Original Article

Comparative Study of Bacterial Culture Isolates and Drug Resistance Patterns Among Elderly Patients with Bacterial Community-Acquired Pneumonia Before and During the COVID-19 Pandemic

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ABSTRACT

Background: The COVID-19 pandemic has changed the microbiological distribution and drug-resistance patterns of pathogens in community-acquired pneumonia (CAP). This study aimed to evaluate these among elderly patients with CAP before and during COVID-19.

Methodology: Data was collected from patients aged 65 to 85 years with a diagnosis of bacterial pneumonia admitted to the Veterans Memorial Medical Center pre-COVID-19 and during COVID-19. The study compared bacterial pathogens, antimicrobial resistance patterns, length of hospital stay, and mortality between the two groups.

Results: Data from 243 patients was analyzed. The COVID-19 group was younger and had more males compared to the pre-COVID-19 group (median age 70 [IQR 67–75] vs 74 [IQR 67–80] years; p = 0.015 and 74.50% vs 56.45%; p = 0.005, respectively). Hypertension was the most common comorbidity in the pre-COVID-19 group while diabetes was most common in the COVID-19 group. Similar proportions of almost all bacterial pathogens were observed. Among patients without COVID-19 co-infection, antimicrobial resistance was higher in the pre-COVID-19 group but was not significant (61.90% vs 55.56%; p = 0.316). Multidrug-resistant (MDR) pathogens were found to be higher in the COVID-19 group (21.37% vs 9.52%; p = 0.010). The majority of patients in both groups (~61%) had prolonged hospital stays. Overall mortality was lower in the COVID-19 group (41.88% vs. 56.35%; p = 0.024) while, for patients with MDR, mortality was higher in the COVID-19 group (24.49% vs 8.45%, p = 0.016).

Conclusions: The distribution of bacterial isolates did not differ significantly between pre-COVID-19 and COVID-19 periods. MDR was higher during the COVID-19 period. For MDR-infected patients, mortality was higher in the COVID-19 group. The findings of this study help inform the antimicrobial stewardship program of the institution. Vigilant surveillance and regular reporting of bacterial pathogens are needed to improve patient outcomes.

Keywords: bacterial pneumonia, COVID-19, antimicrobial resistance

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INTRODUCTION

Pneumonia was the third leading cause of death in the Philippines as reported by the Philippine Statistics Authority in 2016, and it remains a major health problem associated with high morbidity and mortality across all age groups worldwide.[1] In the elderly population, pneumonia is the single most common cause of death from infectious diseases as this group is often characterized by impaired immunity caused by multiple factors such as immune senescence, malnutrition, comorbidities, and functional impairments.[2,3]

Pneumonia is categorized as community-, hospital-, and ventilator-associated pneumonia. The most common agents of community-acquired pneumonia (CAP) are *Streptococcus pneumoniae*, *Haemophilus influenzae, Mycoplasma pneumoniae, Staphylococcus aureus, Moraxella catarrhalis,* and *Legionella* species.[4-6]

Most of the pathogens mentioned above were based on studies done before the COVID-19 pandemic. But with the outbreak of SARS-CoV-2, the virus responsible for the pandemic, accompanied by the aging population, the microbiological distribution, epidemiology, antimicrobial consumption, and resistance were changed.[7] Tang et al conducted studies proving that the COVID-19 pandemic has changed the epidemiological distribution of respiratory pathogens. Non-pharmacological interventions such as social distancing, cancellation of social gatherings, travel restrictions, lockdowns, mask-wearing, and frequent hand hygiene significantly contributed to the changing epidemiology of respiratory infections.[7] Moreover, with the implementation of the above measures, hospitalization due to CAP was reduced. This may reflect the direct effect of non-pharmacological interventions as well as the implementation of virtual consultations and avoidance of exposure in the emergency department. In terms of virological and bacteriological epidemiology, there was a noted huge shift because SARS-CoV-2 became the most predominant virus causing upper respiratory tract infection and pneumonia, casting aside other viruses such as respiratory syncytial virus, parainfluenza, and adenovirus.[7] Various studies revealed similar results.[8-13] A study by Li et al documented a decline in the overall detection rate of common respiratory viruses from 26.9% in 2019 to 10.5% in 2020 in the pediatric population, with the same declining trend noted among adults and elderly population.[8,14,15] *S. pneumoniae,* which causes pneumococcal pneumonia and invasive pneumococcal disease, was significantly decreased during the pandemic.[7,15-19] *M. pneumoniae* was also found to decrease during the pandemic.[7,16,17]

After an extensive search, no local study on the epidemiology of bacterial respiratory pathogens in patients with respiratory

tract infection during COVID-19 was found, hence, this study was conducted. This study aimed to determine the microbiological distribution, antibiotic resistance, and clinical outcomes in cases of bacterial CAP before and during COVID-19. Specifically, it aimed to determine and compare the proportion of the different bacterial isolates among patients admitted for bacterial CAP before and during the COVID-19 pandemic; the proportion of drug-resistant pathogens; and lastly, the clinical outcomes in terms of length of hospital stay and mortality.

METHODOLOGY

Study design

The study used an observational analytical study design comparing the microbiological distribution, antibiotic resistance, and clinical outcomes among elderly patients with bacterial CAP before and during COVID-19. A records review was conducted.

Setting

The study was conducted at Veterans Memorial Medical Center for 12 months.

Study population

The study population consisted of elderly patients admitted for bacterial CAP. The first group was a historical cohort of elderly patients admitted from March 2017 to December 2019. The second group was a historical cohort of elderly patients admitted from March 2020 to December 2022.

Eligibility criteria

Inclusion criteria

1. Patients aged 65 to 85 years
2. Patients admitted to the general ward or intensive care unit
3. Diagnosed with CAP with bacterial isolates from a respiratory specimen
4. Bacterial isolates with specimen showing Gram stain satisfactory for interpretation (neutrophil count >25 per low power field and <10 epithelial cells)

Exclusion criteria

1. Patient records with incomplete data
2. Neutropenic patient
3. Patients transferred from other hospitals and being managed as a case of hospital acquired-pneumonia or ventilator-associated pneumonia

Sampling design

The principal investigator obtained a list of respiratory specimens submitted for culture studies from the Department of Pathology from January 2017 to December 2022. Patients with bacterial isolates from submitted specimens were listed and their records retrieved from the Medical Records Department for review. The medical records of each subject were screened by the principal investigator using the inclusion and exclusion criteria to ascertain if the subject was eligible for study.

Purposive sampling was employed using the list of patients obtained with a diagnosis of bacterial pneumonia as a sampling frame.

Sample size

At a 95% confidence level and 80% power of test, a minimum sample of 226 was required to detect at least 25% difference in clinical outcome. The calculation was based on the bacterial detection rate of 71% in the COVID cohort vs 62% in the pre-COVID cohort by Serigstad et al.[25]

Study procedure

For patients admitted from March 2017 to December 2019, the study collected data on: age, sex, admitting diagnosis, smoking history, comorbidities, bacteria isolated from culture studies, antibiotic sensitivity, antibiotic given during admission, number of days of hospital stay, and outcome (survive or mortality). For patients admitted from March 2020 to December 2022, the study collected data on the same, with the addition of co-infection with COVID-19 (yes or no).

Drug resistance was further classified as multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan drug-resistant (PDR) based on the European Center for Disease Control and Center for Disease Control Atlanta definitions. Prolonged hospital stay was defined as hospitalization lasting 14 days or longer.

Statistical analysis

Shapiro-Wilk test was used to determine the normality of age distribution, which was the only continuous variable. Descriptive statistics were presented as frequencies and percentages for categorical variables, and median and interquartile range (IQR) for the non-normally distributed age variable. Wilcoxon rank-sum and chi-square test were used to compare medians and categorical variables, respectively. STATA 17.0BE was the statistical software used. P-values less than 0.05 were considered statistically significant.

Ethical consideration

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was granted by the Institutional Review Board of the institution (VMMC-IRB Control No. VMMC-2023-034). The primary researcher applied for a waiver of individual informed consent since the study only involved medical records review. Access to medical records was approved by the Department of Pathology and Medical Records Section. Measures to ensure confidentiality, data privacy, and anonymity were employed to reduce the potential risk of breach of confidentiality.

RESULTS

Clinical and demographic profile

A total of 243 patient records met the eligibility criteria and were included in the study (Table 1). The COVID-19 period patients were significantly younger than the pre-COVID-19 period patients (median age 70 [IQR 67–75] vs 74 [IQR 67–80] years; p = 0.015). Males predominated in both groups but significantly more males were in the COVID-19 than in the pre-COVID-19 group (74.50% vs 56.45%; p= 0.005). There was an almost equal distribution of moderate-risk (CAP MR) and high-risk pneumonia (CAP HR) patients in the COVID-19 group while the pre-COVID-19 group was predominated by high-risk pneumonia patients (56.35%). Both groups had a greater proportion of non-smokers. Hypertension was the most common comorbidity in the pre-COVID-19 group while diabetes was most common in the COVID-19 group. There were significantly fewer patients with heart failure in the COVID-19 group than in the pre-COVID-19 group (8.62% vs 17.46%; p= 0.043).

Tables 2 and 3 show the antibiotic/s used upon admission for CAP MR and CAP HR patients. Dual antibiotic therapy with

Table 1. Clinico-demographic profile of elderly patients admitted for bacterial CAP, before and during COVID-19

	Overall (n = 243)	Pre-COVID -19 (n = 126)	COVID-19 (n = 117)	p-value
Age, years (median [IQR])	72 (67–79)	74 (67–80)	70 (67–75)	0.015*
Sex, n (%)				
Male	157 (64.1)	71 (56.45)	86 (74.50)	0.005*
Female	86 (35.39)	55 (43.65)	31 (26.50)	
Diagnosis, n (%)				
CAP MR	114 (46.91)	55 (43.65)	59 (50.43)	0.290
CAP HR	129 (53.09)	71 (56.35)	58 (49.47)	
Smoking, n (%)				
Yes	110 (45.27)	55 (43.65)	55 (47.01)	0.599
No	133 (54.73)	71 (56.35)	62 (52.99)	
Comorbidity, n (%)				
Hypertension	94 (38.68)	48 (38.10)	46 (39.32)	0.845
Diabetes mellitus	87 (35.80)	40 (31.75)	47 (40.17)	0.171
Chronic obstructive pulmonary disease	64 (26.34)	30 (23.81)	34 (29.06)	0.353
Bronchial asthma	11 (4.53)	8 (6.35)	3 (2.56)	0.156
Heart failure	32 (13.22)	22 (17.46)	10 (8.62)	0.043*
Chronic kidney disease	35 (14.40)	15 (11.90)	20 (17.09)	0.250
Liver disease	1 (0.41)	0 (0.00)	1 (0.85)	0.298
Cerebrovascular disease	33 (13.58)	21 (16.67)	12 (10.26)	0.145
Cancer	23 (9.47)	13 (10.32)	10 (8.55)	0.638
No comorbidity	10 (4.13)	3 (2.38)	7 (6.03)	0.154
COVID-19 co-infection		…	46 (39.32)	

*p-values are significant (<0.05)
CAP: community-acquired pneumonia; CAP MR, CAP moderate risk; CAP HR, CAP high-risk

Table 2. Antibiotic/s used upon admission for CAP MR patients

n (%)	Overall (n = 114)	Pre-COVID-19 (n = 55)	COVID-19 (n = 59)
Ampicillin sulbactam	7 (6.14)	2 (3.64)	5 (8.47)
Cefepime	5 (4.39)	3 (5.45)	2 (3.39)
Cefoxitin	1 (0.88)	1 (1.82)	0 (0.00)
Ceftazidime	12 (10.53)	5 (9.09)	7 (11.86)
Ceftriaxone	65 (57.02)	31 (56.36)	34 (57.63)
Cefuroxime	9 (7.89)	6 (10.91)	3 (5.08)
Co-amoxiclav	1 (0.88)	1 (1.82)	0 (0.00)
Levofloxacin	1 (0.88)	1 (1.82)	0 (0.00)
Meropenem	0 (0.00)	0 (0.00)	0 (0.00)
Piperacillin tazobactam	13 (11.40)	5 (9.0)	8 (13.56)
Regimen			
Monotherapy	49 (42.98)	25 (45.45)	24 (40.68)
Dual therapy	65 (57.02)	30 (54.55)	35 (59.32)
Second drug			
Azithromycin	62/65 (95.38)	28/65 (43.08)	34/65 (52.31)
Clarithromycin	1/65 (1.54)	1/65 (1.54)	0/65 (0.00)
Levofloxacin	2/65 (3.08)	1/65 (1.54)	1/65 (1.64)

Table 3. Antibiotic/s used upon admission for CAP HR patients

n (%)	Overall (n = 129)	Pre-COVID-19 (n = 71)	COVID-19 (n = 58)
Ampicillin sulbactam	9 (6.98)	6 (8.45)	3 (5.17)
Cefepime	14 (10.85)	4 (5.63)	10 (17.24)
Cefoxitin	0 (0.00)	0 (0.00)	0 (0.00)
Ceftazidime	11 (8.53)	8 (11.27)	3 (5.17)
Ceftriaxone	29 (22.48)	12 (16.90)	17 (29.31)
Cefuroxime	5 (3.88)	3 (4.23)	2 (3.45)
Co-amoxiclav	0 (0.00)	0 (0.00)	0 (0.00)
Levofloxacin	0 (0.00)	0 (0.00)	0 (0.00)
Meropenem	4 (3.10)	2 (2.82)	2 (3.45)
Piperacillin tazobactam	57 (44.19)	36 (50.70)	21 (36.21)
Regimen			
Monotherapy	87 (67.44)	55 (77.46)	32 (55.17)
Dual therapy	42 (32.56)	16 (22.54)	26 (44.83)
Second drug			
Azithromycin	38/42 (90.48)	14/42 (33.33)	24/42 (57.14)
Clarithromycin	0/42 (0.00)	0/42 (0.00)	0/42 (0.00)
Levofloxacin	4/42 (9.52)	2/42 (4.76)	2/42 (4.76)

ceftriaxone and azithromycin was commonly given for CAP MR in both groups while monotherapy with piperacillin tazobactam was commonly administered for CAP HR in both groups. This study documented 39.32% confirmed COVID-19 co-infection cases during the COVID-19 period (Table 1).

Bacterial isolates

Overall, the top five most common bacterial isolates were *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Enterococcus faecalis* (Table 4). During the COVID-19 period, the most common isolated strains were *K. pneumoniae*, *S. aureus*, *A. baumannii*, *E. faecalis*, and *P. aeruginosa*. Meanwhile, among the pre-COVID-19 group, the most common strains were *A. baumannii*, *K. pneumoniae*, *Enterobacter aerogenes*, *P. aeruginosa*, and *S. aureus/E. faecalis*. The proportion of *A. baumannii* was significantly lower in the COVID-19 group than in the pre-COVID-19 group (10.3% vs 27.0%; p <0.001).

Bacterial sensitivity/resistance profile

As presented in Table 5, antimicrobial-resistant pathogens were lower in the COVID-19 group than in the pre-COVID-19 group but this was not statistically significant (55.56% vs 61.90%; p = 0.316). During COVID-19, 50% (23/46) of the bacterial isolates from COVID-19-confirmed patients were resistant. The proportion of MDR pathogens was significantly higher in the COVID-19 group compared to the pre-COVID-19 group (21.37% vs 9.52%; p = 0.010). Eight isolates (6.84%) were MDR with COVID-19 co-infection. The proportion of XDR pathogens was lower among the COVID-19 group than the pre-COVID-19 group (14.53% vs 21.43%). Nine isolates (7.69%) were XDR with COVID-19 infection. The proportion of PDR pathogens was significantly lower among the COVID-19 group compared to the pre-COVID-19 group (19.66% vs 30.95%; p = 0.044). Six isolates (5.13%) were PDR with COVID-19 co-infection.

The drug resistance patterns of all isolates before and during COVID-19 period are presented in Figures 1 and 2. As presented in Figure 1, pre-COVID-19, the top three MDR isolates (n = 12) were *K. pneumoniae* (n = 5), *A. baumannii* (n = 3), *and Enterococcus faecalis* (n = 2). The most common XDR (n

Table 4. Bacterial isolates from respiratory specimens of elderly patients admitted for bacterial CAP, before and during COVID-19

n (%)	Overall (n = 243)	Pre-COVID-19 (n = 126)	COVID-19 (n = 117)	p-value
Klebsiella pneumoniae	69 (28.4)	33 (26.2)	36 (30.8)	0.429
Acinetobacter baumannii	46 (18.9)	34 (27.0)	12 (10.3)	<0.001*
Pseudomonas aeruginosa	21 (8.6)	10 (7.9)	11 (9.4)	0.685
Staphylococcus aureus	19 (7.8)	6 (4.8)	13 (11.1)	0.065
Enterococcus faecalis	18 (7.4)	6 (4.8)	12 (10.3)	0.102
Enterobacter aerogenes	13 (5.3)	12 (9.5)	1 (0.9)	**
Escherichia coli	9 (3.7)	4 (3.2)	5 (4.3)	
Streptococcus viridans	9 (3.7)	3 (2.4)	6 (5.1)	
Enterobacter cloacae	6 (2.5)	2 (1.6)	4 (3.4)	
Burkholderia cepacia	4 (1.6)	2 (1.6)	2 (1.7)	
Coagulase-negative staphylococci (CONS)	4 (1.6)	3 (2.4)	1 (0.9)	
Klebsiella aerogenes	4 (1.6)	0 (0.0)	4 (3.4)	
Klebsiella oxytoca	4 (1.6)	3 (2.4)	1 (0.9)	
Stenotrophomonas	3 (1.2)	1 (0.8)	2 (1.7)	
Non-*enterococcus*	2 (0.8)	1 (0.8)	1 (0.9)	
Acinetobacter iwoffii	1 (0.4)	1 (0.8)	0 (0.0)	
Enterobacter gergoviae	1 (0.4)	0 (0.0)	1 (0.9)	
Hafnia alvei	1 (0.4)	1 (0.8)	0 (0.0)	
Citrobacter diversus	1 (0.4)	1 (0.8)	0 (0.0)	
Citrobacter	1 (0.4)	0 (0.0)	1 (0.9)	
Methicillin-resistant *Staphylococcus aureus* (MRSA)	1 (0.4)	1 (0.8)	0 (0.0)	
Providencia rettgeri	1 (0.4)	0 (0.0)	1 (0.9)	
Pseudomonas fluorescens	1 (0.4)	0 (0.0)	1 (0.9)	
Serratia rubidaea	1 (0.4)	1 (0.8)	0 (0.0)	
Enterobacter agglomerans	1 (0.4)	0 (0.0)	1 (0.4)	
Streptococcus species	1 (0.4)	1 (0.8)	0 (0.0)	
Streptococcus agalactiae	1 (0.4)	0 (0.0)	1 (0.9)	

*p-values are significant (<0.05)
**p-values cannot be generated due to the violation of the Chi-square test prerequisite: expected cell values of at least more than 5 in 80% of the cells

Table 5. Status of drug-resistance of bacterial isolates from elderly patients with bacterial CAP, before and during COVID-19

n (%)	Overall (n = 243)	Pre-COVID-19 (n = 126)	COVID-19 (n = 117)	p-value
Bacterial isolate				
Sensitive	100 (41.15)	48 (38.10)	52 (44.00)	0.316
With COVID-19 co-infection	23 (9.47)	…	23 (19.66)	
Resistant	142 (58.85)	78 (61.90)	65 (55.56)	0.316
With COVID-19 co-infection	23 (9.47)	…	23 (19.66)	
Subtype of drug resistance				
MDR	37 (15.23)	12 (9.52)	25 (21.37)	0.010*
With COVID-19 co-infection	8 (3.29)	…	8 (6.84)	
XDR	44 (18.11)	27 (21.43)	17 (14.53)	0.163
With COVID-19 co-infection	9 (3.70)	…	9 (7.69)	
PDR	62 (25.51)	39 (30.95)	23 (19.66)	0.044*
With COVID-19 co-infection	6 (2.47)	…	6 (5.13)	

*p-values are significant (<0.05)
MDR: multidrug-resistant; XDR: extremely drug-resistant; PDR: pan drug-resistant

= 27) and PDR (n = 39) isolates were *A. baumannii* (n = 7 and 17, respectively), *K. pneumoniae* (n = 5 and 10, respectively), *and E. aerogenes* (n = 4 and 5, respectively). In contrast, during the COVID-19 period (Figure 2), the top three MDR isolates (n = 25) were *K. pneumoniae* (n = 17), *Escherichia coli* (n = 3), *and E. faecalis* (n = 3). The most common XDR isolates (n = 17) were *K. pneumoniae* (n = 7) *and E. faecalis* (n = 3). For the PDR isolates (n = 23), the most common were *K. pneumoniae* (n = 5), *P. aeruginosa* (n = 4), and *A. baumannii* (n = 3).

Clinical outcomes

Length of hospital stay

Overall, 150 (61.73%) elderly patients had prolonged hospital stay. A higher proportion of patients in the COVID-19 group had prolonged hospital stay compared to the pre-COVID-19 group but the difference was not statistically significant (73/117 [62.39%] vs 77/126 [61.11%]; p = 0.838). The top five common bacteria isolated in the pre-COVID-19 group were *A. baumannii, K. pneumoniae, P. aeruginosa, E. aerogenes, and S. aureus*. Meanwhile, in the COVID-19 group, *K. pneumoniae, A. baumannii, P. aeruginosa, E. faecalis, and S. aureus* were most common (Table 6). The proportion of *A. baumannii*-infected patients was significantly lower in the COVID-19 group than in the pre-COVID-19 group (13.70% vs 29.87%; p = 0.002). The proportion of patients infected by *K. pneumoniae, P. aeruginosa, and S. aureus* was higher among the COVID-19 group than the pre-COVID-19 group.

The proportion of MDR patients with prolonged hospital stay was higher among the COVID-19 group (15.07%) than in the pre-COVID-19 group (5.19%) while the proportion of XDR and PDR patients with prolonged hospital stay was higher among the pre-COVID-19 group than in the COVID-19 group (Table 7).

Mortality

Overall, 120 (49.38%) elderly patients died (Table 8). A significantly lower proportion of elderly patients died in the COVID-19 group compared to the pre-COVID-19 (49/117 [41.88%] vs 71/126 [56.35%]; p = 0.024). In the COVID-19 group, of the 46 COVID-19-confirmed patients, 19 (41.30%) died. Among the mortalities in the pre-COVID-19 group, the top five bacterial isolates were *A. baumannii, K. pneumoniae, E. aerogenes, P. aeruginosa, and E. faecalis* while, in the COVID-19 group, the top isolates were *K. pneumonia, A. baumannii, S. aureus, P. aeruginosa, and E. faecalis.* The proportion of *A. baumannii*-infected patients was significantly lower among the COVID-19 group than in the pre-COVID-19 group (14.29% vs 35.21%; p <0.001).

In terms of resistant strains, the proportion of MDR patients who died was significantly higher in the COVID-19 group compared to the pre-COVID group (24.49% vs 8.45%; p= 0.016). The proportion of XDR patients who died was higher in the pre-COVID-19 group compared to the COVID-19 group (26.76% vs 16.33%; p = 0.179). Lastly, the proportion of PDR patients who died was higher in the pre-COVID-19 group compared to the COVID-19 group (43.66% vs 30.61%; p =

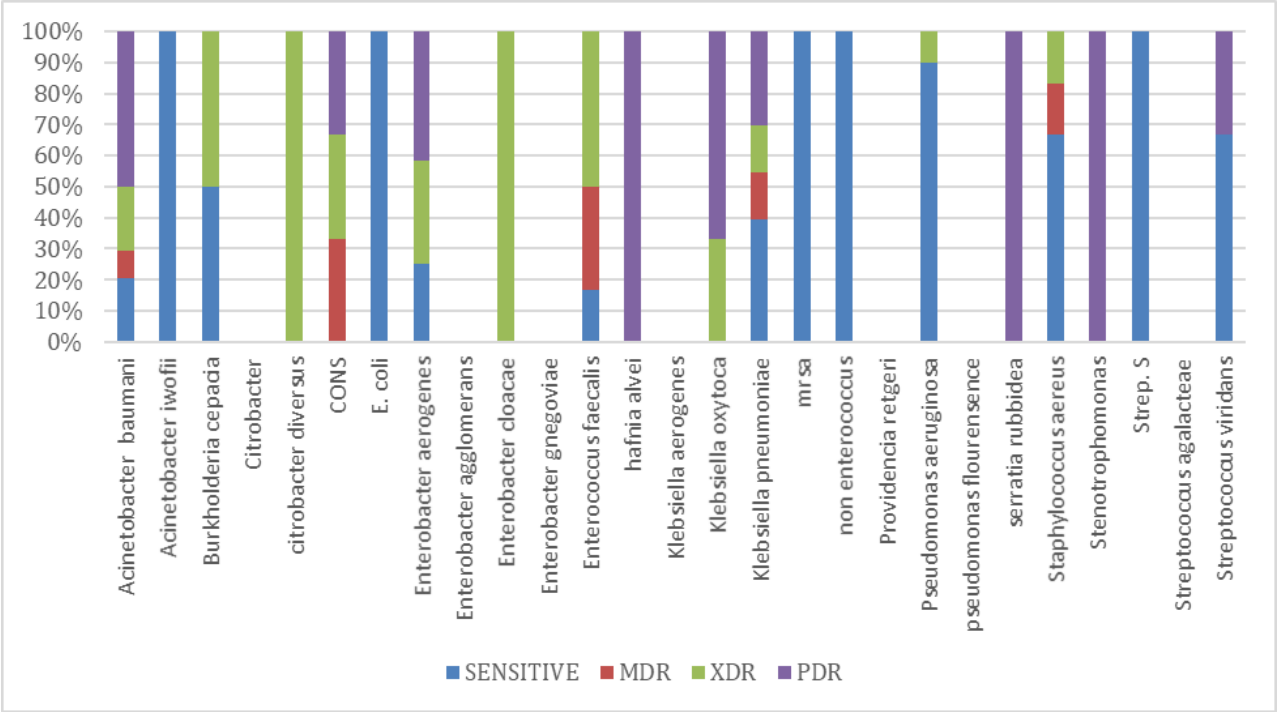

Figure 1. Classification of organisms according to European Center for Disease Control and Centre for Disease Control Atlanta as sensitive, multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan drug-resistant (PDR) strains pre-COVID-19

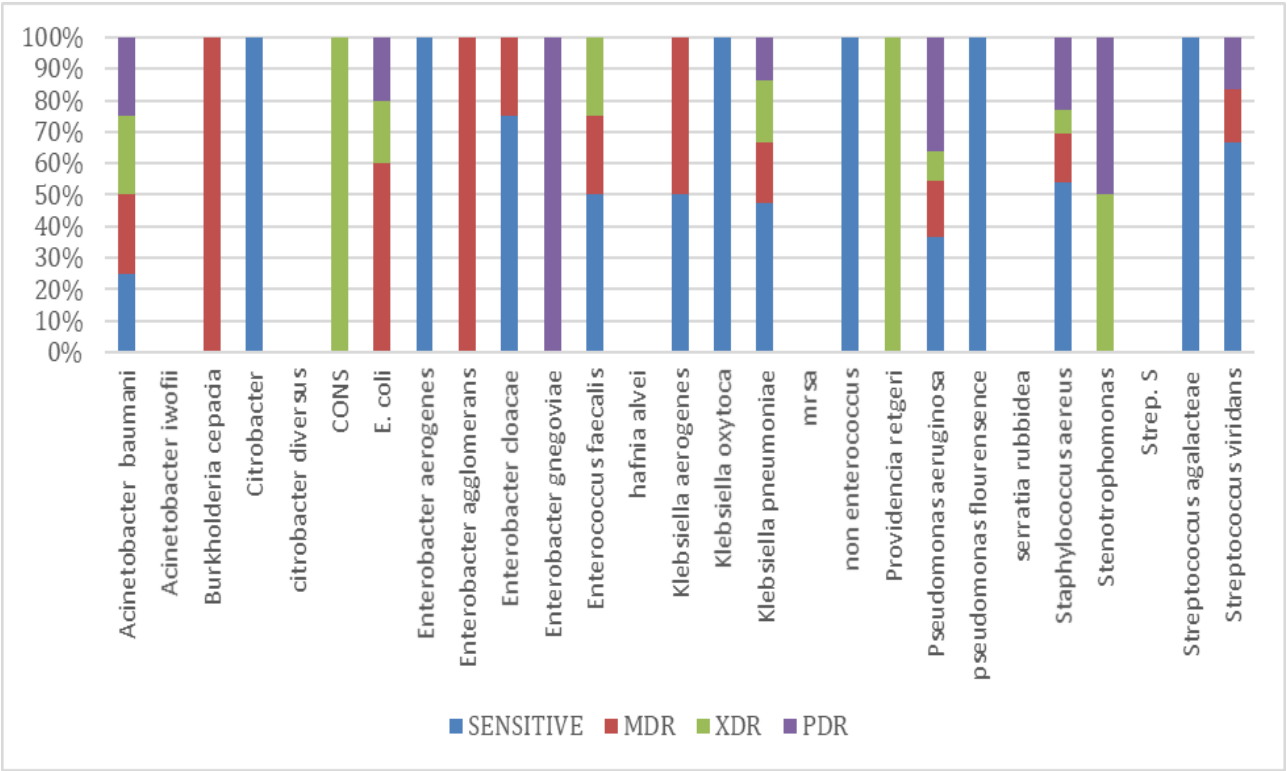

Figure 2. Classification of organisms according to European Center for Disease Control and Centre for Disease Control Atlanta as sensitive, multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan drug-resistant (PDR) strains during COVID-19

Table 6. Bacterial isolates from elderly patients admitted for bacterial CAP with prolonged hospital stay, before and during COVID-19

n (%)	Overall (n = 150)	Pre-COVID-19 (n = 77)	COVID-19 (n = 73)	p-value
A. baumannii	33 (22)	23 (29.87)	10 (13.70)	0.002*
K. pneumoniae	37 (24.67)	17 (22.08)	20 (27.40)	0.450
P. aeruginosa	15 (10)	7 (9.09)	8 (10.96)	0.703
E. aerogenes	6 (4)	5 (6.49)	1 (1.37)	**
S. aureus	10 (6.67)	5 (6.49)	5 (6.85)	0.930
E. faecalis	10 (6.67)	3 (3.9)	7 (9.59)	**

*p-values are significant (<0.05)
**p values cannot be generated due to the violation of the Chi-square test prerequisite: expected cell values of at least more than 5 in 80% of the cells

Table 7. Drug-resistant strains isolated from elderly patients admitted for bacterial CAP with prolonged hospital stay, before and during COVID-19

n (%)	Overall (n = 150)	Pre-COVID-19 (n = 77)	COVID-19 (n = 73)	p-value
MDR	15 (10)	4 (5.19)	11 (15.07)	*
XDR	27 (18)	17 (22.08)	10 (13.70)	0.182
PDR	45 (30)	27 (35.06)	18 (24.66)	0.164

*p-values cannot be generated due to the violation of the Chi-square test prerequisite: expected cell values of at least more than 5 in 80% of the cells
MDR: multidrug-resistant; XDR: extremely drug-resistant; PDR: pan drug-resistant

Table 8. Bacterial isolates from elderly patients admitted for bacterial CAP who died, before and during COVID-19

n (%)	Overall (n = 120)	Pre-COVID-19 (n = 71)	COVID-19 (n = 49)	p-value
A. baumannii	32 (26.67)	25 (35.21)	7 (14.29)	<0.001*
K. pneumoniae	29 (24.17)	16 (22.54)	13 (26.53)	0.615
E. aerogenes	7 (5.83)	6 (8.45)	1 (2.04)	**
P. aeruginosa	9 (7.5)	5 (7.04)	4 (8.16)	**
E. faecalis	7 (5.83)	3 (4.23)	4 (8.16)	**
S. aureus	8 (6.67)	2 (2.82)	6 (12.24)	**

*p-values are significant (<0.05)
**p-values cannot be generated due to the violation of the Chi-square test prerequisite: expected cell values of at least more than 5 in 80% of the cells

0.148) (Table 9).

Table 9. Drug-resistant strains isolated from elderly patients admitted for bacterial CAP who died, before and during COVID-19

n (%)	Overall (n = 120)	Pre-COVID-19 (n = 71)	COVID-19 (n = 49)	p-value
MDR	18 (15.00)	6 (8.45)	12 (24.49)	0.016*
XDR	27 (22.50)	19 (26.76)	8 (16.33)	0.179
PDR	46 (38.33)	31 (43.66)	15 (30.61)	0.148

*p-values are significant (<0.05)
MDR: multidrug-resistant; XDR: extremely drug-resistant; PDR: pan drug-resistant

DISCUSSION

Our study revealed that the distribution of bacterial isolates did not differ between the periods studied. The most common bacterial pathogens documented in both the pre-COVID-19 and COVID-19 periods were *A. baumannii, K. pneumoniae, P. aeruginosa, E. aerogenes, E. faecalis, and S. aureus.* Comorbidities such as chronic obstructive pulmonary disease, renal disease, and diabetes mellitus put elderly patients at risk of community-acquired infection due to these bacteria.[3] *A. baumannii* was isolated less frequently during COVID-19 which contrasts with published literature.[20,21] The disparity may be attributed to differences in bacterial colonization across centers, clinical profiles of the patients, and sensitivity of available antibiotics. Our results support recent reports of increased prevalence of *K. pneumoniae* and *S. aureus* in COVID-19 cohorts.[7,22-24] In the study by Serigstad et al, *S. aureus* was the second most common bacterial pathogen detected during the pandemic at about 23% following *H. influenzae*.[25] *S. aureus* is a frequent colonizer of the upper respiratory tract, and nasal carriage is associated with infection and risk for bacteremia. It is also a common co-infecting pathogen in COVID-19 patients because of the molecular interaction between SARS-CoV-2 and *S. aureus*.[25] This might explain why *S. aureus* remained prevalent during the COVID-19 period.

Multidrug resistance was significantly higher during the COVID -19 period which may be due to multiple factors. First, was the reversal of already implemented preventive measures as institutions focused more on COVID-19, and personnel, resources, and attention were diverted from antimicrobial resistance surveillance and diagnosis. Secondly, studies claimed that, because of the pandemic, empiric utilization of antimicrobial agents increased.[7,17,26]

For both periods, the majority of patients had prolonged hospital stay. Prolonged hospital stay may not be solely associated with the causative agent's bacterial profile but also with disease severity, patient's comorbidities, and duration of antibiotic treatment.

The present study also documented significantly higher mortality among patients with bacterial CAP in the pre-COVID-19 period compared to the COVID-19 period. However, mortality in patients with MDR strains was significantly higher during the COVID-19 period. This finding is congruent with the analysis of other published literature.[27-31] Boral et al concluded that MDR *A. baumannii* infections occurred more frequently during COVID-19, and the case fatality rate was higher than pre -COVID-19 (83.3% vs 81.5%; p = 0.835).[20] The lack of effective antimicrobial treatments against resistant strains of *A. baumannii* may have contributed to the mortality rate. Meanwhile, disease severity was the underlying cause of mortality for those patients harboring resistant strains, based on Rao et al's study.[32]

This study had limitations being a single-center study where bacterial colonization may be different from other centers. The chart review nature of the study limited the investigator in the data that can be collected and validated. This study did not investigate other factors that might have an impact on resistance, for instance, the association between patient's comorbidities and resistant strains, as this was beyond the scope of the present study.

CONCLUSIONS

Our study concluded that the distribution of bacterial isolates did not differ significantly between the pre-COVID-19 and COVID-19 periods. The most common bacterial pathogens documented both in the pre-COVID-19 and COVID-19 periods were *A. baumannii, K. pneumoniae, P. aeruginosa, E. aerogenes, E. faecalis, and S. aureus.* Multidrug resistance was significantly higher during the COVID-19 period. The majority of patients had prolonged hospital stay for both periods. Mortality in

patients with MDR strains was significantly higher during the COVID-19 period.

These findings are essential in informing the antimicrobial stewardship program of the institution. Vigilant surveillance and regular reporting of bacterial pathogens, especially those with resistant strains, are needed to improve clinical outcomes. We recommend that similar studies be carried out for hospital-acquired pneumonia including ventilator-associated pneumonia.

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