

Marcelo Petean Amaro, Lucas Mira Gon, André Canetti Rubes, Caio Di Donato Ribeiro, Antônio Luis Eiras Falcão, Cássio Luís Zanettini Riccetto

Division of Urology, Department of Surgery, Hospital das Clínicas, School of Medical Sciences, State University of Campinas

Introduction and Objectives

Bacterial coinfections have been reported in 7% of hospitalized coronavirus disease (COVID-19) patients and in up to 14% of COVID-19 patients in intensive care units (ICUs), (1) The lungs, bloodstream, and urinary tract are among the most common sites of coinfection.

In 2020, Haoheg et al. reported bacterial lung infections (55%) as the most common coinfection among 38 critically ill hospitalized patients with COVID-19, followed by sepsis (34%) and urinary tract infection (UTI) (7.8%). (2) Although UTIs play an important role in coinfections, it is unclear whether there is a relation between UTI and COVID-19. There is still a lack of evidence of epidemiological data, microbiological profiles, and risk factors for the possible association.

Therefore, the objective of this study was to identify the main risk factors for UTI in hospitalized COVID-19 patients and to find the most common etiological agents.

Methods

This retrospective study analyzed the data of patients admitted to a regional hospital between March 2020 and August 2021. As a reference center, most wards and ICUs were reassigned to treat COVID-19 patients during that period. The study included all patients who had SARS-CoV-2 infection confirmed by polymerase chain reaction (PCR) testing and at least one urine culture sample available.

UTI was diagnosed if 100,000 or more colony-forming units were detected in the urine culture. Only samples collected by sterile catheterization or mid-stream urine samples after disinfection were considered.

The variables studied as possible risk factors for UTI in COVID-19 patients were age, sex, leukopenia (defined as a white blood cell count below 4,000 leukocytes/μL (3)), comorbidities [such as diabetes mellitus (DM) and obesity], ICU admission, orotracheal intubation (OTI), indwelling urinary catheter (IUC) use, and length of hospital stay.

Tables

Table 1: General descriptive analysis.

Variables	average ± SD min - max	Data (n = 447)
Age (years)	57.8 ± 16.78 19 - 98.00	
White Blood Count (per microliter)	average ± SD min - max 8.84 ± 5.14 0.30 - 30.80	
Hospital stays (days)	average ± SD min - max 26.5 ± 29.82 1.00 - 348.00	
Gender	Female Male	158 (41.6%) 281 (58.4%)
Hospitalization site (ICU)	Ward Intensive Care Unit	188 (41.4%) 252 (58.6%)
Urine culture	Positive Negative	185 (41.4%) 262 (58.6%)
Death	Yes No	143 (32.1%) 303 (67.9%)
Diabetes Mellitus (DM)	Yes No	172 (38.5%) 275 (61.5%)
Obesity	Yes No	108 (23.9%) 340 (76.1%)
DM and Obesity	none both	226 (50.7%) 221 (49.3%)
Leukopenia	Yes No	37 (8.3%) 410 (91.7%)
Indwelling Urinary Catheterization (IUC)	Yes No	280 (62.6%) 167 (37.4%)
Orotracheal Intubation (OTI)	Yes No	238 (53.2%) 209 (46.8%)
IUC or OTI	None Both	156 (35.1%) 228 (51.2%)
> 60 years old	Yes No	210 (46.9%) 231 (51.7%)
Hospital stay > 7 days	Yes No	363 (81.2%) 84 (18.8%)

Table 2: Description of COVID-19 patients with or without Urinary Tract Infection (UTI)

Variables	Urine Culture No (n=252)	Urine Culture Yes (n=195)	P Value	Pathogens	Frequency (n=185)	Percentage
Age (average ± SD)	55.41 ± 13.13	61.38 ± 13.01	0.0002	<i>Candida albicans</i>	54	29.2%
White Blood Cells (average ± SD)	9.40 ± 4.97	10.47 ± 5.32	0.0276	<i>Klebsiella pneumoniae</i>	33	17.8%
Hospital Stay (average ± SD)	18.72 ± 21.94	37.51 ± 35.15	<0.001	<i>Enterococcus faecalis</i>	28	15.1%
Female	80 (34.4%)	86 (51.3%)	0.0002	<i>Candida tropicalis</i>	26	14.1%
Male	172 (65.6%)	92 (48.7%)		<i>Candida glabrata</i>	25	13.5%
Ward	155 (61.7%)	46 (25.2%)	<0.001	<i>Escherichia coli</i>	22	11.9%
Intensive Care Unit (ICU)	128 (48.3%)	139 (74.7%)		<i>Pseudomonas aeruginosa</i>	20	10.8%
Death No	200 (76.6%)	103 (55.7%)	<0.001	<i>Candida parapsilosis</i>	9	4.9%
Death Yes	61 (23.4%)	82 (44.3%)		<i>Enterococcus faecium</i>	9	4.9%
DM [†] Yes	181 (69.1%)	94 (50.3%)	<0.001	<i>Toothospora asahi</i>	6	3.2%
DM [†] No	81 (30.9%)	91 (49.2%)		<i>Proteus mirabilis</i>	5	2.7%
Obesity No	204 (78.2%)	138 (73.5%)	0.2559	<i>Acinetobacter baumannii</i>	4	2.2%
Obesity Yes	57 (21.8%)	49 (26.5%)		<i>Serratia marcescens</i>	4	2.2%
DM [†] and Obesity (none)	146 (55.6%)	80 (42.2%)	0.0023	<i>Staphylococcus epidermidis</i>	3	1.6%
DM [†] and Obesity (both)	23 (8.9%)	25 (12.9%)		<i>Klebsiella variicola</i>	3	1.6%
Leukopenia No	235 (89.7%)	175 (94.6%)	0.0641	<i>Enterobacter cloacae</i>	3	1.6%
Leukopenia Yes	27 (10.3%)	19 (9.4%)		<i>Klebsiella aerogenes</i>	3	1.6%
IUC ^{**} No	133 (50.8%)	32 (17.5%)	<0.001	<i>Microbota Multicola</i>	2	1.1%
IUC ^{**} Yes	128 (49.2%)	151 (82.5%)		<i>Staphylococcus haemolyticus</i>	2	1.1%
OTI ^{**} No	155 (59.2%)	54 (28.2%)	<0.001	<i>Morganella morganii</i>	2	1.1%
OTI ^{**} Yes	107 (40.8%)	131 (70.8%)		<i>Staphylococcus aureus</i>	2	1.1%
Elderly No	156 (59.6%)	75 (40.3%)	<0.001	<i>Clostridium cloacii</i>	1	0.5%
Elderly Yes	106 (40.4%)	119 (65.8%)				
IUC ^{**} and OTI ^{**} (none)	128 (49.1%)	35 (18.4%)	<0.001			
IUC ^{**} and OTI ^{**} (Both)	100 (38.2%)	128 (69.6%)				
Hospital Stay < 7 days	75 (28.6%)	9 (4.4%)	<0.001			
Hospital Stay > 7 days	187 (71.4%)	179 (95.1%)				

[†] Diabetes Mellitus; ^{**} Intensive Care Unit (ICU); ^{††} Orotracheal Intubation (OTI)

Results

A total of 447 hospitalized patients with PCR-confirmed SARS-CoV-2 infection were included in the study. Their mean age was 57.8 ± 16 years, 58% were male, and 81% required hospitalization for >7 days. ICU admission and ventilatory assistance with OTI were required in 58.6% and 53% of the patients, respectively. An association between UTI and COVID-19 during hospitalization was found in 41.4% of the patients. (Table 1.)

IUC use and OTI were the main risk factors for UTI (odds ratio (OR) = 4.86 and 3.51, respectively; p<0.0001). When combined, these two factors increased the risk of UTI by more than five times (OR = 5.3, p<0.001). The necessity of intensive care was associated with a three-fold higher chance of UTI development than that in patients hospitalized only in non-ICU wards (p<0.0001). Other risk factors for UTI in hospitalized COVID-19 patients were age, sex, and DM. Patients aged over 60 years were 2.8 times more likely to acquire UTI (p<0.0001). Female patients were twice as likely as male patients (p=0.0002) and patients with DM were 2.16 times more likely than those without diabetes (p=0.0001) to acquire UTI. However, obesity and leukopenia were not associated with UTI development, contrary to the expectation based on previous findings (4, 5) (Table 2).

The most prevalent microorganisms in the positive urine culture samples were *Candida* spp. (64.2%), *Klebsiella pneumoniae* (17.8%), *Enterococcus faecalis* (15.1%), *Escherichia coli* (11.9%), *Pseudomonas aeruginosa* (10.8%), and *Enterococcus faecium* (4.9%) (Table 3).

Conclusion

Hospitalized patients with moderate-to-severe pulmonary infections caused 'by SARS-CoV-2 are associated with higher incidence of UTI than previously reported; this suggests a relationship between COVID-19 and UTIs. The main associated factors of UTI in COVID-19 patients were IUC use and mechanical ventilation, other factors such as age, female sex, and DM also contributed to a higher risk of UTI and were associated with worse clinical outcomes

The incidence of *Candida* spp. in our study was still higher than those in other reports from ICU (6). This finding can be related to regional characteristics or indicate a possible association with COVID-19. SARS-CoV-2 can be detected in different tissues, and its presence in urine and urothelial could be related to a higher risk of UTI.

The limitation of this study was that owing to its retrospective nature, only available data could be used. Other information, such as obesity, body mass index, sarcopenia, and weight loss during hospitalization could not be investigated because of a lack of records. Nonetheless, we found high incidence of UTIs in a large cohort, which consistently pointed toward an association of UTI with COVID-19.

References

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