

## Letter to the Editor

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# Urinalysis parameters for predicting severity in coronavirus disease 2019 (COVID-19)

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To the Editor,

We read with interest the recent article by Liu et al., who described the clinical significance of urinalysis for predicting the severity of coronavirus disease 2019 (COVID-19) in a group of 119 Chinese patients [1]. It is now undeniable that the managed care of patients with COVID-19, which has recently been upgraded to a pandemic disease by the World Health Organization (WHO) after causing over 200,000 deaths worldwide [2], encompasses the identification of clinical and laboratory parameters, enabling accurate risk stratification of progressing toward severe or critical disease.

As it has now been clearly established that urinary tract involvement is commonplace in patients with COVID-19, and that progressive deterioration of renal function shall be considered an unfavorable prognostic factor [3], we present here the first report of urinalysis abnormalities

in a series of COVID-19 Italian patients admitted to the emergency department (ED) of Valcamonica Hospital of Esine, between March 13 and April 8, 2020.

The study population of this retrospective observational investigation consisted of 226 patients consecutively admitted to the local ED for COVID-19. Disease diagnosis was based on current standards, thus encompassing suggestive findings on chest computed tomography (CT) and positive results of real-time reverse transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV-2 on oropharyngeal and nasopharyngeal swabs. Overall, 154 of our patients were male (median age, 66 years; interquartile range [IQR], 57–75 years), whilst

**Table 1:** Urinalysis data in urine samples collected at emergency department admission in 226 patients who have been diagnosed with coronavirus disease 2019 (COVID-19).

Parameter	Results
Median pH (IQR)	6.0 (5.5–6.5)
Median SW (IQR)	1.022 (1.019–1.026)
Protein presence	203/226 (89.8%)
Blood presence	163/226 (72.1%)
Urinary sediment	
WBC	184/226 (81.4%)
RBC	159/226 (70.4%)
Bacteria	45/226 (19.9%)
Casts	111/226 (49.1%)
Hyaline	59/226 (26.1%)
Granular	15/226 (6.6%)
Hyaline-granular	72/226 (31.9%)
Leucocytes	1/226 (0.4%)
Epithelial	4/226 (1.8%)

Results are reported as number and % of patients with pathological data on the total number of 226 urinary samples collected at the emergency department unless otherwise specified. Presence: if  $\geq 1$  element/hpf is present. Absence: no element is visible in one of the 20 optic fields of SediMax images. IQR, interquartile range; RBC, red blood cells; WBC, white blood cells.

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72 were female (median age, 69 years; IQR, 57–76 years). Urinalysis was carried out in the local laboratory with the Aution Max AX-4030 (Arkray, Kyoto, Japan) and SediMax (Menarini, Firenze, Italy) systems, using proprietary reagents, whilst microscopic assessment was performed when necessary, according to results of biochemical urinalysis. Exclusion criteria were past history of diabetes and kidney disease. From the initial group of 226 patients, 51 were immediately discharged from the ED after results of chest CT, showing non-severe disease, whilst the remaining 175 patients were hospitalized. From this group of patients, 45 were selected for inclusion, divided into two groups, the former including 20 patients who died during hospital stay and the latter encompassing 25 patients who displayed clinical improvement and

could hence be discharged. The remaining 130 patients were still hospitalized at the time of writing this report, so no final information on disease outcome had become available.

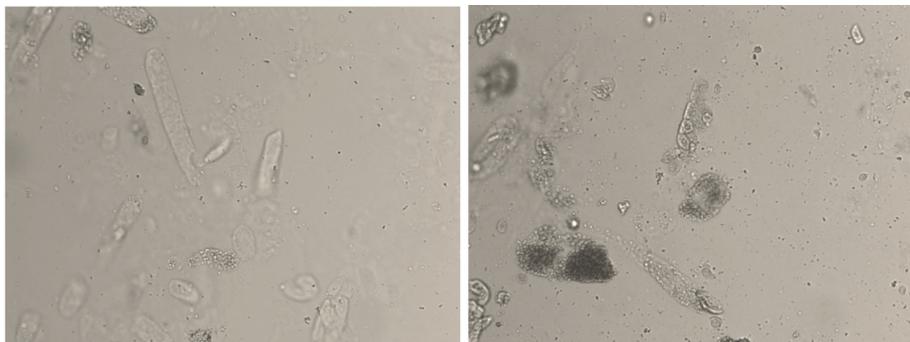
The results of urinalysis in all the 226 COVID-19 patients originally admitted to the local ED are shown in Table 1. Cumulatively, proteinuria and hematuria were present in most patients, already at ED admission. The analysis of the urine sediment also revealed the presence of erythrocytes and casts in nearly half of all patients.

The comparison of urinalysis in the two study cohorts (i.e. in patients who died or in those who could be discharged) is shown in Table 2. Notably, most urinalysis parameters were not found to be substantially different in patients who died during hospital stay and those who

**Table 2:** Comparison of urinalysis data in urine samples collected at emergency department admission in patients who have been diagnosed with coronavirus disease 2019 (COVID-19), divided according to clinical outcome.

Parameter	In-hospital death (n=20)	Discharged (n=25)	p-Value
Age, years	73.5 (64.5–79.0)	64.0 (56.3–71.5)	0.005
Plasma creatinine >URL	16 (80%)	5 (20%)	<0.001
Plasma urea >URL	15 (75%)	6 (24%)	0.001
eGFR <60, mL/min per 1.73 m <sup>2</sup>	6 (30.0%)	5 (20.0%)	0.443
Median pH (IQR)	5.75 (5.5–6.0)	6.0 (5.5–6.0)	0.889
Median SW (IQR)	1.022 (1.019–1.025)	1.022 (1.0187–1.0255)	0.670
Protein			
Negative	0 (0.0%)	1 (4.0%)	0.371
± and 1	8 (40.0%)	14 (56.0%)	0.291
+2 and +4	12 (60.0%)	10 (40.0%)	0.187
Blood			
Negative	5 (25.0%)	4 (16.0%)	0.458
± and 1	9 (45.0%)	18 (72.0%)	0.069
+2 and +4	6 (30.0%)	3 (12.0%)	0.138
Urinary sediment			
Mucus	2 (10%)	10 (40%)	0.025
Bacteria	6 (30%)	6 (24%)	0.655
WBC	15 (75%)	17 (68%)	0.611
Negative	9 (45%)	7 (80%)	0.242
<20 by optic field	11 (55%)	16 (64%)	0.545
≥20 by optic field	0 (0%)	2 (8%)	0.201
RBC			
Negative	6 (30%)	6 (24%)	0.655
<20 by optic field	12 (60%)	17 (68%)	0.582
≥20 by optic field	2 (10%)	2 (8%)	0.817
Tubular cells	8 (40.0%)	3 (12.0%)	0.032
Urothelial cells	3 (15.0%)	2 (8%)	0.463
Hyaline casts	9 (45%)	5 (25%)	0.075
Hyaline-granular casts	6 (30%)	6 (24%)	0.652
Granular casts	12 (60%)	2 (8%)	<0.001

Statistical evaluation was performed by the  $\chi^2$  test and by the Mann-Whitney test for independent samples for continuous variables; a p-value <0.05 or less was considered significant. Plasma creatinine reference interval, males: 55.4–90.8, females: 44.6–76.2  $\mu\text{mol/L}$  and urea: 3.2–7.9 mmol/L for the Valcamonica population. eGFR, estimated glomerular filtration rate; IQR, interquartile range; RBC, red blood cells; SW, specific weight; URL, upper reference limit; WBC, white blood cells.



**Figure 1:** SediMax images of urinary sediment in bright-field in COVID-19 patients at hospital admission.

In the left image are clearly visible hyaline and hyaline-granular casts. In the right image, a granular cast is present while a cluster of tubular cells is visible at the center of it.

could be discharged, though some interesting aspects can be highlighted. One paradigmatic feature was the more frequent presence of granular cylinders and tubular cells in the urine of patients who died, as also shown in Figure 1. Renal impairment was also found to be more frequent in patients who died compared to those who could be discharged. This is clearly reflected by the higher rate of abnormal urea and creatinine values at admission in patients who died (i.e. between 75% and 80%) compared to those who could be discharged (i.e. between 20% and 24%).

Taken together, these urinalysis findings in a population of Italian COVID-19 patients seem in keeping with data earlier published in a Chinese cohort [1, 4], thus confirming the frequent presence of proteinuria and hematuria in this infectious disease [1, 4]. Nevertheless, the values of these urine parameters were found to be consistently higher than in previous studies, thus suggesting that our COVID-19 population was perhaps in worst clinical conditions at ED admission, as mirrored by the considerably high mortality in our setting (i.e. 26%). Another important aspect that emerged from this retrospective investigation is that renal involvement may be a significant predictor of unfavorable disease progression, thus confirming previous assumptions [3], and ultimately reaffirming the importance of laboratory testing in risk stratification of COVID-19 [5, 6].

We can hence conclude that urinalysis shall be regularly performed in all patients with COVID-19, whereby it may provide important information for clinical management and risk prediction.

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**Ethical approval:** The local Institutional Review Board deemed the study exempt from review.

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