

## Increase in levels of Serum Ferritin in COVID 19.

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### Abstract

Corona virus is a type of virus that commonly cause infection to your upper respiratory tract (sinuses, nose, and throat) and also radiates to lower respiratory tract and infects it. Most of these viruses are not life threatening. Recently in the past year, 2020 there was an outbreak initiated in December 2019 in China after which the WHO (World Health Organization) identified SARS-CoV-2 as a variant of new Corona virus. This outbreak soon spread all around the globe affecting many people. The disease caused by the virus SARS-CoV-2 is Covid-19 that cause infection in the respiratory tract hence you can call the infection as respiratory tract infection. It affects both the upper and lower respiratory tract which includes sinuses, nose, throat, lungs and windpipe. The epidemiology of this virus type is same as the other variants of corona viruses. They are communicable in nature. They spread more commonly through person to person by aerosols. The damage caused to the person ranges from mild to severe even life threatening (deadly). Ferritin is known as intracellular iron storage. Elevated forms of this iron storage indicate the presence of any type of virus or bacteria in the human body. Thus, the temporary presence of COVID-19 can also be detected by measuring the level of ferritin. It has been observed in research that high ferritin levels in serum indicate the severity of COVID-19 as 50 percent of cases of patients with COVID-19 having extremely high ferritin levels have died. Research on ferritin is ongoing. Recent studies have also proved that it can also activate the body's macrophages which are like the white blood cells of the immune system, in addition to indicating acuteness of illness.

**Keywords:** Ferritin, COVID-19, Immune system, Cytokines, Interleukin-6, Pro-inflammatory, Immunosuppressive, SARS, MERS, Lung parenchyma.

### Introduction

#### *Serum ferritin*

Ferritin is a protein present in the blood which contains iron. The test for ferritin helps to understand the proportion of iron stored in your body. If the ferritin level in your blood is lower than the normal value, it shows that the iron stores in your body are depleted and you may be diagnosed with iron deficiency. Thereafter, you can become anemic [1].

Ferritin is known as intracellular iron storage. Elevated forms of this iron storage indicate the presence of any type of virus or bacteria in the human body. Thus, the temporary presence of COVID-19 can also be detected by measuring the level of ferritin. It has been observed in research that high ferritin levels in serum indicate the severity of COVID-19 as 50 percent of cases of patients with COVID-19 having extremely high ferritin levels have died. Research on ferritin is ongoing. Recent studies have also proved that it can also activate the body's macrophages which are like the white blood cells of the immune system, in addition to indicating acuteness of illness.

If the ferritin level in your blood is higher than normal, it shows that you may have some other conditions which allow you to store more amount of iron in your body. This may be due to RA (Rheumatoid arthritis) or any other diseases of the liver, some inflammatory conditions or increase in the level of thyroid hormone (hyperthyroidism). Certain types of neoplasms can also elevate the level of ferritin in your blood [2].

### COVID-19

Corona virus is a type of virus that commonly cause ailments to your upper respiratory tract (sinuses, nose, and throat) and also radiates to lower respiratory tract and infects it. Most of these viruses are not life threatening. Recently in the past year, 2020 there was an outbreak initiated in December 2019 in China after which the WHO (World Health Organization) identified SARS-CoV-2 as a variant of new Corona virus. This outbreak soon spread all around the globe affecting many people [3]. The disease caused by the virus SARS-CoV-2 is Covid-19 that cause infection in the respiratory tract hence you

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Received: 27-June-2022, Manuscript No. AABPS-22-67779; Editor assigned: 29-June-2022, PreQC No. AABPS-22-67779(PQ); Reviewed: 14-July-2022, QC No. AABPS-22-67779; Revised: 18-July-2022, Manuscript No. AABPS-22-67779(R); Published: 25-July-2022, DOI:10.35841/2249-622X.91.134

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**Citation:** Kane S. Increase in levels of Serum Ferritin in COVID 19. *Asian J Biomed Pharmaceut Sci.* 2022;12(91):134

can call the infection as respiratory tract infection. It affects both the upper and lower respiratory tract which includes sinuses, nose, throat, lungs and windpipe.

This has come out to be a very dangerous disease. It is affecting human of all the age groups irrespective of gender. It is mainly transmitted through aerosol. Any contact with the patients suffering from COVID-19 can infect healthy individuals mostly if he/she is immuno compromised. The damage caused to the infected individual may be mild to critical depending on its severity. The epidemiology of this virus type is same as the other variants of corona viruses. They are communicable in nature. They spread more commonly through person to person by aerosols. The damage caused to the person ranges from mild to severe even life threatening (deadly).

There are a total of 7 categories of corona virus around globe, among which SARS-CoV-2 is one of the type. The Camel flu or MERS and the Severe Acute Respiratory Syndrome (SARS) can cause severe illness which may be fatal. The other types are not much serious in person with good immunity; they cause normal cold to us during various seasons of the year [4].

Ferritin is known as intracellular iron storage. Elevated forms of this iron storage indicate the presence of any type of virus or bacteria in the human body. Thus, the temporary presence of COVID-19 can also be detected by measuring the level of ferritin. It has been observed in research that high ferritin levels in serum indicate the severity of COVID-19 as 50 percent of cases of patients with COVID-19 having extremely high ferritin levels have died. Research on ferritin is ongoing. Recent studies have also proved that it can also activate the body's macrophages which are like the white blood cells of the immune system, in addition to indicating acuteness of illness.

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### **Normal ranges**

Normal Ferritin levels in blood ranges from:

Males: 24-336 mg/L

Females: 11-307 mg/L [5].

If the ferritin level in your blood is lower than the normal value, it shows that the iron stores in your body are depleted and you may be diagnosed with iron deficiency. Thereafter, you can become anemic. If the ferritin level in your blood is higher than normal, it shows that you may have some other conditions which allow you to store more amount of iron in your body. This may be due to RA (Rheumatoid arthritis) or any other diseases of the liver, some inflammatory conditions

or increase in the level of thyroid hormone (hyperthyroidism). Certain types of neoplasms can also elevate the level of ferritin in your blood.

### **How can the level of ferritin in serum indicate severity of COVID infection?**

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If the ferritin level in your blood is higher than normal, it shows that you may have some other conditions which allow you to store more amount of iron in your body. This may be due to RA (Rheumatoid arthritis) or any other diseases of the liver, some inflammatory conditions or increase in the level of thyroid hormone (hyperthyroidism). Certain types of neoplasms can also elevate the level of ferritin in your blood. Ferritin and IL-6 concentrations reduced as patients recovered, according to Liu et al. This could imply that increase in the concentration of ferritin in the blood is linked to COVID-19 [6].

### **Why is the level of ferritin in serum high in COVID-19?**

COVID-19 disease develops in patients infected with the new coronavirus known as SARS-CoV-2. This new corona virus causes pneumonia in a severe stage and also damages other organs like kidneys, heart and liver. Similar to other infections acquired by pathogenic coronaviruses, an inflammatory cytokine storm has been identified as the underlying cause of death, due to the excessive and uncontrolled release of pro-inflammatory cytokines. In individuals with severe COVID-19 disease, for example, inflammatory cytokines generated by macrophages (IL-6, IL-10, and TNF-) rise, causing lung and other organ damage. As a result, measuring plasma inflammatory markers could be beneficial in predicting disease development.

SARS CoV-2 may have mutated into the virus itself during human-to-human transmission, as these individuals were at the epicenter of the outbreak. As a result, multicenter studies with bigger sample sizes and conducted in different countries should be conducted to confirm hyperferritinemia in affected patients. Nonetheless, it is established that longitudinal ferritin monitoring during hospitalization may aid in the identification of critical patients

### **Based on previous studies**

In research on patients of COVID-19, the concentration of certain inflammatory markers such as C-reactive protein, ESR, procalcitonin and serum amyloid A in the serum have been recorded. Nevertheless, despite the fact that hyperferritinemia

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has been linked to problems in other viral infections including dengue fever, ferritin has received little attention.

Ferritin levels in patients with non-critical and critical COVID-19 infection during hospitalization (and patients who have survived and failed to survive). Only the concentration of ferritin in the patients of COVID-19 infection at the time of admission in the hospital is reported in these investigations. The concentration of ferritin in patients with non-severe illness is within the normal range (30–400 g/L), as may be seen (according to the National Health Commission guidelines of China for COVID-19 severity classification). On admission, still the patients with severe illness had hyper ferritinemia (ferritin level more than 400 g/L) [7].

In fact, patients with severe illness had a mean ferritin content of >800 g/L. Furthermore, ferritin levels were 1.5 and 5.3 times more in patients with critical COVID-19 infection than in patients with less critical COVID-19 infection at the time of admission. There have also been researches comparing ferritin levels at admission between COVID-19 patients who died in hospital and patients who were successfully discharged after therapy. Non-survivors had ferritin levels of roughly 1400 g/L upon admission, which were 3 to 4 times greater than those of survivors, according to these investigations.

In these investigations, blood cytokines like IL-6 were shown to be particularly high upon admission in individuals who acquired severe illness. According to one study, non-survivors had higher ferritin and IL-6 concentrations throughout the clinical course than discharged patients, and the difference grew as the patient's condition worsened. Ferritin and IL-6 concentrations reduced as patients recovered, according to Liu et al. This could imply that increase in the concentration of ferritin in the blood is linked to COVID-19 infection and its inflammation, and that ferritin could be a helpful indicator for estimating illness severity and cytokine storm size.

However, we must consider the origin of the elevated concentration of ferritin in the plasma as well as the protein's probable role in the inflammation following the onset of COVID-19 disease. Inflammatory disorders can result in active ferritin production. The release of serum ferritin may be mediated by macrophages, which produce cytokines and are responsible for the major amount of immune cells in the lung parenchyma. Ferritin production can also be triggered by inflammatory stimuli such as cytokines like IL-6. High concentrations of the interleukin-6 in patients of COVID-19 have been connected to disease chronicity, which is interesting. The epidemiology of this virus type is same as the other variants of corona viruses. They are communicable in nature. They spread more commonly through person to person by aerosols. The damage caused to the person ranges from mild to severe even life threatening (deadly).

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Research on ferritin is ongoing. Recent studies have also proved that it can also activate the body's macrophages which are like the white blood cells of the immune system, in addition to indicating acuteness of illness [8].

Because ferritin is secreted actively near the site of infection, it's probable that ferritin serves a purpose other than iron storage. Ferritin appears to be a signaling molecule and a direct immune system modulator, according to growing evidence. Since cytokines can drive the development of pro- and anti-inflammatory cytokines, complicated feedback mechanisms between ferritin and cytokines under the control of pro-inflammatory and anti-inflammatory mediators may exist. The harmful significance of ferritin during inflammation is a subject of discussion amongst different schools of thinking.

The composition of ferritin in the plasma of patients suffering from COVID-19 might be an intriguing field for further research. H and L are the two subunits that make up ferritin. Several studies have demonstrated that inflammatory stimuli stimulate H subunit production, and that H-ferritin is a pro-inflammatory and immunosuppressive immunomodulatory molecule [9].

### ***Significance of ferritin in COVID-19***

If ferritin is a pathogenic mediator in COVID-19, then therapeutic plasma exchange, which lowers ferritin and cytokines, could be advantageous for SARS-CoV-2 infected individuals. Plasma exchange is an automated procedure in which the patient's plasma is removed and replaced with donor plasma from a blood bank. It has been shown to be extremely beneficial in the treatment of certain diseases. Finally, during the early embarkation of the pandemic, some research were undertaken in Wuhan, where hospitals with inadequate medical facilities and staff were packed with patients. SARS-CoV-2 may have mutated into the virus itself during human-to-human transmission, as these individuals were at the epicenter of the outbreak. As a result, multicenter studies with bigger sample sizes and conducted in different countries should be conducted to confirm hyperferritinemia in affected patients. Nonetheless, it is established that longitudinal ferritin monitoring during hospitalization may aid in the identification of critical patients and prediction of the progression of the disease (COVID-19) to a poorer clinical outcome. SARS CoV-2 may have mutated into the virus itself during human-to-human transmission, as these individuals were at the epicenter of the outbreak. As a result, multicenter studies with bigger sample sizes and conducted in different countries should be conducted to confirm hyperferritinemia in affected patients. Nonetheless, it is established that longitudinal ferritin monitoring during hospitalization may aid in the identification of critical patients [10-15].

## Conclusion

In these investigations, blood cytokines like IL-6 were shown to be particularly high upon admission in individuals who acquired severe illness. According to one study, non-survivors had higher ferritin and IL-6 concentrations throughout the clinical course than discharged patients, and the difference grew as the patient's condition worsened. Ferritin and IL-6 concentrations reduced as patients recovered, according to Liu et al. This could imply that increase in the concentration of ferritin in the blood is linked to COVID-19.

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