with a mild to moderate disease.^{5,11,12}

SARS-CoV-2 remains viable for hours in aerosols and days on many surfaces.¹³ The SARS-CoV-2 transmission is done by contacting or inhaling infected droplets and the human to human transmit may happen throughout the first few days after the onset of symptoms in symptomatic patients and within initial days of disease in asymptomatic patients.^{4,9,13} The incubation period of COVID-19 is 5.1 days ranging from 2 to 14 days.^{4,9} The approval process for vaccine production through various methods is being reviewed and under Confirmation.¹⁴ The SARS-CoV-2 must bind with ACE2 receptor to be able to enter the host cells in human body, particularly in alveolar epithelial cells.^{7,15} Hence, it is necessary to release and express ACE2 to have target organs be infected by SARS-CoV-2 infection.^{7,15} At the time of this study about 3,181,642 patients and approximately 224,301 deaths were reported for this disease.¹⁶ Rapid laboratory testing of SARS-CoV-2 is essential to achieve early diagnose, reporting, quarantine and treatment of patients in which will lead to prevent disease transmission.¹⁷ Laboratory findings such as lymphocyte count and inflammatory indices including LDH, CRP and IL-6 may help to diagnose the patients.¹⁸ Studies demonstrates that Computed Tomography has a high sensitivity and specificity in the diagnosis of COVID-19 and shows multiple patchy areas of ground glass opacity, consolidation predominately in the periphery of the lungs, adjacent pleura thickening, interlobular septal thickening and air bronchograms.¹⁹⁻²¹

Anemia and iron deficiency

Anemia is diagnosed by a reduction in hemoglobin absolute value or red blood cells count.²² Anemia is identified by Hb level below 13.0 g/dl, 12.0 g/dL and 11.0 g/dL in male adults, female adults and pregnant women, respectively.²³ However, its level may vary based on age and race criteria.²⁴ It shows to be high levels of Hb in smokers and resident of higher altitudes.²⁵ Anemia can occur at all stages of life cycle, but exhibits more outbreaks in elders, pregnant women and young children.^{26,27} Anemia has many causes but the most important reason is iron deficiency.²⁶

Iron is an essential element required for many metabolic functions.²² Iron deficiency is the most common reason of anemia and may occur as a result of low iron intake and absorption or increased iron demand or loss.^{26,28} Iron deficiency can increase the risk of mortality in some diseases such as Chronic Heart failure due to the reduces in Hb status.²⁹

CASE REPORT

According to the following 4 reasons, we mentioned that, it is strongly suggested to investigate the serum iron level in patients with COVID-19:

- Patients with COVID-19 may present with respiratory dysfunctions including pneumonia, dyspnea, respiratory distress and acute respiratory distress syndrome (ARDS). These complications reduce blood O₂ saturation, and may damage vital organs due to hypoxemia.^{3-5,9,10} Therefore, RBCs and Hb, play an important role in determining the prognosis of these patients. In other words, any defects, dysfunction and decrease in performance (operation) and levels of RBCs and Hb, such as anemia and Iron deficiency, may increase the mortality and organ failure.^{29,30}
- Previous retrospective studies indicated that Inflammatory cytokines, including interleukin-6, interleukin-10 and interleukin-1 β were significantly elevated in COVID-19 patients and completely related to severity and fatality of COVID-19.³¹⁻³⁶ Furthermore, based on other studies, IL-6 directly regulates hepcidin and increases hepcidin's level in both acute and chronic inflammation.³⁷⁻⁴⁰ Hepcidin is an antimicrobial peptide hormone, secreted by hepatocytes that blocks the iron releasing from macrophages and inhibit absorption of iron from intestinal lumen.^{37-39,41} So, as a result of hepcidin elevation due to IL-6 elevation in covid-19 patients, serum Iron level may decrease significantly.
- Iron deficiency is related with weakness of skeletal muscles and may decrease respiratory capacity. As a result of respiratory capacity reduction, may induce the deterioration and mortality of patients with COVID-19.⁴²⁻⁴⁴
- Various studies show that, Iron has an essential role in suppression of infectious and inflammatory response and may reduce in febrile and autoimmune disease.⁴⁵⁻⁵¹ However, it is reported to be deposited in some viral and inflammatory diseases.^{52,53}

METHODS

In this study, we have selected patients without underlying hematologic disorders who were referred to Alinasab Hospital and diagnosed with COVID-19. Our diagnosis is performed according to the laboratory and radiological criteria including absolute lymphopenia and involved Chest computed tomography. The patients are divided into 3 main categories based on the severity of their respiratory symptoms and need for respiratory support.

- Patients with COVID-19 who have severe respiratory symptoms and are admitted to the ICU due to the need for respiratory support.
- Patients with COVID-19 who have mild respiratory symptoms and are admitted to the Department of Infectious Diseases without the need for respiratory support.
- Patients with COVID-19 without significant respiratory symptoms that are treated on an outpatient basis and sent to quarantine with no need for hospitalization.

Due to our study's purpose, we proceeded to check serum Iron level randomly for 6 patients selected from each group (in total 18 patients) with different sexes and ages who were referred to Alinasab Hospital at a time point. The data were collected in April 2020. About of 3 ml of the venous blood was extracted from the all samples. After the centrifuging, the separated serum was placed in Mindray BS 800 chemistry analyzer in Alinasab hospital's laboratory. According to our laboratory reference, the normal conventional range for serum iron level is 65-175 mcg/dL for males and 50-170 mcg/dL for females.⁵⁴

DISCUSSION

Authors found that serum iron levels were lower than normal range in admitted patients and in the patients without apparent respiratory symptoms who referred to quarantine, the serum Iron levels were in the lower limit of normal range (Table 1). Moreover, serum Iron levels in ICU admitted patients were significantly lower than the others.

Table 1: Table of patients divided by sex, age, place of treatment and serum iron level.

Patient no.	Subgroup	Sex	Age	Serum iron
1	ICU admitted	F	76	27
2	ICU admitted	M	63	18
3	ICU admitted	M	80	38
4	ICU admitted	F	85	20
5	ICU admitted	F	71	22
6	ICU admitted	M	68	26
7	Infectious diseases department	F	59	30
8	Infectious diseases department	M	62	47
9	Infectious diseases department	F	67	33
10	Infectious diseases department	F	79	32
11	Infectious diseases department t	M	82	42
12	Infectious diseases department	M	54	49
13	Outpatient clinic	F	76	45
14	Outpatient clinic	M	59	60
15	Outpatient clinic	M	54	66
16	Outpatient clinic	F	78	47
17	Outpatient clinic	F	57	50
18	Outpatient clinic	M	81	69

Suggestions

- Due to the laboratory results, measuring serum Iron levels may be helpful in Therapeutic and diagnostic process of COVID-19 disease.

- Based on the results obtained, it can be an inverse communication between serum Iron and the severity of respiratory symptoms (Table 1).
- Due to the high prevalence of iron deficiency in different societies, control and treat of Iron deficiency can be an important factor in preventing the exacerbation of respiratory symptoms in COVID-19 disease.
- Prescribing iron in the acute phase of the disease can be helpful and needs more investigation.
- Iron deficiency in these patients can indicate Iron deposition in various organs that requires further investigation.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Alipour R, Hashemi SH, Mikaeili F. Serum iron level in patients with COVID-19: a case report study. *Int J Res Med Sci* 2020;8:2658-62.