



## URINE BIOCHEMICAL MARKERS AS A PREDICTOR OF SEVERE COVID 19 INFECTION

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## ABSTRACT

**BACKGROUND-** The study aimed to assess the role of various urinary biochemical markers in predicting the severity of the COVID 19 infection.

**METHODOLOGY-** This study was conducted as a retrospective study on patients admitted in COVID ICU, HDU and COVID Care centre of tertiary care centreduring the 3 months period with reporting of urine biochemical parameters such as Urinary Occult Blood, Leukocyte esterase, Urinary Protein, Specific Gravity (SG) and pH. Using a questionnaire, sociodemographic variables, clinical features, condition of patient and findings of urinalysis were obtained and documented. Also, the outcome of the patients i.e. weather discharged or death was also noted.

**RESULTS-** A total of 194 patients were enrolled, of them, 96 were severe cases whereas 98 were mild to moderate cases. Mean age of patients with severe COVID 19 infection was significantly higher ( $57.9 \pm 7.5$  years) as compared to mild to moderate infections ( $49.6 \pm 10.6$  years) ( $p < 0.05$ ). Urinary occult blood and urine protein were observed in significantly higher proportions of patients with severe COVID infection as compared to mild to moderate COVID infections ( $p < 0.05$ ). Both urinary occult blood and urine protein were significant predictors of severe COVID 19 infections on univariate as well as multivariate analysis ( $p < 0.05$ ).

**CONCLUSIONS-** Urine biochemical parameters may be utilized for both diagnosis and predicting severe COVID 19 infection. In patients with suspected COVID 19 infection, urinalysis must be performed routinely. This may help in better clinical management and predicting severe illness.

**KEYWORDS :** urinary markers, covid infection, severity, protein

## INTRODUCTION

COVID 19 infection, a RNA viral disease is caused by SARS Co-V virus. First case was reported in China in 2019 and later, this deadly virus affected population all over the world leading to pandemic.<sup>[1,2]</sup> As a result, the pandemic burdened the health care systems Globally and India is no exception. The patient present with variable symptoms i.e. from asymptomatic to pneumonia to severe form of respiratory illness viz. acute respiratory distress syndrome in the adult (ARDS) along with involvement of multiple organs.<sup>[3,4]</sup>

Literature suggest that urinary system involvement is one of the common feature of COVID 19 infection and is characterized by progressive deterioration of renal functions.<sup>[5]</sup> Thus it was postulated that various urinary biochemical markers which are useful in diagnosis of UTI and monitoring treatment can be utilized for predicting severity of COVID 19 infections. Previous studies have shown some correlation of urine biochemical parameters and COVID 19 infection.<sup>[6,7]</sup> The present study was therefore conducted to assess the role of various urinary biochemical markers in predicting the severity of the COVID 19 infection.

## METHODOLOGY

This study was conducted as a retrospective study on patients admitted in COVID ICU, HDU and COVID Care centre of LN Medical College and associated JK Hospital during the 3 months period i.e. 1<sup>st</sup> May- 31<sup>st</sup> July 2021. All the RTPCR confirmed cases belonging to age range of more than 18 years and patients with reporting of urine biochemical parameters such as Urinary Occult Blood, Leukocyte esterase, Urinary Protein, Specific Gravity (SG) and pH were included. Patients not requiring admission, with comorbidities such as CKD, diabetes, hypertension and with positive urine culture were excluded from the study. Patients admitted in ICU and HDU were considered as severe cases whereas those admitted in COVID care centre were considered as mild to moderate cases.

After obtaining ethical clearance from Institute's ethical committee, records of all the patients were retrieved from MRD Department. All the cases in whom urinary findings were

available and fulfilling inclusion criteria were separated and accessed. Using a questionnaire, sociodemographic variables, clinical features, condition of patient and findings of urinalysis were obtained and documented. Also, the outcome of the patients i.e. weather discharged or death was also noted.

**STATISTICAL ANALYSIS-** Data was compiled using MsExcel and analysed with the help of IBM SPSS software version 20. Continuous variables were expressed as mean and standard deviation whereas continuous variables were represented as frequency and proportions. T test and Chi square test were used for comparison of continuous and categorical variables respectively between mild to moderate and moderate to severe cases. The data was considered statistically significant when P-value was  $< 0.05$ .

## RESULTS

A total of 372 patients were admitted during the study period, of them, 194 cases met the inclusion and exclusion criteria and thus were enrolled in our study. Of them, 96 were moderate to severe cases whereas 98 were mild to moderate cases.

**Table 1- Distribution according to sociodemographic variables**

Sociodemographic variables		Mild to moderate (n=98)	Severe (n=96)	Total (n=194)	P value
Age (years)	Mean $\pm$ SD	49.6 $\pm$ 10.6	57.9 $\pm$ 7.5	53.7 $\pm$ 9.5	0.001
	Gender				
	Male	61 (62.2)	64 (66.7)	125 (64.4)	0.52
	Female	37 (37.8)	32 (33.3)	69 (35.6)	
Place of residence	Urban	74 (75.5)	77 (80.2)	151 (77.8)	0.43
	Rural	24 (24.5)	19 (19.8)	43 (22.2)	

Mean age of patients with severe COVID 19 infection was significantly higher ( $57.9 \pm 7.5$  years) as compared to mild to moderate infections ( $49.6 \pm 10.6$  years) ( $p < 0.05$ ). However, place of residence and gender composition was similar in the two groups ( $p > 0.05$ ).

**Table 2- Comparison of urine biochemical parameters**

between the groups

Urine biochemical markers		Mild to moderate (n=98)	Severe (n=96)	Total (n=194)	P value
Urinary occult blood	Present	8 (8.2)	21 (21.9)	29 (14.9)	0.007
	Absent	90 (91.8)	75 (78.1)	165 (85.1)	
Urine glucose	Present	24 (24.5)	26 (27.1)	50 (25.8)	0.68
	Absent	74 (75.5)	70 (72.9)	144 (74.2)	
Urine protein	Present	7 (7.1)	24 (25)	31 (16)	0.006
	Absent	91 (92.9)	72 (75)	163 (84)	
Leucocyte esterase	Present	3 (3.1)	4 (4.2)	7 (3.6)	0.69
	Absent	95 (96.9)	92 (95.8)	187 (96.4)	
Urine ketones	Present	75 (76.5)	78 (81.3)	153 (78.9)	0.42
	Absent	23 (23.5)	18 (18.7)	41 (21.2)	
Specific gravity	Mean±SD	1.02±0.005	1.03±0.007	1.02±0.006	0.26
pH	Mean±SD	5.9±0.77	5.7±0.75	5.8±0.76	0.07

In present study, urinary occult blood and urine protein were observed in significantly higher proportions of patients with severe COVID infection as compared to mild to moderate COVID infections (p<0.05).

**Table 3- Univariate and multivariate analysis of urine biochemical markers for predicting severity of COVID 19 infection**

Urine biochemical markers	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Urinary occult blood	1.34 (0.78-3.32)	0.007	2.27 (1.29-3.33)	0.002
Urine glucose	1.17 (0.23-2.79)	0.68	1.26 (1.01-1.97)	0.35
Urine protein	2.12 (1.23-4.25)	0.006	3.14 (1.13-5.15)	0.001
Leucocyte esterase	1.27 (0.57-1.87)	0.69	1.71 (0.92-3.24)	0.21
Urine ketones	1.12 (0.71-2.93)	0.42	1.24 (0.39-1.79)	0.30

Among these urine biochemical markers, both urinary occult blood and urine protein were significant predictors of severe COVID 19 infections on univariate as well as multivariate analysis (p<0.05).

**DISCUSSIONS**

Novel coronavirus, a SARS COV-2 infection has been originated from Wuhan, China and spread across the countries via respiratory route. COVID 19 infection was declared pandemic by World health Organization (WHO) on 11<sup>th</sup> March 2020.<sup>[8]</sup> Since then, pandemic lead to rapid surge of cases of varying severity leading to enormous burden on health care system. The COVID 19 virus has a strong affinity for angiotensin converting enzyme 2 (ACE 2) receptors, the virus bind to this receptor and initiate infection.<sup>[9]</sup> ACE-2 enzyme is predominantly present in lung epithelial cells (type II alveolar cells) as well as other organs such as kidney, gut, heart etc.<sup>[10]</sup> Thus, involvement of renal and urinary system is reported to be higher in COVID 19 infection. The spectrum of infection may varies from asymptomatic illness, to acute respiratory illness, to severe form of illness including ARDS and multiple organ failure.<sup>[11,12]</sup>

Previous literature have suggested various systemic factors predicting the severity of COVID 19 infection. These factors include advanced age, dyspnea, fatigue, sputum production, presence of comorbidities and various blood parameters such as D dimer, CRP, serum ferritin and LDH levels.<sup>[13-15]</sup> Our study aimed at assessing the role of urinary biomarkers in predicting the severity of COVID 19 infection. Urine routine microscopy and urine dipstick was not being performed routinely initially, but as we went through literature<sup>[6,7]</sup>, the importance of urine examination in COVID 19 infection was

realized and then urine examination was being advised in each case admitted either in HDU, ICU or COVID care centre. Our study documented that presence of occult blood in urine as well as proteinuria were significant predictors of severity of COVID 19 infection on univariate and multivariate analysis indicating significant effect of COVID 19 infection on occult blood in urine and proteinuria. Similar findings were documented by previous studies in which urine protein and occult urine blood were significantly higher in moderate and severe cases as compared to mild cases or healthy controls (p<0.05).<sup>[6,7]</sup> Liu et al however documented significantly higher occult blood in urine and specific gravity in patients with COVID 9 infection of varying severity as compared to healthy controls. Also, urinary glucose and urinary protein were significantly higher in severe and critical COVID cases as compared to moderate cases supporting the findings of our study.<sup>[16]</sup> Cytokine storm secondary to COVID 19 infection is one of the major cause of ARDS and renal damage. As the ACE-2 receptors are also present in urinary tract, cellular damage to renal and urinary system may be responsible for urine occult blood and proteinuria.<sup>[17-19]</sup> Renal involvement has been described as an unfavorable factor associated with disease progression and severe illness.<sup>[7]</sup>

In present study, urinary ketone were observed in higher proportions of severe cases but the difference was statistically insignificant (p>0.05), indicating the effect of virus on urinary and renal system due to lung function impairment rather than ketoacidosis. These findings were concordant with the findings of Murgod et al<sup>[7]</sup> and Liu et al<sup>[16]</sup>.

Our study had certain limitations, mild asymptomatic cases were not included in our study as due to overburdened health care system, mild asymptomatic cases were advised home quarantine and though investigations were suggested in them, but the maintenance of record for OPD based patients could not be maintained at our centre. The study was conducted as a retrospective study but a prospective study would have yielded a true scenario.

**CONCLUSIONS**

Urine biochemical parameters may be utilized for both diagnosis and predicting severe COVID 19 infection. In patients with suspected COVID 19 infection, urinalysis must be performed routinely. This may help in better clinical management and predicting severe illness.

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