Is the Urine Analysis, a Diagnostic Value in COVID-19 Patients?

Sonti Sulochana a≡, Lakshmi Priya Asokan a*e, Mathesh a# and Chitra Srinivasan a†

a Department of Pathology, Saveetha Medical College and Hospital, Saveetha Medical College and Hospital Saveetha Nagar, Thandalam, Chennai 602105, Tamil Nadu, India.

Authors’ contributions
This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information
DOI: 10.9734/JPRI/2021/v33i58B34198

Original Research Article

ABSTRACT

Background: Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2), a novel coronavirus causing Coronavirus disease 19 (COVID-19) in December 2019, is now a pandemic infectious disease, primarily affecting the respiratory tract. To date, many investigations are available for the diagnosis of SARS-CoV-2. A viral nucleic acid test has been used for the diagnosis of COVID-19, and some hematological indicators have been used in the auxiliary diagnosis and identification of the severity of COVID-19. There are very few studies available in routine urine biochemical parameters and their relation with Covid-19 patients.

Aim: This study is aimed to study the changes in urine parameter values in COVID-19 disease and to predict the severity of the disease with the changes in urine parameters.

Materials and Methods: A total of 150 patients with COVID-19 were admitted at Saveetha Medical College and Hospital during the study period. All cases tested positive for SARS-CoV-2 by RT-PCR test done on nasopharyngeal swabs during the study period were included. Patients who tested negative by RT-PCR test were considered as controls. The relationship between the results of urine biochemical parameters and the severity of COVID-19 were analysed by Descriptive statistics, Chi-squared test.
Results: The positive rates of proteinuria (PRO) and leucocytes were more significant in COVID-19 patients than in healthy controls. The urine specific gravity (SG) value was highly significant (p <0.001) while the blood, nitrites in urine, and potential of hydrogen (pH) value was insignificant.

Conclusion: There were some considerable changes in few urine biochemical parameters between patients with the SARS-CoV-2 and healthy controls. So from this study we conclude, proteinuria is helpful for predicting COVID-19 severity and kidney function.

Keywords: SARS-CoV-2; COVID-19; urine biochemical parameters; hematuria.

1. INTRODUCTION

SARS-CoV-2, a novel coronavirus, was first discovered in 2019 in Wuhan, China [1]. The virus is a novel human pathogen and can infect multiple host species [2]. It is an RNA virus with an enveloped positive-sense RNA that can grow in epithelial cells and mainly cause respiratory infection, including severe acute respiratory syndrome. The WHO named coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 [3] and this term mainly refers to the ongoing outbreak of SARS-CoV-2-infected pneumonia [1, 4, 5]. Patients with severe cases of COVID19 show symptoms of dyspnea associated with hypoxemia, while septic shock, multiple organ failure, and acute kidney injury was observed in severely ill patients [6]. Initially many studies concentrated on lung infections and complications [7,8,9,10] and less attentiveness was given to the AKI incidence in those patients, and oversight to kidney involvement was considered [11]. Many studies have been done on the hematological parameters and the abnormal hematology results of patients with COVID-19 include lymphopenia, increased lactate dehydrogenase (LDH), increased creatine kinase (CK) and its isoenzymes, and increased C-reactive protein (CRP) and inflammatory factors. Urine dry chemical tests have the characteristics of being quick, convenient, and economical, and the urine parameters can be used for the additional diagnosis of urinary tract infections (UTIs), the diagnosis of kidney diseases, and the monitoring of treatment effects [12,13,14]. To date, there have been very few studies about the correlation between urine biochemical parameters and COVID-19. This study aims to investigate the changes in urine parameters and their value in the prediction of the severity of COVID-19.

2. MATERIALS AND METHODS

This is a retrospective study done for a period of four months at Saveetha Medical College and Hospital, Chennai, Tamilnadu. The center caters to semi urban and rural population. Random enumeration sampling was done. The study cohort included the cases tested positive for SARS-CoV-2 by reverse transcription polymerase chain reaction (RT-PCR) test done on nasopharyngeal swabs within the study period. Exclusion criteria included patients who had urinary tract infection confirmed by positive for urine culture on microbiology, not hospitalized or treated on outpatient basis; lacking SARS-COV-2 RT-PCR testing; without necessary laboratory data, clinical data, and/or mortality data; pregnant females. Control cohort included healthy adults who were COVID-19 negative.

Patient information on demographics, comorbidities, complains and data on laboratory tests were obtained. As a part of routine investigations, urinary parameters were ordered in hospitalised cases and the values on the first day of admission were considered. Approximately 20 mL of clean midstream urine samples were obtained and tested within 2 h. In case of delay, the samples were refrigerated. The values of Urine parameters such as urine occult blood (BLOOD), proteinuria (PRO), the potential of hydrogen (pH), specific gravity (SG), ketone (KET), urine glucose (GLU-U), nitrite, and leukocytes (LEU) were obtained by using a fully automatic urine analyzer SIEMENS(Clinitek advantus) with 10 parameters urostrip. This study was approved by the Institutional Ethics Board of Saveetha Medical College and Hospital.

2.1 Statistical Methods

Data was entered in MS excel sheet and statistical analysis was done with SPSS version 22.0 software. Categorical variables were expressed as frequencies and percentages. Nominal categorical data between the groups were compared using Chi-square test. A p-value of <0.05 is taken as a statistical significance.
3. RESULTS AND DISCUSSION

The study population included a total of 150 individuals which included 120 cases who were tested positive for covid 19 and 30 healthy controls. The P-value of protein (<0.009), blood (0.056) and leucocytes (<0.008) were significant in patients with COVID-19 than in healthy controls.

In this study we observed a significant increase in proteins, leukocytes and blood in urine in COVID patients as compared to the healthy adults.

In this study there is no significant changes in urine glucose, ketone, pH, and nitrites values covid 19 patients compared to the healthy adults. Though not significant, there is an increase in ketones and nitrates in patients compared to helathy controls. The results were shown in Table 1-8.

In this study there is no significant increase in the urine glucose in covid 19 patients and controls. No statistical significance made out.

From this study we observe that there is increase in urine protein in covid 19 patients as compared to the control and also statistical significance is established.

In this study, we could find significant presence of blood in urine in covid 19 patients compared to the non covid persons, which was also statistically significant.

This study shows statistically significant presence of leukocytes in covid patients as compared to healthy controls.

In this study we noticed increase in urine nitrates in covid cases as compared to non covid cases, but it was not statistically significant.

In this study we observed increase in urine ketones in covid 19 patients compared to healthy controls, but statistical significance was not established.

This study didn’t show any significant changes in SG in both cases and controls.

In this study we couldn’t find any statistically significant change in ph values between the covid cases and non covid controls.

| Table 1. Insignificant P-value of urine glucose in Covid-19 |
|----------------------------------------------------------|
| **Urine Glucose** |  |  |  |  | |
| Category | 1+ | 2+ | 3+ | Nil | Trace | Total |
|-----------|----|----|----|-----|------|------|
| Covid     | 6  | 3  | 3  | 104 | 4    | 120  |
| Non Covid | 2  | 0  | 1  | 27  | 0    | 30   |
| Total     | 8  | 3  | 4  | 131 | 4    | 150  |

| Chi-Squared tests |
|-------------------|
| **Value** | **df** | **P** |
| $\chi^2$ | 2.427 | 4 | 0.658 |
### Table 2. Significant $P$-value of protein in Covid-19

| Category  | 1+ | 2+ | 3+ | Nil | Trace | Total |
|-----------|----|----|----|-----|-------|-------|
| Covid     | 16 | 15 | 8  | 63  | 18    | 120   |
| Non Covid | 1  | 0  | 1  | 27  | 1     | 30    |
| Total     | 17 | 15 | 9  | 90  | 19    | 150   |

**Chi-Squared tests**

| $X^2$ | df | $P$ |
|-------|----|-----|
| 13.415 | 4  | 0.009 |

### Table 3. Significant $P$ value of blood in Covid-19

| Category | Absent | Present | Total |
|----------|--------|---------|-------|
| Covid    | 94     | 26      | 120   |
| Non Covid| 28     | 2       | 30    |
| Total    | 122    | 28      | 150   |

**Chi-Squared tests**

| $X^2$ | df | $P$ |
|-------|----|-----|
| 2.311 | 1  | 0.056 |

### Table 4. Significant $P$-value of leucocytes in Covid-19

| Category | Absent | Present | Total |
|----------|--------|---------|-------|
| Covid    | 111    | 9       | 120   |
| Non Covid| 24     | 6       | 30    |
| Total    | 135    | 15      | 150   |

**Chi-Squared tests**

| $X^2$ | df | $P$ |
|-------|----|-----|
| 7.126 | 1  | 0.008 |

### Table 5. Insignificant $P$ value of Nitrite in Covid-19

| Category | Absent | Present | Total |
|----------|--------|---------|-------|
| Covid    | 107    | 13      | 120   |
| Non Covid| 26     | 4       | 30    |
| Total    | 133    | 17      | 150   |

**Chi-Squared tests**

| $X^2$ | df | $P$ |
|-------|----|-----|
| 0.010 | 1  | 0.918 |

### Table 6. Insignificant $P$ value of ketone in Covid-19

| Category | Absent | Present | Total |
|----------|--------|---------|-------|
| Covid    | 96     | 24      | 120   |
| Non Covid| 27     | 3       | 30    |
| Total    | 123    | 27      | 150   |

**Chi-Squared tests**

| $X^2$ | df | $P$ |
|-------|----|-----|
| 2.750 | 1  | 0.097 |
### Table 7. Specific gravity in Covid-19

| Category  | Abnormal | Normal | Total |
|-----------|----------|--------|-------|
| Covid     | 0        | 120    | 120   |
| Non covid | 0        | 30     | 30    |
| Total     | 27       | 150    | 177   |

| Chi-Squared tests |
|-------------------|
| Value             | df  | P       |
| $X^2$             | 71.336 | 1 | < 0.001 |

### Table 8. Insignificant P-value of pH in Covid-19

| Category    | Abnormal | Normal | Total |
|-------------|----------|--------|-------|
| Covid       | 1        | 119    | 120   |
| Non Covid   | 0        | 30     | 30    |
| Total       | 1        | 149    | 150   |

| Chi-Squared tests |
|-------------------|
| Value             | df  | P       |
| $X^2$             | 0.173 | 1 | 0.677 |

### 3.1 Discussion

At the end of 2019, in Wuhan, China an epidemic outbreak of the COVID-19 started and it has spread worldwide and has led to a large number of patient deaths and huge economic losses. The cause of COVID-19 was determined to be SARS-CoV-2 by an RNA-based metagenomic next-generation sequencing approach [15]. SARS-CoV-2 likely infects the host cells via the ACE-2 receptors resulting in macrophage activation, B-cell mediated antibody production, T-cell activation, cytokine release [19,20,21]. Some COVID-19 patients develop cytokine storm syndrome, which is characterized by increased production of pro-inflammatory cytokines like TNF, IL-6, and IL-1β. This causes an increase in vascular permeability, hyperinflammation, and loss of procoagulant-anticoagulant balance [22,23].

COVID-19 disease has shown abnormalities in the routine laboratory parameters. The clinical symptoms of COVID-19 were fever, cough, diarrhoea, nausea, and myalgia[10,16]. Elderly men and women associated with comorbidities like diabetes, hypertension, etc are more likely to have respiratory failure, and the disease onset of some patients has shown rapid progression to multiple organ dysfunction and many patients died from severe illness COVID-19[4]. ARDS is the main symptom of patients with COVID-19 [17]. SARS-CoV-2 infection may trigger cytokine storm which causes multiple organ dysfunction syndromes (MODS) including kidney damage caused by cytokine storm [18].

Biochemical parameters in urine can be used for UTI diagnosis, monitoring of kidney diseases and the follow-up of treatment effects, due to the easy sample collection, test automation and cost-effectiveness [25]. The correlation between urine biochemical parameters and the prediction of progress of COVID-19 disease has been analysed in few literature and found to be significant.

In our study, the positive rates of protein, leucocyte, and blood in COVID-19 patients were found to be more significant than those in healthy controls, and the values of ketones, nitrites, SG and pH of p values were not significantly different between COVID-19 patients and healthy controls. The results indicate that the differences in protein, leucocyte and blood are caused by SARS-CoV-2 infection but not a bacterial infection as patients with urine culture positivity were excluded from the study. So these indicators can be used for the differentiation of COVID-19 patients from healthy individuals.

In a study done by Liu et al [24], there was significant change in the proportion of positive blood and protein in the urine dipstick between patients with COVID-19 and healthy controls. While analysing the severity of the COVID-19, it is seen that the groups with the highest
proportion of positive glucose and protein results were from samples of patients who were critically ill i.e. up to 60% of critical patients showed positive for glucose in the urine dipstick and 50% for protein. Our study showed concordance with the above study in case of proteinuria, which showed increased percentage of positive values for protein in covid patients.

In an other study done by, Pei G.et al [27], it is found that in about 75.4% of COVID-19 patients who had renal involvement upon admission, 65.8% had proteinuria and 41.7% had hematuria. They reported in their study, that the presence of AKI is associated with a higher incidence during hospital stay (86.4%) than upon admission (13.6%). It was also seen that critically ill patients showed a high incidence of proteinuria (85.7%) and also that of AKI (42.9%). So proteinuria can be used as good indicator of renal disease progression in covid cases.

In a study done by Liu et al [27], they found that increase in protein and glucose correlated significantly with the severity of the patients. So thereby, it states that proteinuria can be used as a significant marker of severity in covid 19 patients.

It is seen that in this study there is a positive rate of ketone and nitrate in patients but it was not statistically significant. So its association in COVID 19 infection and with severity of disease cannot be drawn with this study.

It is known that SARS-CoV-2 infection causes increase in cytokines which in turn leads to cytokine storm. This is seen to be the cause of multiple organ dysfunction syndrome including renal system [28]. Renal damage caused by cytokine storm could be the causative factor for difference in protein, blood and leukocytes between the covid 19 patient and control group.

4. CONCLUSION

In our study significant value of proteinuria, leukocytes and blood was noted. The changes in urine biochemical parameters are useful in evaluating the progress of covid-19 patients and can be used for prognosis.

Hence, we conclude that urine analysis shall be regularly performed in all patients with covid-19, whereby it may provide important information for clinical management and risk prediction.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL CLEARANCE

Institutional Ethics Board of Saveetha Medical College and Hospital approval was obtained.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. a novel coronavirus from patients with pneumonia in china, 2019. N Engl J Med. 2020;382:727–33.

2. Fung Ts, Liu DX. Human coronavirus: host-pathogen interaction. Annu rev microbiol 2019; 73:529–57.

3. World health organization. Who director-general’s remarks at the media briefing on 2019-ncov on 11 february 2020.

4. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in wuhan, china, Lancet 2020;395:497–506.

5. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in wuhan, china, of novel coronavirus-infected pneumonia. N Engl J Med 2020;382:1199–207.

6. Peerapornratana S, Manrique-Caballero CL, Gómez H, Kellum JA. Acute kidney injury from sepsis: current concepts, epidemiology, pathophysiology, prevention and treatment. Kidney Int 2019;96: 1083–1099.

7. Grasselli G, zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with sars-cov-2 admitted to icus of the lombardy region, italy. Jama; 2020.

8. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in critically ill patients in the seattle region–case series. N Engl J Med; 2020.

9. Arentz M, Yim E, Klaff L, et al. characteristics and outcomes of 21critically ill patients with covid-19 in washington state. JAMA; 2020.
10. Guan W-J, Ni Z-Y, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in china. N Engl J Med; 2020.

11. Wang I, li X, Chen H et al. coronavirus disease 19 infection does not result in acute kidney injury: an analysis of 116 hospitalized patients from wuhan, china. Ajn; 2020.

12. Berger RE. The urine dipstick test useful to rule out infections.a meta-analysis of the accuracy. J Urol. 2005;174:941–2.

13. Falbo R, Sala MR, Signorelli S, Venturi N, Signorini S, Brambilla P. Bacteriuria screening by automated whole-field image-based microscopy reduces the number of urine cultures. J Clin Microbiol. 2012;50: 1427–9.

14. Erdman P, Anderson B, Zacko JC, Taylo, K, Donaldson k. The accuracy of the sysmex uf-1000i in urine bacterial detection compared with the standard urine analysis and culture. Arch Pathol Lab Med. 2017;141:1540–3.

15. Chen L, Liu w, Zhang q, Xu k, Ye g, Wu w, et al. RNA based mngs approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 wuhan outbreak. Emerg microbes infect 2020;9:313–9.

16. Chen I, Liu w, Zhang q, Xu k, Ye g, Wu w, et al. RNA based mngs approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 wuhan outbreak. Emerg microbes infect 2020;9:313–9.

17. Wu Z, Mcgoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (covid-19) outbreak in china: summary of a report of 72314 cases from the chinese center for disease control and prevention. J Am Med Assoc; 2020.

18. Tetro JA. Is COVID-19 receiving ade from other coronaviruses? Microbes infect 2020;22:72–3.

19. Chen n, zhou m, dong x, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in wuhan, china: a descriptive study. Lancet 2020;395:507-13.

20. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus– infected pneumonia in wuhan, china. Jama 2020;323:1061–9.

21. 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

22. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46: 846–8.

DOI: 10.1007/s00134-020-05991-x

23. Vaninov N. In the eye of the COVID-19 cytokine storm. Nat Rev Immunol. 2020; 20:277.

DOI: 10.1038/s41577-020-0305-6

24. Liu R, et al. Te value of urine biochemical parameters in the in the prediction of the severity of coronavirus disease 2019. Clin. Chem. Lab. Med. 2020;58:1121–1124.

25. Erdman P, Anderson B, Zacko JC, Taylo, K. & Donaldson, K. Te accuracy of the Sysmex UF-1000i in urine bacterial detection compared with the standard urine analysis and culture. Arch. Pathol. Lab. Med. 2017;141:1540– 1543.

26. Pei G, et al. Renal involvement and early prognosis in patients with COVID-19 pneumonia. J. Am. Soc. Nephrol. 2020;31: 1157–1165.

27. Liu R, Ma Q, Han H, Su H, Liu F, Wu K, Wang W, Zhu C. The value of urine biochemical parameters in the prediction of the severity of coronavirus disease 2019. Clin Chem Lab Med. 2020;58(7):1121- 1124.

28. Tetro JA. Is COVID-19 receiving ADE from other coronaviruses? Microbes Infect. 2020;22:72–3.

© 2021 Sulochana et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here: https://www.sdiarticle5.com/review-history/75830

249