

Co-infection in patients with COVID-19 in Tripoli Northern Lebanon: germs involved and antibiotic sensitivity profile

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Abstract

Introduction: Patients hospitalized with coronavirus disease 2019 (COVID-19) acquired bacterial infections. The aim of this study was to investigate the etiology and antimicrobial resistance of bacterial co-infection to provide informed antimicrobial treatment.

Methods: This retrospective study reviewed the electronic medical records of 873 patients hospitalized with COVID-19 in Northern Lebanon, Nini Hospital between August 2020 and September 2021. According to the inclusion and exclusion criteria, patients who acquired bacterial infection were enrolled. Demographic, etiology and antimicrobial resistance data of the co-infection were collected.

Results: The rate of infection by Gram-negative bacteria was 29/47 (61.7%), while the rate of infection by Gram-positive bacteria was 11/47 (23.4%). *Escherichia coli* was the dominant species isolated in this study (25.5%), followed by *Stenotrophomonas maltophilia* (12.7%) and *Pseudomonas aeruginosa* (10.6%). Regarding fungal infection, there were 7/47=14.9% cases of yeast infection. Respiratory infection was the majority 20/47 (42.5%), followed by blood infection 15/47 (32%) and urine infection 12/47 (25.5%). The analysis of antibiotics sensitivity results showed us that 44.4% of isolated *Enterobacteriaceae* were resistant to carbapenem, 16.7% were secretors of extended-spectrum beta-lactamase (ESBL). We noted that 27.8% of *Enterobacteriaceae* were extended drug-resistant (XDR). All isolates of *Staphylococcus aureus* were resistant to methicillin.

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Conclusions: Bacterial co-infection may occur in patients hospitalized with COVID-19 and lead to high mortality. Gram-negative bacteria, especially *E. coli*, *S. maltophilia*, and *P. aeruginosa*, were the main bacteria isolate, and the resistance rates of the major isolated bacteria were generally high.

Keywords

COVID-19, Co-infection, Antibiotic Resistance, Lebanon.

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Introduction

The severe acute respiratory coronavirus 2 (SARS-Cov-2), which was first discovered in Wuhan, China, Huanan market in December 2019 [1, 2] is named as 2019 novel coronavirus by WHO and the International Committee on Taxonomy of Viruses on January 12 and its disease as COVID-19 on February 11 [3, 4]. It has spread to most countries around the world and has progressed into a global pandemic [5]. Globally, as of October 8, 2021, there have been 236,599,025 confirmed cases including 4,831,486 deaths [3]. Bacterial co-infection is frequently determined as co-infection in viral respiratory tract infections, such as influenza, and is a significant cause of mortality and morbidity [6]. Bacterial/fungal co-infection is defined as new microorganisms identified 48 hours after hospital admission. In 14 observational studies, the incidence of bacterial co-infection in hospitalized COVID-19 patients reported was 16% and ranged between 4.8-42.8% [7]. According to 18 observational studies, the incidence of fungal co-infection in hospitalized COVID-19 patients was 6.3% and ranged between 0.9-33.3% [7]. A retrospective study of 918 COVID-19 patients from Wuhan China, showed that 7.1% had a fungal or bacterial co-infection [8].

In previous studies [6, 8-11], bacterial co-infection occurred at rates of 3%~15%. It's a dangerous and common complication in patients hospitalized

with COVID-19. According to existing reports, 50% of COVID-19 deaths developed from bacterial co-infection; thus, patients with co-infection have a higher risk of mortality [12, 13]. Bacterial and fungal co-infection in COVID-19 patients is not well described and represents an important knowledge gap. Most of the death cases that occurred during the 1918-9 influenza pandemic were the result of bacterial co-infection [11, 14].

The initial antibiotic treatment was administered to patients with COVID-19 to prevent adverse events and because of the concerns of complications. The overuse of antibiotics leads to resistance to bacterial and fungal pathogens acquired in hospitals, which cause healthcare-associated infection [14]. This routine use contradicts the objectives and principles of the antimicrobial stewardship program. For this reason, it is crucial to identify the patients with COVID-19 who develop a co-infection and to administer a specific antibiotic [5]. Furthermore, the rate of bacterial co-infection in COVID-19 patients could have an important effect on refining empirical antibiotic management guidelines for patients with COVID-19.

The purpose of this study is to investigate the etiology and antimicrobial resistance of bacterial co-infection with COVID-19 to develop a more informed antimicrobial treatment.

Materials and methods

Study population

This study was carried out at Nini Hospital (having a capacity of 120 beds, and covers treatments in all specialties). This hospital was designated to treat patients with COVID-19 in Tripoli, Northern Lebanon. A total of 873 patients were diagnosed with COVID-19 and treated in the department of COVID-19 between August 2020 and September 2021. According to the severity of illness on admission, 710 of the patients were classified as severe (i.e., dyspnea, respiratory frequency $\geq 30/\text{min}$, blood oxygen saturation $\leq 93\%$, the partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300 , and/or lung infiltrates $> 50\%$ within 24 to 48h). Other 163 patients were critical (i.e., respiratory failure, septic shock, and/or multiple organ dysfunction or failure). Demographic, clinical course, laboratory, and treatment data were collected from electronic medical records for each patient.

Study design

Bacterial co-infection is identified when patients showed clinical characteristics of bacterial infections, and at least one positive etiology of bacteria was acquired from qualified microbiological specimens (sputum, endotracheal aspirate, Broncho alveolar lavage, pleural fluid, blood samples, and urine) after SARS-CoV-2 infection. We performed a retrospective review of medical records in collaboration with the Ethical Committee, Microbiology, and Molecular Biology Laboratory of Nini Hospital. Inclusion criteria were: patient with common symptoms of COVID-19 illness including fever and cough, abnormal findings on chest computed tomography (CT scan), positive nucleic acid testing in the form of real-time reverse transcriptase-polymerase chain reaction (RT-PCR), met the diagnostic criteria of bacterial co-infection. Patients were excluded if: before being infected with SARS-CoV-2 they had another infectious disease, the medical records were incomplete. This study

was approved by the Research Ethics Committee of Nini Hospital (Reference; IRB F 04).

Pathogen detection and antimicrobial susceptibility.

The different microbiological specimens of patients with COVID-19 were processed and cultured in the microbiological sector within the laboratory of Nini Hospital according to the Remic Standard in medical microbiology [15]. Bacterial identification was done using the Vitek®-MS Plus, MALDI-TOF (Bio-Mérieux, France). This step was realized in collaboration with the Laboratoire Microbiologie Santé et Environnement (LMSE) at the Doctoral School in Science and Technology, and the Faculty of Public Health, in the Lebanese University, Tripoli Lebanon. Antimicrobial susceptibility testing was performed using the disk diffusion method (Bio-Rad® France). The results were interpreted according to the criteria of the European Committee on Antibiotic Susceptibility Testing (EUCAST 2021). List of antibiotics used for fermenting *Enterobacteriaceae* were: ampicillin (10 μg), amoxicillin/clavulanic acid (20-10 μg), ticarcillin (75 μg), ticarcillin/clavulanic acid (75-10 μg), piperacillin (30 μg), piperacillin/tazobactam (30-6 μg), aztreonam (30 μg), imipenem (10 μg), meropenem (10 μg), ertapenem (10 μg), cefalexin (30 μg), cefuroxime (30 μg), cefoxitin (30 μg), cefepime (30 μg), ceftazidime (10 μg), cefixime (5 μg), cefotaxime (5 μg), gentamicin (10 μg), amikacin (30 μg), ciprofloxacin (5 μg), levofloxacin (5 μg), trimethoprim/sulfamethoxazole (1,25-23,75 μg), Fosfomycin (200 μg), tigecycline (15 μg). For *P. aeruginosa* the list of antibiotics was: piperacillin/tazobactam (30-6 μg), imipenem (10 μg), meropenem (10 μg), cefepime (30 μg), ceftazidime (10 μg), gentamicin (10 μg), amikacin (30 μg), ciprofloxacin (5 μg), levofloxacin (5 μg) and fosfomycin (200 μg). ceftazidime (10 μg), levofloxacin (5 μg), trimethoprim/sulfamethoxazole (1,25-23,75 μg) and minocycline (30 μg) were used for *S. maltophilia*.

For *S. aureus* spp the antibiotics used were: penicillin G (1 unit), oxacillin (1 μg), ampicillin (2 μg),

cefoxitin (30µg), erythromycin (15µg), clindamycin (2µg), gentamycin (10µg), minocycline (30µg), ciprofloxacin (5µg), levofloxacin (5µg), nitrofurantoin (100µg), rifampicin (10µg), linezolid (10µg), tigecycline (15µg), vancomycin (5µg) and teicoplanin (30µg). For *Streptococcus* spp, the list of antibiotics used were: penicillin G (1µg), erythromycin (15µg), clindamycin (2µg), gentamycin (500µg), minocycline (30µg), moxifloxacin (5µg), levofloxacin (5µg), nitrofurantoin (100µg), rifampicin (5µg), linezolid (10µg), vancomycin (5µg), teicoplanin (30µg) and tigecycline (15µg). The list of antibiotics for *Enterococcus* spp was: oxacillin (1µg), ampicillin (2µg), erythromycin (15µg), clindamycin (2µg), gentamycin (30µg), minocycline (30µg), levofloxacin (5µg), linezolid (10µg), tigecycline (15µg), vancomycin (5µg) and teicoplanin (30µg). The same isolates from one patient were counted only once.

Results

After excluding 12 patients who had other infectious disease before being infected with SARS-CoV-2, and 4 patients with incomplete medical records, a total of 873 patients infected by COVID-19 were admitted to the Nini Hospital. Among them, 710 patients were admitted to the non-intensive care unit (n-ICU) and 163 patients were admitted to the intensive

care unit (ICU). As clinical outcomes, 795 patients remained alive and 78 patients died. The number of infected patients with bacterial co-infection was 33/873 (3.8%). The mean age was 66.2 +/- 11.2 years (ranging from 37-84 years), 25 patients were males (75.8%) and 8 (24.2%) patients were females. Among them, 30 patients were admitted to the ICU and 3 patients were admitted to the n-ICU. By the end of the study period, 22 patients died and 11 patients survived. Among these alive patients, three patients discharged; one patient transferred to other hospital; and seven patients persisted (**Table 1**). The overall in-hospital mortality rate was found to be 9% (78/873), 22 of the 78 fatal patients also developed nosocomial infection with 66.7% (22/33) as the mortality rate. The most common causes of death were septic shock with respiratory failure and cardiac arrest.

The proportions of bacterial co-infections in the lungs, bloodstream, and urinary tract were 20/47 (42.5%); 15/47 (31.9 %) and 12/47 (25.5%) respectively. Moreover, 4/33 patients (12.1%) had lung infections mixed with bloodstream infection, 2/33 (6%) patients had lung infections mixed with urinary tract infection, and 1/33 (3%) patient had lung infections mixed with bloodstream infection and urinary tract infection.

Table 1. Demographic characteristics of COVID-19 patients who had co-infection.

Demographic			Admission				Clinical Outcomes			
			Non-ICU		ICU		Alive		Dead	
	n	%	n	%	n	%	n	%	n	%
Co-infection										
Gender										
Male	25	75.8	2	66.7	23	70	5	45	20	90
Female	8	24.2	1	33.3	7	30	6	55	2	10
Age (years)										
0-49	5	15.1	0	0	5	16.6	1	9	4	18.1
>50	28	84.8	3	100	25	83.3	10	90.9	18	81.8
Total Admission	873		710	81.3	163	18.7	795	91	78	9
Patients having	33		3	9	30	91	11	33.3	22	66.7

Etiology of the bacterial co-infection

A total of 47 strains of bacteria were isolated from 33 patients. Among the isolated bacteria; Gram-negative bacteria were the main bacteria, accounting for 61.7%. The top three bacteria of co-infection were *Escherichia coli* (*E. coli*, 25.5%); (*Stenotrophomonas maltophilia*, 12.7%); and (*Pseudomonas aeruginosa*, 10.6%). The distribution and composition ratios of bacteria are shown in (Table 2). Among them, 10 patients had infections with mixed bacteria 10/33 (30.3%) (Table 3).

Table 2. Distribution of isolated species according to the different types of samples.

Bacteria	different sites							
	Lungs		Blood stream		Urinary tract		Total	
	n	%	n	%	n	%	n	%
Gram-negative	15	75	6	40	8	66.7	29	61.7
<i>Escherichia coli</i>	5	25	3	20	4	33.3	12	25.5
<i>Klebsiella</i> spp	2	10	0	0	2	16.7	4	8.5
<i>E. cloacae</i>	0	0	1	6.7	1	8.3	2	4.3
<i>S. maltophilia</i>	6	30	0	0	0	0	6	12.8
<i>P. aeruginosa</i>	2	10	2	13.3	1	8.3	5	10.6
Gram-positive	2	10	8	53.3	1	8.3	11	23.4
<i>S. aureus</i>	1	5	3	20	0	0	4	8.5
<i>Streptococcus</i> spp	1	5	1	6.7	1	8.3	3	6.4
<i>Enterococcus</i> spp	0	0	4	26.7	0	0	4	8.5
Yeast	3	15	1	6.7	3	25	7	14.9
<i>Candida</i> spp	3	15	1	6.6	3	25	7	14.9
Total	20	100	15	100	12	100	47	100

Antimicrobial susceptibility

The antimicrobial resistance rate of bacteria isolated from patients with co-infection was generally high. The isolation rates of carbapenem-resistant *Enterobacteriaceae* were 44.4%. The infection rates for *E. coli* extended-spectrum Ampc cephalosporinase

Table 3. Etiological distribution of bacterial co-infection caused by multiple bacteria in patient hospitalized with COVID-19.

Mixed infection	n	%
<i>E. coli</i> (ESAC) + <i>Stenotrophomonas maltophilia</i>	1	10
<i>E. coli</i> + <i>Pseudomonas aeruginosa</i>	1	10
<i>Klebsiella</i> spp + <i>Enterobacter cloacae</i>	1	10
<i>Staphylococcus aureus</i> + <i>Enterococcus</i> spp	1	10
<i>Staphylococcus aureus</i> + <i>Streptococcus</i> spp	1	10
<i>Enterococcus</i> spp + <i>Stenotrophomonas maltophilia</i>	1	10
<i>Pseudomonas aeruginosa</i> + <i>Klebsiella</i> spp	1	10
Other combinations	3	30
Total	10	100

ESAC: extended spectrum Ampc cephalosporinase; spp: species.

(ESAC) were 33.3%. Methicillin resistance was present in 100% of *Staphylococcus aureus* (*S. aureus*) and vancomycin resistant was not found. The isolation rates of ESBL-producing *Enterobacteriaceae* was 16.7% and the resistance rates of XDR-*Enterobacteriaceae* were 27.8% (Table 4). The results of the antimicrobial susceptibility testing for the major bacteria are shown in Table 5 and Table 6.

Table 4. Resistant phenotype caused by different bacterial isolates in patients with bacterial co-infection.

Resistant phenotype	N/total	%
<i>E. coli</i> ESAC	4/12	33.3
<i>Enterobacteriaceae</i> ESBL	3/18	16.7
<i>Enterobacteriaceae</i> XDR	5/18	27.8
MRSA	4/4	100
Carbapenem-resistant <i>Enterobacteriaceae</i>	8/18	44.4

MRSA: methicillin resistant staphylococcus aureus, ESBL: extended spectrum beta-lactamase, XDR: extended drug resistant, ESAC: extended spectrum Ampc cephalosporinase

Table 5. Antimicrobial susceptibility of major Gram-negative bacteria.

Major Gram-negative bacteria, (N) of resistant strains										
Antibacterial	<i>E. coli</i>		<i>Klebsiella spp</i>		<i>E. cloacae</i>		<i>P. aeruginosa</i>		<i>S. maltophilia</i>	
	n=12	%	n=4	%	n=2	%	n=5	%	n=6	%
Ampicillin	12	12	4	4	2	2	-	-	-	-
Amoxicillin/Clavulanic acid	6	8	4	4	2	2	-	-	-	-
Ticarcillin	12	12	4	4	2	2	-	-	-	-
Ticarcillin/Clavulanic acid	8	8	2	2	2	2	-	-	-	-
Piperacillin	12	12	4	4	2	2	-	-	-	-
Piperacillin/Tazobactam	6	7	3	3	2	2	0	5	-	-
Aztreonam	9	12	3	3	-	-	-	-	-	-
Imipenem	312	3	4	2	2	0	5	-	-	-
Meropenem	3	12	3	4	2	2	2	5	-	-
Ertapenem	3	12	3	4	2	2	-	-	-	-
Cefalexin	11	11	4	4	2	2	-	-	-	-
Cefuroxime	11	11	4	4	2	2	-	-	-	-
Cefoxitin	8	10	3	4	2	2	-	-	-	-
Cefepime	8	9	4	4	1	2	0	5	-	-
Ceftazidime	9	11	4	4	2	2	0	5	4	5
Cefixime	10	10	4	4	1	1	-	-	-	-
Cefotaxime	10	10	4	4	2	2	-	-	-	-
Gentamicin	0	9	0	4	-	-	0	5	-	-
Amikacin	0	12	0	4	2	2	0	5	-	-
Ciprofloxacin	4	11	3	4	2	2	0	4	-	-
Levofloxacin	3	8	3	4	2	2	1	5	0	6
SXT*	2	7	0	4	2	2	-	-	3	6
Fosfomycin	2	6	3	4	0	1	0	5	-	-
Tigecycline	2	6	1	4	1	2	-	-	-	-
Minocycline	-	-	-	-	-	-	-	-	1	5

*: SXT Trimethoprim/sulfamethoxazole; Note: - Not tested, n: Number of isolates tested, N: Number of resistant strains,

Table 6. Antimicrobial susceptibility of major Gram-positive bacteria.

Major Gram-positive bacteria, Nn of resistant strains						
Antibacterial	<i>S. aureus</i>		<i>Streptococcus spp</i>		<i>Enterococcus spp</i>	
	n=4	%	n=3	%	n=4	%
Penicillin G	4	4	2	3	-	2
Oxacillin	-	-	4	4	2	2
Ampicillin	-	-	2	4	2	2
Cefoxitin	4	4	-	-	2	2

Antibacterial	<i>S. aureus</i>		<i>Streptococcus</i> spp		<i>Enterococcus</i> spp	
	n=4	%	n=3	%	n=4	%
Erythromycin	4	4	2	3	3	4
Clindamycin	3	4	1	3	4	4
Gentamycin	4	4	1(3*	3	4	
Minocycline	0	4	1	2	4	4
Moxifloxacin	4	4	2	3	2	3
Ciprofloxacin	3	3	-		2	2
Levofloxacin	3	3	2	3	2	4
Nitrofurantoin	-	1	1	-	2	2
Rifampicin	1	3	1	1	-	2
Linezolid	1	4	0	3	0	4
Tigecycline	0	4	0	2	0	3
Vancomycin	0	4	0	3	0	4
Teicoplanin	0	4	0	3	0	4

Note: - Not tested; n: Number of isolates tested, N: Number of resistant strains; *: Gentamicin high concentration was used.

Discussion

Previous studies showed that *Klebsiella* spp, methicillin susceptible *S. aureus* (MSSA), methicillin resistant *S. aureus* (MRSA), *E. coli*, *P. aeruginosa*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *S. maltophilia* and *Aspergillus* were the main causative of co-infection in patients with COVID-19 [5, 6, 16-18].

Respiratory failure or multiple organ failure is the direct cause of death in patients with COVID-19, and bacterial/fungal co-infection has an important role in this process [19-20]. Among the 873 patients with COVID-19, the incidence rate of co-infection was 3.8% in our study which was consistent with studies described in Wuhan China, United Kingdom, and Barcelona Spain [5, 7, 8, 10, 11]. The incidence of bacterial co-infection in the critical group is much higher than in the severe group, which was consistent with the higher rate of central catheter placement and invasive mechanical ventilation in critical patients [12].

In a study carried out by Bordi et al. the detected *M. pneumoniae* in five patients (4.0%) with only one patient was infected with *Legionella pneumophila* and *Streptococcus pneumoniae* (0.8%) and mixed infections were also observed in a small number of cases [21]. Zhou et al. found that 50% (27/54) of patients who died from COVID-19 had bacterial co-infection, and ventilator-associated pneumonia ensued in 10 of 32 patients (30%) needing invasive mechanical ventilation [12]. Chen et al. have reported fungal and bacterial co-infection in patients with COVID-19 [22]. In 45 critically ill patients, we identify 19 (42.2%) with bacterial co-infection [23]. Verroken et al. showed 13/32 (40.6%) patients with a bacterial co-infection [24]. Rawson et al. found that 62/806 (8%) of patients were reported as experiencing bacterial/fungal co-infection during hospital admission [9]. Huang et al. showed that among 41 individuals infected with COVID-19 four cases (9.8%) had bacterial co-infection [25]. Zhang et al. found that 221 patients with SARS-CoV-2 pneumonia were admitted to Zhong-

nan hospital, Wuhan China, among them 25.8% (57/221) patients were afflicted with co-infection and among these patients with co-infection 29.8% (17/57) were co-infected with bacteria [26]. Blasco et al. found one patient who was positive for *Mycoplasma pneumoniae* (*M. pneumoniae*) co-infection among patients with COVID-19 pneumonia [27]. Clarie et al. reported a fatal case of necrotizing pneumonia induced by Panton-Valentine- Leucocidin (PVL) secreting *Staphylococcus aureus* (*S. aureus*) in a patient who was affected by COVID-19 [28]. Of the 33 patients, 22/33 (66.7%) of patients' deaths were caused by nosocomial infection during hospitalization. The common pathogens identified in our study were *E. coli* (in eight patients), *Klebsiella* spp (in four patients), *Enterobacter cloacae* (in two patients), *P. aeruginosa* (in five patients), *S. maltophilia* (in six patients), *S. aureus* (in four patients), *Streptococcus* spp (in three patients), *Enterococcus* spp (in four patients), and *Candida* spp (in five patients). These pathogens are commonly associated with hospital acquired pneumonia (HAP), Ventilator acquired pneumonia (VAP), bacteremia and urinary tract infection are reported as common co-pathogens in COVID-19 infections [3, 29, 30]. Co-infections occurred mostly in the lungs; this may be related to the decrease in airway defense function after a SARS-CoV-2 infection. Invasive operations such as trachea intubation and ventilator-assisted breathing during hospitalization may also be the cause of co-infection in the lungs [5, 11]. Our study showed 19 patients had lungs infection, 15 patients had bloodstream infections and nine patients had urinary tract infections. Among patients with lungs infection, four patients had lung infections mixed with bloodstream infections, two patients had lung infections mixed with urinary tract infections, and one patient had lungs infection mixed with bloodstream and urinary tract infections. We compared the bacteria in mixed infection and found that one patient had the same bacteria in the lungs and bloodstream,

including *E. coli* (ESAC), and two patients had the same pathogen in the lungs and the urinary tract that include *E. coli* (1/2), and *Candida* spp (1/2). It is possible that the migration of these pathogens from the lungs resulted in the bloodstream and urinary tract infections in these patients.

A total of 47 isolates of bacteria isolated in this study were mainly Gram-negative bacteria 29/47 (61.7%). The top three bacteria of lung infections were *S. maltophilia*, *E. coli* and *P. aeruginosa*. The etiological distribution was different from the previously reported bacteria of hospital-acquired pneumoniae (HAP) [5, 6, 16]. The proportion of *S. maltophilia* and *E. coli* was significantly higher, and the proportion of *P. aeruginosa* and *S. aureus* was less, suggesting that the initial empirical antimicrobial program of HAP should not be completely automatically copied if co-infection occurs in the lungs. The lower proportion of *P. aeruginosa* and *S. aureus* suggests that it is not necessary to first choose an antimicrobial with antibacterial activity against *P. aeruginosa* and *S. aureus* for lung infections. The choice of antimicrobial program could be more suitable to treat the infections of *S. maltophilia* and *E. coli*. However, the bacteria that cause bloodstream infection were mainly Gram-positive bacteria 11/47 (23.4%) as showed in our study. The main bacteria were *Enterococcus* spp (26.7%) and *S. aureus* (MRSA) (20%).

Previous studies [3, 6, 16, 18] reported that *K. pneumoniae*, *A. baumannii*, *S. aureus* (MRSA) were the main bacteria detected. Our study revealed that bloodstream infections were associated with the implantation of a central venous catheter. Therefore, we suggest that the proper management of venous catheters in severe patients should be adapted to avoid bloodstream infections. The number of urinary tract infections was relatively small, *E. coli* was still the main bacterium (33.3%), followed by *Candida* spp (25%). According to previous studies, *Candida* spp, *E. coli*, and *Proteus mirabilis* are the main bacteria in this type

of specimen [5, 16, 18]. According to antimicrobial susceptibility tests, our study showed that 44.4% of *Enterobacteriaceae* isolates were resistant to imipenem. 25% of *E. coli* isolates were resistant to this drug. Three isolates of *Klebsiella* were resistant and all *Enterobacter cloacae* isolates were resistant to this molecule. The resistance rate of ESBL-producing *Enterobacteriaceae* was 16.7%, XDR-*Enterobacteriaceae* was 27.8 %, and 33.3% for ESAC-producing *E. coli*. The resistance rate of *Enterobacteriaceae* to ciprofloxacin and levofloxacin was 50% respectively; and was 22.2% to tigecycline, 30.7% to trimethoprim/sulfamethoxazole, 45.4% to Fosfomycin and 33.3% to nitrofurantoin. Two isolates of *P. aeruginosa* were resistant to meropenem and one isolate to levofloxacin. There was no resistance to the other tested beta-lactam-molecules (imipenem, ceftazidime, and piperacillin/tazobactam). All isolates were sensitive to fosfomycin, colistin, amikacin, netilmicin, gentamicin, and tobramycin. Three isolates of *S. maltophilia* were resistant to trimethoprim/sulfamethoxazole, one isolate was resistant to minocycline, and all isolates were sensitive to levofloxacin. All *S. aureus* isolates were resistant to cefoxitin, gentamicin, moxifloxacin, and fusidic acid. Three isolates were resistant to clindamycin and tetracycline; no resistance was found to vancomycin, teicoplanin, and linezolid. Two isolates of *Streptococcus* were resistant to penicillin, erythromycin, tetracycline, moxifloxacin, and levofloxacin. Two *Enterococcus* isolates were resistant to ampicillin, pristinamycin, streptomycin high charge, moxifloxacin, levofloxacin, and trimethoprim/sulfamethoxazole. All isolates were resistant to erythromycin, clindamycin, and tetracycline.

As compared to previous study, Li and colleagues found that the isolation rate of ESBL-producing *E. coli* was 75%. The isolation rate of carbapenem-resistant *A. baumannii* and carbapenem-resistant *K. pneumoniae* were 91.7% and 76.6% respectively. MRSA was persisted in 100% of *S. aureus*, van-

comycin resistance was not found [5]. In another study described by Gysin et al. *Enterobacteriaceae* isolates showed resistance to piperacillin/tazobactam (32%), ceftriaxone (32%), ceftazidime (36%), cefepime (8%) and trimethoprim/sulfamethoxazole (4%). *P. aeruginosa* isolates was found to be resistant to cefepime (56.3%), ceftazidime (46.9%), meropenem (50%), piperacillin/tazobactam (65.6%) and ciprofloxacin (15.6%) [17]. Mahmoudi et al. found that *Enterobacteriaceae* isolates had the highest resistance to cotrimoxazole (74%), piperacillin (67.5%), ceftazidime (47.5%), cefepime (42.5%). All isolates were susceptible to amikacin (100%). *P. aeruginosa* isolate was susceptible to imipenem (90%). All *S. aureus* isolates were susceptible to vancomycin, but the rates of resistance to oxacillin, erythromycin, and clindamycin were over than (90%) [6]. Vijay et al. showed that the highest resistance was seen in *K. Pneumoniae* isolates against third-generation cephalosporine, ceftriaxone (91.7%), fluoroquinolone (82%), piperacillin/tazobactam (79.2%), cefoperazone-sulbactam (76.4%), Ertapenem (79%), meropenem (72%) and imipenem (66.8%). *A. baumannii* isolates were resistant to ceftazidime (96%), meropenem (94%), fluoroquinolone (93.5%), imipenem (92%), and piperacillin/tazobactam (91%). (76.8%) of *K. pneumoniae* and (90.3%) of *A. baumannii* isolates were intermediated to colistin. Among *Enterobacteriaceae*, ESBL detected in (83.2%) of isolates and (74.2%) of Gram-negative isolates were resistant to carbapenem. All *S. aureus* and (68%) of *Enterococcus* spp isolates were susceptible to vancomycin [18]. Khurana et al. [16] found the overall resistance ranged from (9%) to (84%) amongst all organisms. The highest observed was to amoxicillin/clavulanic acid (84%), followed by levofloxacin (83%), ciprofloxacin (79%), piperacillin/tazobactam (77%), and trimethoprim/sulfamethoxazole (75%). In addition, all resistance to third-generation cephalosporine and carbapenem was found to be (64-69%). All isolates were sensitive to colistin. Amongst Gram-

positive, pathogen isolates were sensitive to vancomycin, teicoplanin, tigecycline, linezolid, and daptomycin [16].

A limitation of this study is that during the period of study, Lebanon was passing through economic crisis which led to a lack of antibiotics discs. The company was unable to provide Nini Hospital with several types of antibiotic discs. Consequently, the study was based on a limited number of antibiotics

Conclusion

In Conclusions, Gram-negative bacteria, especially *E. coli*, *P. aeruginosa*, and *S. maltophilia*, were the main bacteria isolated in our study. In present study, aminoglycosides were the most effective drug class *in vitro* for the respiratory clinical isolates among *Enterobacteriaceae* and with full coverage of all isolates of *P. aeruginosa*. Glycopeptides were the most effective drug against the Gram-positive isolates. Levofloxacin was the most effective drug against *S. maltophilia*. A high rate of co-infection with resistant pathogens in COVID-19 patients highlights the importance of antimicrobial stewardship programs focusing on supporting the optimal selection of empiric treatments and rapid de-escalation, based on culture reports.

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