

# Investigation Of Bacterial Coinfection Among Hospitalized Patients With COVID-19: A Retrospective Study In A Turkey Training And Research Hospital

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## ABSTRACT

**Objective:** In the present study, we aimed to determine the distribution and antibiotic resistance rates of bacteria isolated from endotracheal aspirates (ETA), blood, catheters, urinary, and sputum taken from COVID-19 patients who hospitalized in the Siirt Training and Research Hospital.

**Methods:** A retrospective observational analysis of all COVID-19 patients hospitalized in Siirt Training and Research Hospital was undertaken. We determined the distribution and antibiotic resistance rates of bacteria isolated from endotracheal aspirates (ETA), blood, catheters, urinary, and sputum taken from COVID-19 patients who hospitalized in the Siirt Training and Research Hospital. between March 2020 and July 2020.

**Results:** In this study, we identified a total of 720 patients with confirmed SARS-CoV-2 during the study period (15 March 2020 to 1 July 2020). Significant growth was detected in 64 (8.9%) of Endotracheal aspirate (ETA), blood, catheter and urinary samples admitted to our laboratory in 3.5 months period. Most bacteria detected in blood (41) and ETA (15) samples. In the 36 Gram-positive bacteria detected in the blood cultures, 19 Coagulase negative Staphylococcus (CNS), 7 Enterococcus spp., 5 Staphylococcus epidermidis, 2 Staphylococcus hominis, 2 Staphylococcus capitis and 1 staphylococcus haemolyticus were identified. In the 4 Gram-positive bacteria detected in the catheter samples, 2 CNS, 1 Staphylococcus aureus and 1 S. capitis were identified. No Gram-positive bacteria were grown in the ETA. In the 15 Gram-negative bacteria detected in ETA, 13 Acinetobacter baumannii and 2 Klebsiella spp. were identified. In the 5 Gram-negative bacteria detected in blood cultures, 3 A. baumannii, 1 E. coli 1 Klebsiella spp. were identified and In the 3 Gram-negative bacteria detected in catheter, 2 A. baumannii and 1 Pseudomonas aeruginosa were identified. Among Gram-positive bacteria, methicillin resistances were detected in 57.9 % (n=11) of CNS and vancomycin resistance rates were 14.3% in Enterococcus spp. isolated from blood samples. The A. baumannii isolates from ETA were found to be resistance at least three antibiotics. We detected that 100% (n=13) of A. baumannii isolated from ETA were resistant to piperacillin-tazobactam, meropenem, ciprofloxacin, ceftazidime and 61.5% of resistant to amikacin. 2 Klebsiella spp. isolated from ETA were resistant to ciprofloxacin, amikasin, piperacillin-tazobactam, meropenem, tigecycline, trimethoprim-sulfamethoxazol and ceftazidime and 1 P. aeruginosa isolated from catheter cultures was found to be resistant to amikasin, piperacillin-tazobactam, meropenem, ciprofloxacin, trimethoprim-sulfamethoxazol and ceftazidime.

**Conclusion:** As a result, the frequency of microbiologically confirmed bacterial co-infections was found low in confirmed SARS-CoV-2 patients admitted to our hospital. Nevertheless, when present, they can cause serious illness with worse consequences. Since the incidence, nature, and effect of late secondary bacterial infections are less clear, more studies are needed.

**Keywords:** SARS-CoV-2; Bacterial co-infection; Antimicrobial stewardship

## Introduction

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a pandemic coronavirus that greatly affects healthcare worldwide and also propounded a formidable medical challenge to healthcare systems and clinicians [1,2]. It is known that

COVID-19 is as mainly a respiratory illness and mostly leads to pneumonia [3-6]. Bacterial, particularly Streptococcus pneumoniae and Staphylococcus aureus, have been reported as common complications arising in other pandemics caused by influenza viruses [2,7,8]. However, It hasn't fully understood bacterial coinfection in hospitalized patients with

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coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [9]. Wider SARS-CoV-2 data shows that the lack of information about the frequency, nature, and susceptibility profiles of secondarily infecting pathogens continues [5,10]. For this reason, we aimed to determine the distribution and antibiotic resistance rates of bacteria isolated from endotracheal aspirates (ETA), blood, catheters, urinary, and sputum taken from COVID-19 patients who hospitalized in the Siirt Training and Research Hospital.

### Materials and Methods

A retrospective observational analysis of all COVID-19 patients hospitalized in Siirt Training and Research Hospital was undertaken. We determined the distribution and antibiotic resistance rates of bacteria isolated from endotracheal aspirates (ETA), blood, catheters, urinary, and sputum taken from COVID-19 patients who hospitalized in the Siirt Training and Research Hospital, between March 2020 and July 2020. In samples sent from the same patient at different times, these samples were excluded when the same microorganism reproduced. Clinical samples were transferred on 5% sheep blood agar and “eosin methylene blue” (EMB) agar. Plates were incubated at 37°C for 18-24 hours; Plaques that produced  $\geq 100,000$  cfu/ml in pure culture were included in the study. Microorganisms that could not be identified by conventional methods were identified with the automated system VITEK® 2 (bioMérieux, Marcy l’Etoile, France). Antibiotic susceptibility of growing bacteria was investigated by the disc diffusion method in line with Clinical and Laboratory Standards Institute recommendations. Bloody agar was used for streptococci and Mueller-Hinton agar (Becton, Dickinson and Company, Franklin Lakes, New Jersey, USA) was used for other microorganisms.

### Results And Discussion

In this study, we identified a total of 720 patients with confirmed SARS-CoV-2 during the study period (15 March 2020 to 1 July 2020). Significant growth was detected in 64 (8.9%) of ETA, blood, catheter and urinary samples admitted to our laboratory in 3.5 months period. No growth observed in sputum samples and only one bacterial species identified as *Escherichia coli* was grown in urinary samples. Growth was observed in 41 blood samples, 15 ETS samples,

7 catheter and one urinary sample. 36 (87.48%) Gram-positive and 5 (12.2 %) Gram-negative bacteria were isolated and identified from blood samples, 15 (100%) Gram-negative bacteria were isolated and identified from ETA, 4 (57.1%) Gram-positive, 3 (42.9%) Gram-negative bacteria were isolated and identified from catheter and only one Gram-negative bacterium was isolated and identified from urinary samples. In the 36 Gram-positive bacteria detected in the blood cultures, 19 (52.8 %) samples were identified as Coagulase negative *Staphylococcus*, 7 (19.4%) samples were identified as *Enterococcus* spp., 5 (13.9%) samples were identified as *Staphylococcus epidermidis*, 2 (5.6%) samples each were identified as *Staphylococcus hominis* and *Staphylococcus capitis* and 1 sample was identified as *staphylococcus haemolyticus* and in the 4 Gram-positive bacteria detected in the catheter samples, 2 (50%) samples were identified as CNS, 1 sample (25%) was identified as *Staphylococcus aureus* and 1 sample (25%), was identified as *S. capitis*. No Gram-positive bacteria were grown in the ETA (Table 1). In the 15 Gram-negative bacteria detected in ETA, 13 samples (86.7%) were identified as *Acinetobacter baumannii* and 2 samples (13.3%) were identified as *Klebsiella* spp.. In the 5 Gram-negative bacteria detected in blood cultures, 3 samples (60%) were identified as *A. baumannii*, 1 sample was identified as *E. coli* and 1 sample was as *Klebsiella* spp., and In the 3 Gram-negative bacteria detected in catheter, 2 samples (66.7%) were identified as *A. baumannii* and 1 sample (33.3%) was identified as *Pseudomonas aeruginosa* (Table 1). Our results are consistent with a recent review that summarizes nine studies reporting on co-infections in COVID-19 patients. An 8% rate has been defined for bacterial and fungal co-infections (Rawson et al. 2020) (Table 1).

In the recent study, Acer and Özüdoğru [11], reported that the mostly bacteria isolated from catheter samples of patients under mechanical ventilation in intensive care units (ICUs) of Siirt Training and Research Hospital were Coagulase-negative *Staphylococcus*, *S. aureus*, *Klebsiella* spp., *A. baumannii*, *P. aeruginosa*, *Enterococcus faecium* and *Enterobacter* spp. and another recent study conducted by Acer and Özüdoğru [12] reported that that the mostly bacteria isolated from endotracheal aspirate samples of patients under mechanical ventilation in intensive care units (ICUs) of Siirt Training and Research Hospital were *S. aureus*, *S. pneumoniae*, *Klebsiella* spp., *A. baumannii*, *P. aeruginosa*,

*E. coli* and *Enterobacter spp.* We detected a low laboratory-confirmed bacterial infection rate in COVID-19 patients in our observational study.

The identified low bacterial co-infection rates are notable as they are in contradiction sharply with the observed antibiotic exposures [1]. In a more recent study, Rawson et al. [10] conducted a study to review early data on bacterial and fungal co-infections with SARS-CoV-2. They reported that only 62 of the 806 people (8%) had an identified bacterial or fungal co-infection. However, they reported that 72% of COVID-19 patients were received systemic antibacterials.

In the recent studies, Hughes et al. [9] reported that 36 coagulase-negative staphylococci, one *Streptococcus oralis*, one *Acinetobacter sp.* (none *A. baumannii*) and one *Sphingobacterium multivorum*, one each *Klebsiella pneumoniae* and ventilator-associated *Enterobacter cloacae*, 2 *Enterococcus spp.* and 1 *Pseudomonas aeruginosa* were identified from blood cultures of 836 COVID-19 patients and they reported that a positive respiratory culture was detected in low yield; *Staphylococcus aureus* was found to be the most common respiratory pathogen isolated in community-acquired coinfection (4/24; 16.7%), with *Pseudomonas*, Garcia-Vida et al. [2] reported that 74 bacterial infections were determined in 989 COVID-19 patients. They mostly isolated *P. aeruginosa*, *E. coli*, 6; *Klebsiella spp.*, *S. aureus*, and Coagulase-negative

staphylococci. Nori et al. (2020) identified 155 isolates from blood cultures of COVID-19 patients. They reported that the most frequently isolated bacteria from blood cultures of COVID-19 patients were *Staphylococcus aureus* (30%), *S. epidermidis* (12%), *Streptococcus spp* (10%), *Enterococcus spp* (7%), *Escherichia coli* (7%), *P. aeruginosa* (6%), *Klebsiella spp* (3%), and *Enterobacter spp* (3%). They identified 112 isolates from respiratory cultures. They reported the 5 most commonly identified organisms were *S. aureus* (44%), *P. aeruginosa* (16%), *Klebsiella spp* (10%), *Enterobacter spp* (8%), and *E. coli* (4%).

In the present study, we also evaluated antibiotics resistance rates of bacteria isolated from hospitalized patients with COVID-19. Among Gram-positive bacteria, methicillin resistances were detected in 57.9 % (n=11) of Coagulase-negative *Staphylococcus* and vancomycin resistance rates were 14.3% in *Enterococcus spp.* isolated from blood samples (Table 2).

We also determined resistance and sensitive rates of growing Gram-negative bacteria isolated from hospitalized SARS-CoV-2 patients. As shown in Table 3, The *A. baumannii* isolates from ETA were found to be resistance at least three antibiotics. We detected that 100% (n=13) of *A. baumannii* isolated from ETA were resistant to piperacillin-tazobactam, meropenem, ciprofloxacin, ceftazidime and 61.5% of

Table 1: Microbiologic culture results from hospitalized SARS-CoV-2 patients.

Bacteria	Blood cultures (n=41/214)	Endotracheal aspirate (n=15/37)	Catheter (n=7/26)	Urinary (n=1/39)
Coagulase negative <i>Staphylococcus</i> (n= 21)	19	-	2	-
<i>A. baumannii</i> (n=18)	3	13	2	-
<i>Enterococcus spp.</i> (n=7)	7	-	-	-
<i>S. epidermidis</i> (n=5)	5	-	-	-
<i>S. capitis</i> (n=3)	2	-	1	-
<i>Klebsiella spp.</i> (n=3)	1	2	-	-
<i>S. hominis</i> (n=2)	2	-	-	-
<i>S. haemolyticus</i> (n=1)	1	-	-	-
<i>S. aureus</i> (n=1)	-	-	1	-
<i>P. aeruginosa</i> (n=1)	-	-	1	-
<i>E. coli</i> (n=2)	1	-	-	1
Mortality	19	7	5	1

**Table 2:** Resistance and sensitive rates of growing Gram-positive bacteria isolated from hospitalized SARS-CoV-2 patients (%).

Bacteria	Antibiotics resistance and sensitive (%)												
	Oxacilin		Vancomycin		Teicoplanin		Linezolid		Ciprofloxacin		Tigecycline		
	-	+	-	+	-	+	-	+	-	+	-	+	
<b>Blood cultures (n=36)</b>													
Coagulase negative Staphylococcus	42.1	57.9	100	0	100	0	100	0	21.1	78.9	100	0	
(n= 19)	n=8	n=11	n=19	n=0	n=19	n=0	n=19	n=0	n=4	n=11	n=19	n=0	
<i>Enterococcus spp.</i>	*50	*50	85.7	14.3	100	0	100	0	42.9	57.1	100	0	
(n=7)	n=3	n=3	n=6	n=1	n=7	n=0	n=7	n=0	n=3	n=4	n=7	n=0	
<i>S. epidermidis</i>	20	80	100	0	100	0	100	0	20	80	100	0	
(n=5)	n=1	n=4	n=5	n=0	n=5	n=0	n=5	n=0	n=1	n=4	n=5	n=0	
<i>S. hominis</i>	0	100	100	0	100	0	100	0	50	50	100	0	
(n=2)	n=0	n=2	n=2	n=0	n=2	n=0	n=2	n=0	n=1	n=1	n=2	n=0	
<i>S. capitis</i>	0	100	100	0	100	0	100	0	0	100	100	0	
(n=2)	n=0	n=2	n=2	n=0	n=2	n=0	n=2	n=0	n=0	n=2	n=2	n=0	
<i>S. haemolyticus</i>	0	100	100	0	100	0	100	0	0	100	100	0	
(n=1)	n=0	n=1	n=1	n=0	n=1	n=0	n=1	n=0	n=0	n=1	n=1	n=0	
<b>Catheter cultures (n=4)</b>													
Coagulase negative Staphylococcus	50	50	100	0	100	0	100	0	100	0	100	0	
(n=2 )	n=1	n=1	n=2	n=0	n=2	n=0	n=2	n=0	n=2	n=0	n=2	n=0	
<i>S. aureus</i>	100	0	100	0	100	0	100	0	100	0	100	0	
(n=1)	n=1	n=0	n=1	n=0	n=1	n=0	n=1	n=0	n=1	n=0	n=1	n=0	
<i>S. capitis</i>	0	100	100	0	100	0	100	0	0	100	100	0	
(n=1)	n=0	n=1	n=1	n=0	n=1	n=0	n=1	n=0	n=0	n=1	n=1	n=0	

“-” = sensitive; “+” = resistant

**Table 3:** Resistance and sensitive rates of growing Gram-negative bacteria isolated from hospitalized SARS-CoV-2 patients (%).

Bacteria	Antibiotics resistance and sensitive (%)															
	Cholistin		Amicasin		Piper- acillintazo- bactam		Meropenem		Cipro- floxacin		Tigesicline		Trimetho- prim-sulfa methoxazole		Cefta- zidime	
	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+
<b>Endotracheal Aspirate cultures (n=15)</b>																
<i>A. baumannii</i>	92.3	7.7	38.5	61.5	0	100	0	100	0	100	69.2	30.8	61.5	38.5	0	100
(n=13)	n=12	n=1	n=5	n=8	n=0	n=13	n=0	n=13	n=0	n=13	n=9	n=4	n=8	n=5	n=0	n=13
<i>Klebsiella spp.</i>	100	0	0	100	0	100	0	100	0	100	0	100	0	100	0	100
(n=2)	n=2	n=0	n=0	n=2	n=0	n=2	n=0	n=2	n=0	n=2	n=0	n=2	n=0	n=2	n=0	n=2
<b>Blood cultures (n=5)</b>																
<i>A. baumannii</i>	0	0	33.3	66.7	0	100	0	100	0	100	33.3	66.7	66.7	33.3	0	100
(n=3)	n=3	n=0	n=1	n=2	n=0	n=3	n=0	n=3	n=0	n=3	n=1	n=2	n=2	n=1	n=0	n=3
<i>Klebsiella spp.</i>	100	0	100	0	0	100	100	0	0	100	100	0	0	100	0	100
(n=1)	n=1	n=0	n=1	n=0	n=0	n=1	n=1	n=0	n=0	n=1	n=1	n=0	n=0	n=1	n=0	n=1
<i>E. coli</i>	100	0	100	0	0	100	100	0	100	0	100	0	100	0	0	100
n=1	n=1	n=0	n=1	n=0	n=0	n=1	n=1	n=0	n=1	n=0	n=1	n=0	n=1	n=0	n=0	n=1
<b>Catheter cultures (n=3)</b>																
<i>A. baumannii</i>	100	0	100	0	0	100	0	100	0	100	100	0	100	0	0	100
(n=2)	n=2	n=0	n=2	n=0	n=0	n=2	n=0	n=2	n=0	n=2	n=2	n=0	n=2	n=0	n=0	n=2
<i>P. aeruginosa</i>	100	0	0	100	0	100	0	100	0	100	100	0	0	100	0	100
(n=1)	n=1	n=0	n=0	n=1	n=0	n=1	n=0	n=1	n=0	n=1	n=1	n=0	n=0	n=1	n=0	n=1

“-” = sensitive; “+” = resistant

resistant to amikacin. 2 *Klebsiella* spp. isolated from ETA were resistant to ciprofloxacin, amikacin, piperacillin-tazobactam, meropenem, tigecycline, trimethoprim-sulfamethoxazol and ceftazidime and 1 *P. aeruginosa* isolated from catheter cultures was found to be resistant to amikacin, piperacillin-tazobactam, meropenem, ciprofloxacin, trimethoprim-sulfamethoxazol and ceftazidime (Table 3).

Our study has some clear limitations that should be acknowledged because the retrospective project decreases control over multiple confounding factors and data collection, our study was limited to one hospital and respiratory samples were not present for all patients; Only 17 sputum cultures were taken.

In conclusion, the frequency of microbiologically confirmed bacterial co-infections was found low in confirmed SARS-CoV-2 patients admitted to our hospital. Nevertheless, when present, they may cause serious illness with worse consequences. Since the incidence, nature, and effect of late secondary bacterial infections are less clear, more studies are needed.

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#### Ethical approval

This study was approved by the SIIRT University Non-Interventional Clinical Research Ethics Committee and Republic of Turkey Ministry of Health as well.

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#### Statistical Analysis

SPSS software version 22.0 was used for statistical analysis. All quantitative data in non-normal or unknown distribution were expressed as median and interquartile range.

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#### Disclosure Statement

The authors declare that they have no conflict of interest.

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#### Funding Information

The authors declared that this case has received no financial support.

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