

Study of Association of Proteinuria as Prognostic Marker in COVID-19 Patients

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ABSTRACT

Introduction: COVID-19 Pandemic is a part of the worldwide Pandemic of the Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). This research work was planned with an objective to assess proteinuria as prognostic marker in COVID-19.

Material and methods: This was an observational prospective single-center study. The patients were admitted from June 2020 to December 2020 were included in present study. The study was approved by an ethics committee. The sample size was estimated using online Epi-calculator. In our study we included 50 patients older than 18 years admitted to our hospital with a positive COVID-19 test (reverse transcriptase polymerase chain reaction (RT-PCR, Cobas SARS CoV-2 Test with Cobas 8800) via nasal swab or antigen testing). We collected urine sample at the time of admission, on 7th day and on discharge.

Results: Mean age of patients was 57.52 + 14.64 years with 23 % female patients and 77 % male patients. In our present study, we found higher prevalence of the patients with abnormal proteinuria (87%). In our study, there was found statistically significant changes in proteinuria in patients of COVID-19 in comparison to date of admission ($P < 0.5$ as significant with considering 95% confidence interval). Conclusion: From present study, we conclude that a incidence of proteinuria is found positively associated with morbid COVID-19 patients. There was found statistically significant results in patients on DOD with DOA. Hence we can conclude that proteinuria is to be an important prognostic marker in COVID-19 patients.

Keywords: COVID-19, Proteinuria, Urine Examination, Serum Creatinine

INTRODUCTION

COVID-19 Pandemic is a part of the worldwide Pandemic of the Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).¹ During this time, strong major impact is observed on the healthcare services and practices of ethics in medicine.² Proteinuria has been commonly reported in patients with COVID-19, suggesting a renal involvement in this infection. However, only dipstick tests have been used thus far. Though numbers of investigations were carried out to assess COVID-19 as diagnostic as well as prognostic importance in various viewpoints as worldwide scenario. Renal damage was found, resulting in rearranged various kidney function tests with proteinuria found to be one of the important prognostic marker in this COVID-19 situation.³ India is a

developing country where there are costly investigations are not available every place. Simple investigations such as proteinuria can help to segregate patients and aid in their management. With this background, this research work was planned with an objective to assess proteinuria as prognostic marker in COVID-19. We planned to assess association with mortality with proteinuria.

MATERIAL AND METHODS

This was an observational prospective single-center study. The patients were admitted from June 2020 to December 2020 were included in present study. The study was approved by an ethics committee. The sample size was estimated using online Epi-calculator. In our study we included 50 patients older than 18 years admitted to our hospital with a positive COVID-19 test (reverse transcriptase polymerase chain reaction (RT-PCR, Cobas SARS CoV-2 Test with Cobas 8800) via nasal swab or antigen testing). We collected urine sample at the time of admission and on discharge.

We excluded patients with previous associated any form of renal diseases.

We included age, gender history of hypertension (based on medical records and/or the presence of antihypertensive medications at admission), history of diabetes (based on medical records and/or the presence of specific therapy at admission), Chronic renal disease (CRD), active cancer, active smoking etc.

We collected urine sample with other investigations.

1. The day when the urine was collected was considered as

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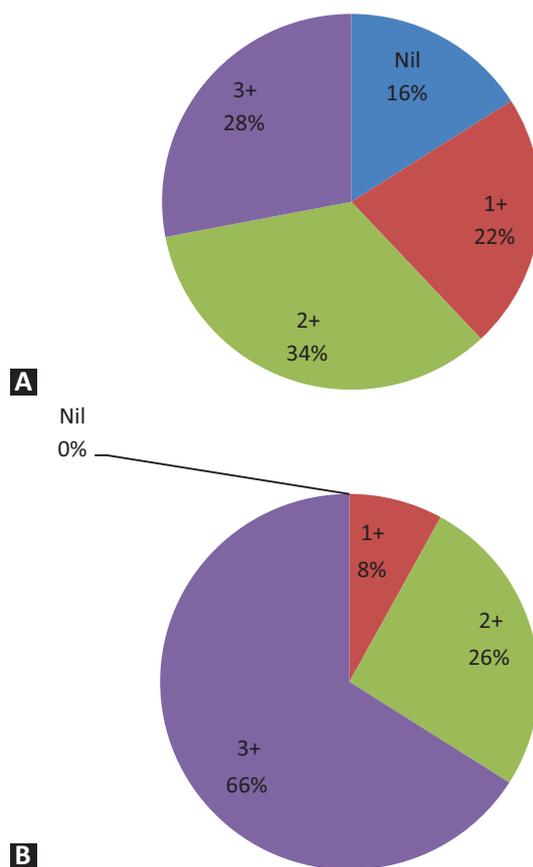
- Day 0 (D0). (Date of admission)
- 2. A second urine analysis was performed in some patients on Day 7 (D7).
- 3. However in this study we included urine sample report on the DOD (Day of discharge)
- 4. Total proteinuria was measured by qualitative method by dipstick analysis as +, ++, +++
- 5. Because proteinuria can be impacted by urinary catheter (UC), analyses were repeated in subgroups without UC at D0.

All other investigations were done with maintaining uniformity with all patients' records. Data was collected from patient's computer record data. Data was tabulated in MS EXCEL sheet and was further analysed using SPSS software.

RESULTS

In our study 50 patients were included. Mean age of patients was 57.52 ± 14.64 years with 23 % female patients and 77 % male patients.

Measurement of proteinuria by dipstick analysis, one plus proteinuria indicates first sign of kidney damage while two plus protein means that can be a sign of kidney disease. The 2 plus means that this was not quantitative. It means that there is "some" protein in urine but does not tell us how much. While patients with proteinuria have unusually high amounts of protein in their urine are noted as three plus. The condition is often a sign of kidney disease.



Graph-1: (A) Measurement of proteinuria by dipstick analysis – DOA; (B) Measurement of proteinuria by dipstick analysis – DOD

Gender	Number of patients	Percentage
Male	46	77
Female	14	23

Table-1: Gender wise distribution of patients

Investigations	Date of admission (DOA)	Date of discharge (DOD)
Total Leucocyte Count (TLC) (Mean \pm SD) (/cmm)	10,815 \pm 4542	17,665 \pm 8550
Erythrocyte Sedimentation Rate (ESR) (Mean \pm SD)	46.86 \pm 1.73	48.01 \pm 0.50
Platelet count (Mean \pm SD) (In lakhs)	1.94 \pm 1.18	3.40 \pm 4.38
CRP (Mean \pm SD)	25.50 \pm 7.80	26.41 \pm 5.11
D – Dimer (Mean \pm SD) (μ g/L)	0.72 \pm 0.08	0.77 \pm 0.31

Table-2: Laboratory investigations of patients

Proteinuria	Date of admission (DOA)	Date of discharge (DOD)
Nil	8	0
1+	11	4
2+	17	13
3+	14	33

Table-3: Measurement of proteinuria by dipstick analysis

In our study, mean proteinuria in DOA patients was one plus, while in DOD patients it was found three plus, strongly indicate found high prevalence of patients with abnormal proteinuria (87%).

In our study, there was found significant changes in proteinuria in patients of COVID-19 in comparison to date of admission ($P < 0.5$ as significant with considering 95% confidence interval).

DISCUSSION

In our study, total of 50 patients were hospitalized with COVID-19 confirmed after investigations and RT PCR test as per guidelines of government. In our present study, we found high prevalence of patients with abnormal proteinuria (87%). In our study, there was found significant changes in proteinuria in patients of COVID-19 in comparison to date of admission ($P < 0.5$ as significant with considering 95% confidence interval).

Dipstick analysis is used in most outpatient settings to semi quantitatively measure the urine protein concentration. The urine protein dipstick test measures the presence of proteins, such as albumin, in a urine sample. If the glomeruli are damaged, protein from the blood leaks into the urine. Normally, there should have less than 150 milligrams (about 3 percent of a teaspoon) of protein in the urine per day. Having more than 150 milligrams per day is called proteinuria. Less than 150 150 milligrams per day results are considered as Nil while more than it to be stated as +, ++, +++ depending on their severity.

It has been observed that, Proteinuria has been commonly reported in patients with COVID-19.³ Our objective was to correlate this factor statistically and confirm it. Coronavirus disease 2019 (COVID-19) is a novel disease resulting from infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has quickly risen since the beginning of 2020 to become a global pandemic.⁴ The rapid spread of the novel SARS-CoV-2 virus and our limited knowledge of its clinical course have caused a unique shift in our healthcare system.

As reported in non-US cohorts, we observed a high prevalence of proteinuria in patients hospitalized with COVID-19. We noted that even after adjustment of significant baseline differences, proteinuria at admission significantly influenced in-hospital outcomes.^{4,5,6} The associations between the proteinuria in hospitalized patients before COVID-19 is well-documented.

SARS-CoV-2 utilizes angiotensin-converting enzyme 2 (ACE2) as a port of entry into cells⁷, which is found mainly in the proximal tubules and to a lesser extent in podocytes.⁷ Recent pathology data from autopsy and kidney biopsy studies are against direct viral toxicity being a primary mechanism of kidney injury in COVID-19.⁸ These studies suggest acute tubular injury⁸ and cytokine-mediated hyperimmune response as potential mechanisms of kidney injury. It has been postulated that SARS-CoV-2 binding to ACE2 on endothelial cells induces an inflammatory response leading to a systemic vasculitis-

like syndrome.⁹ Some cases of COVID-19 pneumonia have presented with kidney injury, and autopsy findings for patients with COVID-19 have revealed renal involvement.^{10,11} Guangchang Pei, et al found, renal abnormalities occurred in the majority of patients with COVID-19 pneumonia. Although proteinuria, hematuria, and AKI often resolved in such patients within 3 weeks after the onset of symptoms, renal complications in COVID-19 were associated with higher mortality.¹²

In our view point, this is the first study reported from our region to highlighting potential of proteinuria in COVID-19 cases and their strong association as an important prognostic factor.

Study limitations:

1. It was a monocentric study
2. This study included limited number of cases
3. This study was with limited duration of observations of patients
4. We consider only proteinuria in present study while other investigations though carried out in hospital, however not included in present study.

CONCLUSION

From present study, we conclude that incidence of proteinuria is found positively associated with hospitalized COVID-19 patients. There was found statistically significant results in patients on DOD with DOA. Hence we can conclude that proteinuria is to be an important prognostic marker in COVID-19 patients.

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