

The prognostic value of serum uric acid in critically ill Covid-19 patients

Ali Ahmad Alhasan^{1*}, Qussai Hassan², Yaser Ahmad Alhasan³

Department of Internal Medicine, Al Assad and Al Mouwasat University hospitals, Damascus University- Faculty of medicine, Damascus, Syria¹

Prof and chief of Nephrology Department, Al Assad University hospital, Damascus University- Faculty of medicine, Damascus, Syria²

Faculty of science, Department of Mathematics, Albaath university, Syria³

Correspondence author: 1*



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ABSTRACT

The severity of infection with Covid-19 ranging from asymptomatic infection to a serious infection that requires mechanical ventilation. This discrepancy underscores the need for new biomarkers related to the course and progression of the disease. Our aim in our article was to evaluate the effect of serum uric acid, which is an easily available, low-cost, and reliable marker on the severity of Covid-19, and the possibility of using it as a warning indicator and a useful indicator in the follow-up of patients due to the scarcity of qualitative studies we have in this regard. The data of patients severely infected with the emerging corona virus who were admitted to the isolation departments at Al-Mowasat University Hospital in Damascus will be studied and collected from the date of approval of the research in September 2022 until September 2023, including: age, name, gender, smoking, medical history, drug history, vital signs, nasopharyngeal swab to detect the emerging corona virus, and laboratories, and then analyze these results using the SPSS-25 program and writing it in its final form after making the necessary modifications to it, along with the tables and diagrams shown thereto. The study sample consisted of 35 patients, where the average age was 70.2 years with a deviation of +/- 11.9, the percentage of males was 65.7%, the vitals of patients upon admission, the average value of systolic pressure was 133.2 mm Hg +/- 20.4, the diastolic pressure was 79 mm Hg +/- 12.1, Sao₂ was 79.7% +/- 8.3, heart rate was 92 +/- 26, while respiratory rate was 32 +/- 10, as all swabs conducted for patients were positive. And according to the uric acid analysis, the mean was 1.9 with a deviation of +/- 0.4 for all sample. Moving on to the inferential statistics, we have studied the relationship between the value of uric acid in each of the patients, where the P-value <0.05, and thus the existence of a statistical relationship between the value of uric acid and the critical general condition of the patient. By applying this study to the sample that was chosen, it was found that, it gave a relative picture of the existence of a statistical relationship between the decrease in the value of uric acid and the critical general condition of patients with COVID-19, and therefore the value of uric acid must be taken into consideration as a warning indicator for patients with corona.



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1. Introduction

The new Coronavirus appeared for the first time in China, specifically in the city of Wuhan, in December 2019, and the first case of infection was caused by eating seafood [1], [2].

The World Health Organization announced that this virus had caused a global epidemic in the month of March of 2020. It was called the emerging virus because it was preceded by two epidemics with two similar viruses descending from the same genus, Beta-Cov, belonging to the family of coronaviruses. These two viruses are MERS-COV and SARS-COV [3], [4]

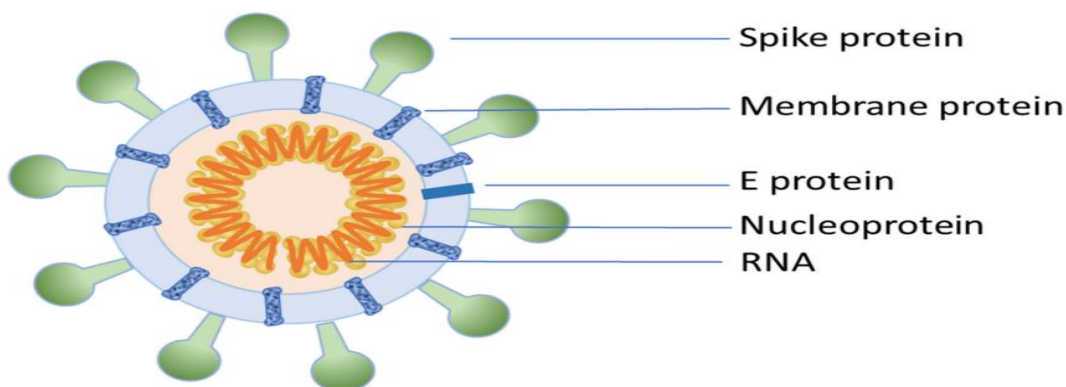


Figure 1: Typical scheme of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virion structure.

Methods of transmission: Through respiratory droplets transmitted from an infected person who is coughing or sneezing, or through tools contaminated with the virus, and just as it is found in the saliva of an infected person, it can also be detected in the urine and feces of infected people [5].

Pathogenic mechanism: The virus suppresses the antiviral immune response by the patient's immune system. It also inhibits the effects of antiviral interferons of the INF-I and INF-III types. The virus also has the ability to incite the host's immune system to distract itself by attacking the host's own tissues in a similar way to autoimmune inflammation.

The virus is also recognized through cellular receptors that are divided into three receptors:

1. Receptors that enable the virus to penetrate the target cell
2. Receptors that transmit information that serves the virus to the target cell
3. Cellular receptors that, after recognizing the virus, stimulate the immune response against the virus, but it inhibits it. [6]

Symptoms and signs:

Symptoms range from asymptomatic infection to acute respiratory distress syndrome (ARDS), causing pneumonia, cough, sneezing, fever, muscle pain, fatigue, shortness of breath, and various other symptoms [7].

Diagnosis:

The RT-PCR method, which is a method of polymerase chain reaction (PCR), is considered the gold standard for diagnosis. It is based on a sample from a nasopharyngeal swab [8].

Radiological findings:

The typical radiographic findings on a chest CT are a ground-glass appearance, especially with a circumferential distribution, and bilateral densities are usually present [9]

Complications associated with Covid-19:

Complications associated with the emerging coronavirus are linked to acute respiratory distress syndrome resulting from excessive activation of the immune system, which causes major damage, including the lungs, acute renal failure, myocarditis, hypercoagulability, elevated liver enzymes, encephalitis, and others [10].

Treatment:

Supportive therapy is the cornerstone of treatment, such as oxygen, hydration, antipyretics, and analgesics as needed. Good nutrition is also important in management. Many antiviral medications have been used, including Remdesivir, which has shown good effectiveness in reducing the viral load [11].

URIC ACID:

Studies revealed that serum uric acid concentrations were noticeably lower in infected patients severe infection with the novel coronavirus, the kidney and gastrointestinal tract are targets of the coronavirus and are the main sites for uric acid excretion, it is likely that infection with the novel coronavirus can affect metabolic regulation of uric acid and its levels in serum., which could be brought about by inflammation-induced renal tubule urine acid reabsorption impairment [12- 14]. And this virus cases nephritis where we find cytoplasmic nephritis, leukocyturia, albuminuria, and hematuria [15]. In addition the Corona virus was discovered in infected patient's urine [16].

The need for readily available and trustworthy markers to identify high-risk patients increases high levels of severe infection with the novel Corona virus in order to give these patients with the best care possible due to the diversity of Covid-19 presentations and development [17].

Based on the information above, uric acid also referred to as a catabolic product of purine that originates from ribonucleic acid and deoxyribonucleic acid was highlighted as a metabolic indicator, is less affected by other factors, however, it is only affected by some medications and a diet high in purines. Studies have shown that acid urine is closely associated with immune system activation and the elimination of oxygen free radicals, and that uric acid [18- 20].

High level of uric acid is an evolutionary benefit that can improve antioxidant defense and lengthen life in humans [21]. Additionally, uric acid regularly enhances vascular endothelial function in smokers through the antioxidant response [22]. Although the exact mechanism is unknown, serum uric acid's antioxidant function may be helpful in highly oxidative situations. It is thought to have a protective effect on the central nervous system [23].

2. Material and methods

The data of patients severely infected with the emerging corona virus who were admitted to the isolation departments at Al-Mowasat University Hospital in Damascus will be studied and collected from the date of approval of the research in September 2022 until September 2023, including: age, name, gender, smoking,

medical history, drug history, vital signs, nasopharyngeal swab to detect the emerging corona virus, and laboratories, and then analyze these results using the SPSS-25 program and writing it in its final form after making the necessary modifications to it, along with the tables and diagrams shown thereto.

3. Statistical analysis

Statistical analysis was performed using the program SPSS-25. We used nonparametric statistics such as the Chi-square test of independence to study whether a relationship exist between tow descriptive variables by applying the Chi-square statistics, and the value of P-value < 0.05 was considered statistically significant to indicate there is a statistical relationship between the studied variables. In addition of T-test. Descriptive analysis was performed using mean and standard deviation (mean \pm SD).

4. Results

In Table 1 we note that the study sample consisted of 35 patients, where the average age was 70.2 years with a deviation of \pm 11.9 , and by dividing the study sample by gender, the percentage of males was 65.7%, and by asking the patients about smoking we found that 68.5% of the patients were smokers ,and when we asked them about medical history we found that Hypertension 74.2% , Diabetes Mellitus 28.5% , Coronary Artery Disease 8.5% ,and with regard to the vitals of patients upon admission, the average value of systolic pressure was 133.2 mm Hg with a deviation of \pm 20.4 , while the average diastolic pressure was 79 mm Hg with a deviation of \pm 12.1 , and the average oxygenation of patients was 79.7% with a deviation of \pm 8.3 , while the average heart rate per minute was 92 beats per minute with a deviation of \pm 26, while the average number of breaths per minute was 32 times per minute with a deviation of \pm 10. As all swabs conducted for patients were positive.

As for the liver functions, the mean for the enzyme alanine aminotransferase (ALT) was 45.2 with a deviation of \pm 39.2, while the aspartate aminotransferase (AST) was 55.3 with a deviation of \pm 49.6 ,when talking about kidney function, the mean for creatinine (Cr) was 3.4 with a deviation of \pm 1.3 while the mean of urine (Ur) was 37.6 with a deviation of \pm 13.4, according to the uric acid analysis (UA), the mean was 1.9 with a deviation of \pm 0.4, the arithmetic mean of the inflammatory index (CRP) was 96.7 with a deviation of \pm 58.1, by analyzing the patients' blood count, the average white blood cell count was 10.4 thousand white blood cells with a deviation of \pm 3.6 thousand cells, while the average percentage of lymphocytes was 4.7% with a deviation of \pm 4.8

Moving on to the inferential statistics, we have studied the relationship between the value of uric acid in each of the patients who were in critical general condition, where the P-value < 0.05, and thus the existence of a statistical relationship between the value of uric acid and the general condition of the patient.

Table 1. Baseline characteristics of patients with COVID-19 according to critical general condition

variables	Critical general condition N=35	Normal range
Age	70.2 \pm 11.9	NA
Male %	23 (65.7%)	NA
Hypertension %	26(74.2%)	NA
DM%	10(28.5%)	NA

CAD%	3(8.5%)	NA
Smokers %	24(68.5%)	NA
SBP (mmHg)	133.2+/-20.4	< 140
DBP (mmHg)	79+/-12.1	< 90
Sao2%	79.7+/-8.3	>94
RR per minute	32+/-10	16-20
HR per minute	92+/-26	60-100
ALT (U/L)	45.2+/-39.2	9-50
AST (U/L)	55.3+/-49.6	10-40
Ur (mg/dl)	37.6+/-13.4	20-40
Cr (mg/dl)	3.4+/-1.3	0.6-1.2
UA	1.9+/-0.4	3.5-7
WBC, 10 ⁹ /L	10.4+/-3.6	4-11
LYM%	4.7+/-4.8	20-50
CRP	96.7+/-58.1	0-5

ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine, DM: Diabetes Mellitus, DBP: diastolic blood pressure; CRP, C- reactive protein, LYM%, Lymphocyte percentage, SBP, systolic blood pressure; UA, uric acid, WBC, white blood cell. CAD: coronary artery disease.

As we note in Table2 that all patients were in acritical general condition and they had the arithmetic mean for uric acid 1.9 +/- 0.4

Table 2. we have studied the relationship between the value of uric acid in each of the patient's critical general condition

variables	Critical general condition N=97	P-value	Normal range
UA	1.9+/-0.4	0.002	3.5-7

5. Discussion

To the best of our knowledge, it is the first study to evaluate the importance of serum uric acid in severe Covid-19 from Syria. We discovered that low serum uric acid levels are commonly seen in patients with severe infection Covid-19, and that they are highly associated with the severity of the disease and the need for mechanical ventilation. Hypouricemia was associated with poor uric acid handling in the tubules and

pathological features that may have indicated a change in the expression of the urate transporter in the kidney's proximal tubule. It was not caused by medication or any other illness that interfered with the production of uric acid. Hypouricemia occurs in 1.2% to 2.5% of hospitalized individuals [24], [25]. In our study, 100% of patients hospitalized for Covid-19 infection reported hypouricemia; among patients requiring mechanical ventilation, this rate increased to 84.3%.

The association between hypouricemia and the development of respiratory failure requiring mechanical ventilation was not affected by age, gender, comorbidities, or biological markers of disease severity, suggesting that hypouricemia may be used as a biomarker to identify patients at risk of more severe SARS-COV-2. As we saw the 2003 SARS outbreak about 25% of patients develop hypouricemia, with high rates in patients requiring mechanical ventilation [26]. The idea that inappropriate tubular processing of urate that leads to the development of hypouricemia is supported by faulty uricosuria and its correlation with other indications of proximal tubule malfunction in individuals with the potentially fatal COVID-19 [27].

As proximal tubule cells and pneumocytes express ACE2, the cellular receptor facilitating viral entrance into host cells, we cannot exclude out a parallel evolution at the tubular and lung level, leading from probable direct cellular infection by SARS-CoV-2 in both organs [27]. Further investigation is required to ascertain the potential contribution of each of these variables to the correlation between low levels of blood uric acid and bad prognosis outcomes in individuals with COVID-19.

The important and notable discovery of uric acid as a biomarker that is easily available, inexpensive, and reliable for determining the level of infection with the novel coronavirus is one of the study's numerous strengths. We acknowledge that there are certain limitations as well, including the single center for the study, the absence of systematic longitudinal follow-up for all biological measures, and the lack of mechanistic insights into the pathophysiology of the relationship between respiratory failure and hypouricemia.

6. Conclusion

By applying this study to the sample that was chosen, it was found that, it gave a relative picture of the existence of a statistical relationship between the decrease in the value of uric acid and the critical general condition of patients with Covid-19, and therefore the value of uric acid must be taken into consideration as a warning indicator for patients with corona.

Author contribution statement

Ali Ahmad Alhasan; write and submit the manuscript, literature review, and collecting data.

Qussai Hassan: makes article corrections, supervisor, and follow-up.

Yaser Ahmad Alhasan: data analysis, wrote and explain the study results.

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Data availability statement

All necessary details are available in the article. Further enquiries can be directed to the corresponding author.

Additional information

No additional information is available for this paper.

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