Original Article

Study of Magnesium, Potassium and Ferritin Levels in the Blood Serum of People Infected with COVID-19

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Abstract

Background: The WHO has declared Coronavirus disease COVID-19 as a worldwide pandemic for the first few months of 2020. Inadequate immunity may result from the immune system's ability to function poorly due to a lack of vitamins and minerals in plasma. **Objective:** This research aimed to evaluate the circulating potassium, magnesium, and ferritin concentrations and their potential to use as a marker in COVID-19 infection. **Materials and Methods:** The study's subjects were split into five age groups based on their respective levels of infection with the coronavirus ($P \sim 0.05$), circulating potassium, magnesium, and ferritin concentrations were measured in the blood serum via the Bioassay Technology laboratory techniques. **Results:** Significant ($P < 0.05$) variations were identified in the previous circulating elements: 25% of patients have low potassium, equally distributed among boys and females. 19% of patients have high potassium levels, particularly in males; In terms of magnesium, the proportion of patients with a high concentration was 58% (males had a greater percentage than females), whereas the reduction was only in 3%; Ferritin was below normal are found in just 3% of patients, and there has been no discernible increase in ferritin levels. **Conclusions:** Due to the nature of everyday jobs, the young and middle-aged populations are the most susceptible to contracting the coronavirus. Hypermagnesemia is a significant indicator of the severity of a viral infection. While COVID-19 patients frequently have hypokalemia as an electrolyte imbalance. It is possible to depend on the ferritin level as a gauge of the infection's severity.

Keywords: corona, COVID-19, ferritin, hypermagnesemia, hypokalemia, Iraqi patients

Introduction

With a global impact never seen before, the coronavirus disease-2019 (COVID-19) pandemic was brought on by the severe acute respiratory illness coronavirus 2. As of January 13, 2022, the WHO SARS-Cov-2 Dashboard showed 312.1 million cases and 5.5 million deaths. The epidemic spurred research on vaccinations that elicit T-cell and antibody responses. Since late 2020, vaccinations have effectively prevented COVID-19 morbidity and mortality. In spite of this outcome, mutations have given rise to newly modified strains with increased rates of transmission, resulting in breakthrough infections in individuals who have had every vaccination possible.[1] As a result, the situation surrounding COVID-19 control has changed, necessitating regular "lockdowns" that affect both domestic and foreign businesses and needing updated estimates of the level of herd immunity needed to avert sickness. Adopting a multipronged strategy that does not rely just on vaccinations is a wise and vital line of action. Certain individuals who have recovered from an acute corona infection—referred to as "long COVID"—experience reduced effectiveness of currently licensed immunizations to stop viral transmission and persistent fibrosis in the kidneys, lungs, and cardiovascular system.[2] Immunosuppressive treatments are becoming more and more common as the globe battles COVID-19 and a lack of treatment options. The immune system is impacted by SARS-CoV-2 COVID-19, thus

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pharmaceutical companies are creating vaccinations and targeted treatments. In addition to helping with infectious disorders, a balanced diet rich in zinc, salt, potassium, calcium, chloride, and phosphorus can also prevent chronic infectious diseases by promoting good health. Insufficient immune system function can result from a lack of vitamins and minerals in plasma.[3]

The most common side effect of COVID-19 is hypokalemia, which exacerbates acute respiratory distress syndrome (ARDS). Angiotensin-converting enzyme 2 (ACE2) is bound by SARS-CoV-2, which also decreases ACE2 expression. This results in an increase in angiotensin-II and hypokalemia. As seen in SARS-CoV animal models, COVID-19 patients showed increased plasma angiotensin-II, which likely caused immediate lung injury Compared to non-severe persons, the potassium concentration of COVID-19 patients with severe disease is lower and less variable than that of salt. Infection with SARS-CoV-2 may also be indicated by low potassium levels.[4] We often overlook magnesium. Magnesium supplements may help manage the stress caused by PTSD, which will affect COVID-19 survivors, medical professionals, and general public. It controls the adherence of immune cells, the synthesis of immunoglobulins, the binding of IgM lymphocytes, antibody-dependent cytolysis, and the response of macrophages to lymphokines. Research both *in vivo* and *in vitro* demonstrates that magnesium aids in the defense against corona infections. Magnesium, vitamin B12 (DMB), and sunlight all assisted in slowing the growth of COVID-19 in the elderly The inflammatory cytokine storm, which is the primary cause of death, has been defined as the excessive and uncontrollable release of pro-inflammatory cytokines, as has been seen in prior infections caused by pathogenic coronaviruses. for example, increased levels of inflammatory cytokines produced by macrophages, which damage the lungs and other organs, are present in patients with severe COVID-19 illness.[5]

Therefore, tracking plasma inflammatory markers could be useful in predicting the course of the illness. Procalcitonin, C-reactive protein, erythrocyte sedimentation rate, and serum amyloid A are a few of the inflammatory markers that have been examined in COVID-19 patient studies. Ferritin has not gotten much attention, despite the fact that it has been shown that hyperferritinemia is associated with problems in other viral infections such as dengue fever.[6] The severity and mortality of the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) can be assessed using ferritin as a biomarker.[7] Elevated ferritin levels and cytokine storms are associated with coronavirus infection. Pro-inflammatory changes and immunosuppression have been associated with elevated ferritin levels.[8] The majority of critically ill diabetic SARS-CoV-2 patients had higher ferritin levels.[9] Ferritin levels in older adults double throughout the course of a lifetime, according to a number of studies, especially when compared to younger adults.[10] A multicenter study on viral infection found that higher levels of hyperferritinemia were associated with higher rates of morbidity and that ARDS was more common.[11] This research aimed to evaluate the circulating potassium, magnesium and ferritin concentrations and their potential to use them to predict COVID-19 infection and its development in Iraqis infected with Coronavirus.

Materials and Methods

Samples collection

This study was carried out at Al-Hillah Teaching Hospital and the medical Mrjan City from the period of January 2022 to May 2022. A total of 100 samples (5 mL) were drawn from individuals with coronavirus infection, ranging in age from 4 to 64 years old and in both genders, using a sterile medical syringe. Numerous questions, including those about marriage, age, family history, recurring infections, smoking, kidney diseases, other disorders, diabetes, and hypertension, were asked of each participant. To keep the blood serum separate, the samples were stored in unique gel tubes. After being left at room temperature for 30 min, the tubes were centrifuged to extract the blood serum and then placed in storage at a temperature of −20°C.

Potassium concentration assay

Using the manufacturer's method (Tetraphenylborate Method Without Deproteinization, code NO. 298 002, spectrum), potassium was measured in the blood serum by the Bioassay Technology Laboratory. To determine the potassium concentration in the blood serum (samples) in relation to the normal range for blood potassium level (3.6–5.2 mmol/L), the following equation was utilized.

$$Sreum\ Potassium\,Conc.\left(\frac{mmol}{L}\right)=\frac{A\,sample}{A\,standard}\times 5$$

Magnesium concentration assay

The Bioassay Technology Laboratory tested the amount of magnesium in the blood serum using the manufacturer's method (Xylidyl Blue Monoreagent, code NO. 285 002, spectrum). The magnesium concentration in the blood serum (samples) was calculated using the following equation, and the results were compared to the normal range of 1.7–2.2 mg/dL for blood magnesium levels.

$$sreum\ Magnesium\,Conc.\left(\frac{mg}{dl}\right)=\frac{A\,sample}{A\,standard}\times 2.5$$

Ferritin concentration assay

Using the Human Ferritin Heavy Chain, FTH1 ELISA Kit, cat. No. E6766Hu, BT LAB, from Bioassay Technology laboratory, ferritin was measured in blood serum and, in accordance with the manufacturer's method, compared to the normal range for blood magnesium level (24–336 μg/L for men, 11–307 μg/L for women.

Statistics

The statistical analyses required for this investigation were carried out using IBM SPSS Statistics version 23.0. To assess sample means from two or more similar groups, the independent samples *t* test and the one-way ANOVA test are useful. *P* value > 0.05 were all regarded as statistically significant.[12]

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number B230501 (including the number and the date in May 8, 2023) to get this approval.

Results

Demographic characteristics

The study's subjects were split into five age groups based on their respective levels of infection with the coronavirus (*P* ~ 0.05). The age groups with the highest rates of infection were (16–30) and (31-45), while the age groups with the lowest rates of infection were (4–15) and (61–75). Table 1 also shows that there were no significant differences in the proportion of males to females in any of the age groups.

Potassium serum concentration

In this study, patients were divided into three groups based on their potassium levels: normal (3.6–5.2 mmol/L) (57%), above normal (19%), and below normal (24%). There were also statistically significant differences between the three groups, and a higher percentage of men (24%) than women (13%) had higher potassium levels (>5.2 mmol/L). The percentages in the other groups converged. As shown in Table 2, there are no differences in the average age of any group.

Magnesium serum levels

Table 3 displays the patient distribution into three groups based on their magnesium levels: normal (1.7–2.2 mg/dL) (39%), above normal (58%), and below normal (3%). Significant differences (*P* < 0.05) were seen between the groups. Furthermore, while the percentage converged in the normal level group, there were no significant differences in the mean ages between all groups. Men (68%) were more likely than women (42%) to have a higher level of magnesium (>2.2 mg/dL), and an increased percentage of men (3%) than women (3%) had a lower level of magnesium (<1.7 mg/dL).

Ferritin serum levels

The ferritin levels of the patients in this study were found to be as follows: normal (24–336 μg/L for men, 11–307 μg/L for women) (97%), above normal (0%), and below normal (3%). Additionally, the proportions of men and women were equal in all groups without statistically significant differences, as shown in Table 4.

Discussion

Being a new virus, the SARS-CoV-2 can infect any member of the human race, regardless of age or gender.[13] Regardless of gender or age, individual variances do occur

Table 1: Distribution of patients with COV-19 according to the age and gender

Age groups (years)	Number of cases (*n* = 100)	Male (%)	Female (%)
1-15	9	5	4
16-30	35	22	13
31-45	35	21	14
46-60	16	12	4
61-75	5	2	3
Sum	100	62	38
P value	0.00	0.79	

Table 2: Distribution of Potassium levels according to normal levels of age and gender

Potassium ranges groups	Number of cases (*n* = 100)	Male (No, %)	Female (No, %)	Mean of age
Normal levels (3.6–5.2 mmol/L)	57	34/62, 55	23/38, 61	33.51
Above the normal level	19	14/62, 23	5/38, 13	33.36
Below the normal level	24	14/62, 23	10/38, 26	32.29
P value	0.00	0.00	0.00	0.228

Table 3: Distribution of magnesium levels according to normal levels of age and gender

Magnesium ranges groups	Number of cases (*n* = 100)	Male (No, %)	Female (No, %)	Mean of age
Normal levels (1.7–2.2 mg/dL)	39	18/62, 29	21/38, 55	33.67
Up to normal levels	58	42/62, 67	16/38, 42	31.45
Down to normal levels	3	2/62, 3	1/38, 3	33.67
P value	0.00*	0.00*	0.00*	0.70

Table 4: Distribution of ferritin levels according to normal levels of gender

Ferritin ranges groups	Number of cases ($n = 100$)	Male (No, %)	Female (No, %)
Normal levels	97	60/62, 97	37/38, 97
Above normal levels	0	0/62, 0.00	0/38, 0.00
Below normal levels	3	2/62, 3	1/38, 3
P value	0.00*	0.00*	0.00*

in physiological processes, immunological responses, and risk factors. Because of this, the probability of getting an infection varies based on age and gender. The present study aimed to investigate the probability, accounting for both gender and age, of an Iraqi population member contracting an infection as they grew older. Numerous studies conducted globally have demonstrated that elderly guys have a higher likelihood of contracting corona infection (>50%).[14,15] Men made about 60.3% of all cases in a survey of 5700 hospitalized COVID-19 patients in the United States. Many assumptions were made about how COVID-19 affected age and gender differently. The COVID-19 susceptibility was further demonstrated using the environmental and socioeconomic factors.[16] A person's daily activities, employment, economic status, level of literacy, and other societal factors all influence how susceptible they are to diseases.[17] The vulnerability to exogenous infections varies due to biological changes between the sexes (male and female) and at different ages.[18] Immune system defense against viruses and other infections is crucial. The normal immune system develops with considerable variation throughout pregnancy, modifies during the fetal to infant stage, and then begins to diminish as senescence approaches.[19] These long-lasting immune system alterations put older people, pregnant women, and children at more risk for issues. Numerous elements are involved in the immune system's differentiation according to age and gender. Differences in the quantity or count of Igs, CD4 and CD8 cells, B-cells, and T-cells between males and females may be the cause of the disparity in COVID-19 cases and deaths.[20-22] According to the study's findings, a sizable portion of men (23%) and women (26%) are deficient in potassium, which is one of the signs of a coronavirus infection. Due to the fact that COVID-19 patients expel high amounts of potassium in their urine, most of them suffer from potassium insufficiency.[23] It has been determined that individuals with COVID-19 typically have hypokalemia. Because of constant K+ loss in the kidneys due to ACE2 breakdown, hypokalemia is difficult to treat.[24] The enzyme ACE2 converts the potent vasoconstrictor angiotensin-II into angiotensin. ACE2 participates in the renin–angiotensin system (RAS) as a result of this activity.[25] End-urinary (K+) loss may be a dependable, timely, sensitive biomarker that indicates bad end-effect on the renin–angiotensin system and is a strong prognostic indicator for the patient. Hypokalemia was observed more frequently in critically ill COVID-19 patients. Ninety-three percent of COVID-19 patients had low potassium levels, according to a recent Chinese study.[26] In patients with COVID-19, ACE2 resistance results in a severe disruption of the (RAS). Those who were out of balance lost less potassium in their urine and responded more favorably to intravenous potassium as indicators of hypokalemia.[27] When people with severe hypokalemia were given 3 g of potassium per day (an average of 34 g over the course of a hospital stay), they got better. Hypokalemia, which is when the potassium level in the blood is below 3.5 mEq/L, can cause problems with fluid and electrolytes in the clinic.[28] Renal potassium loss and hypokalemia can both be exacerbated by hypomagnesemia. A deficiency in magnesium causes the sodium-potassium ATPase pump to function less efficiently. As a result, the cell's potassium content decreases. More potassium waste is produced by distal potassium release through ROMK channels when the body doesn't have adequate magnesium. Potassium loss may worsen with magnesium insufficiency due to elevated aldosterone levels and salt transfer to the extremities. But there are other factors that might lead to hypokalemia as well.[29] Reduced intestine absorption, increased renal loss, and intracellular potassium shifting can also cause hypokalemia. These medications include laxatives, insulin, glucocorticoids, diuretics, antibiotics, and beta 2-receptor antagonists. A magnesium deficit in critically ill patients can cause severe neuromuscular and cardiovascular clinical symptoms in addition to secondary hypokalemia and hypocalcemia. Concomitant magnesium deficiency exacerbates hypokalemia and makes it more resistant to potassium therapy.[30] When treating individuals with hypomagnesemia or borderline low-normal blood concentrations, it is best to treat hypokalemia concurrently with hypomagnesemia to prevent serum potassium levels from falling below normal once potassium medication is stopped.[31]

Among the many nutrients that are necessary for life is magnesium. It is the second most prevalent intracellular cation in the body, after potassium, and is involved in more than 600 enzymatic activities, some of which cause patients' increased inflammatory and immunological responses.[32] Increased phagocyte activity, enhanced granulocyte oxidative stress, activated endothelial cells, and elevated cytokine levels as a result of magnesium shortage are the factors that cause inflammation.[33] Numerous characteristics of the COVID-19 are similar to the metabolic alterations that have been shown to occur with latent subclinical magnesium insufficiency.[34] These alterations include an endothelium-related issue, a decrease in T lymphocytes, and an increase in inflammatory cytokines in the blood. According to our data, magnesium levels were substantially lower in severe COVID-19 patients than in non-severe COVID-19 patients. The shift in COVID-19 symptoms from mild to severe could be attributed in part to the low magnesium level. It was believed that monitoring the body's magnesium levels could help to prevent or reduce the progression of illness.[35]

The majority of studies show that when a person has a coronavirus infection, their blood serum ferritin content rises. Medical professionals who treat a lot of patients and researchers were alerted to the patient's elevated ferritin level since it predicted negative outcomes.[36] In the early stages of the pandemic and following the COVID-19 outbreak. But the possible connection between ferritin and a worse prognosis just scratched the surface of the underlying causes, which calls for more investigation. From a prognostic standpoint, ferritin concentration then evolved to function as a harshness risk factor. More importantly, because of the markedly raised ferritin content, lymphopenia, decreased number of NK cells, impaired liver function, and coagulopathy, researchers hypothesized and subsequently agreed that COVID-19 might be the newest member of the group of hyperserotonemia syndromes.[37]

Serum ferritin concentrations were higher in patients with severe to critical illness than in those with mild to moderate illness, and in non-survivors compared to survivors. Serum ferritin concentrations were greater in patients requiring mechanical ventilation and ICU care than in non-mechanically ventilated patients.[38] Ferritin concentrations were also higher in COVID-19 patients with renal involvement; however, there was inconsistent information about the correlation between ferritin concentrations and COVID-19-associated liver damage. Patients without COVID-19-related thrombotic events showed a lower blood ferritin content. An essential marker of COVID-19 severity is serum ferritin.[39]

Conclusions

Because of the nature of their daily jobs and their frequent interaction with infected people, the young and middle-aged demographics are the most susceptible to contracting the coronavirus. This study shows that in SARS-CoV-2 infections, hypermagnesemia is a reliable marker of the severity of the illness and its unfavorable trajectory. Hypokalemia was a prevalent electrolyte disorder in COVID-19 individuals. Serum potassium and magnesium levels should be part of the panel of tests often ordered in the evaluation of severe SARS-CoV-2 infections. Low potassium levels should be administered intravenously or orally, and the ECG should be carefully examined. Ferritin levels are a reliable predictor of the severity of illness.

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Conflicts of interest

There are no conflicts of interest.

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