

Impact of COVID-19 on the Distribution of Pathogenic Bacteria in the Lower Respiratory Tract of the Elderly

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Abstract

Background: To investigate the distribution of bacterial pathogens of lower respiratory tract infection (LRTI) in hospitalized elderly patients during the COVID-19 epidemic and to explore the influence of COVID-19 on the distribution of bacterial pathogens, in order to provide guidance for clinical diagnosis. **Methods:** Specimens of sputum from elderly LRTIs patients at Fuding Hospital of China were collected from October 2022 to January 2023. Cultures and identification were done, and RT-PCR was employed to detect SARS-Cov-2 nucleic acid. **Results:** A total of 195 isolates were characterized in 163 sputum samples of consecutive hospitalized elderly patients, of which 11.3% were Gram-positive bacteria and 88.7% Gram-negative. The top of frequently isolated pathogens were *Klebsiella pneumonia* (30.3%), *Pseudomonas aeruginosa* (19.0%), *Acinetobacter baumannii* (12.8%), *Stenotrophomonas maltophili*, (7.7%), *Escherichia coli* (7.2%). According to the results of novel coronavirus nucleic acid detection, the 163 patients were divided into COVID-19 group and non-COVID control (CNT) group. The comparison of bacterial distribution between the groups revealed that *Stenotrophomonas maltophilia* was lower in the COVID-19 than in the CNT group, while *Acinetobacter baumannii* was higher in the COVID-19 group, and the difference was statistically significant ($P < 0.05$). **Conclusion:** The major bacteria identified in sputum culture of hospitalized elderly patients were *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Stenotrophomonas maltophilia*, and *Escherichia coli*. Furthermore, the distribution of *Stenotrophomonas maltophilia* and *Acinetobacter baumannii* between the COVID-19 and CNT groups was found to be significantly different ($P < 0.05$), while there were no significant differences in the distribution of other bacteria.

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Conclusion : The major bacteria identified in sputum culture of hospitalized elderly patients were *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Stenotrophomonas maltophilia*, and *Escherichia coli*. Furthermore, the distribution of *Stenotrophomonas maltophilia* and *Acinetobacter baumannii* between the COVID-19 and CNT groups was found to be significantly different ($P < 0.05$), while there were no significant differences in the distribution of other bacteria.

Keywords

Elderly; Lower Respiratory Tract; COVID-19, *Stenotrophomonas maltophilia*, *Acinetobacter baumannii*, Bacterial Infection.

Introduction

Age has been identified as a major factor influencing the outcomes of COVID-19. Elderly individuals (over the age of 60) are more likely to be admitted to the intensive care unit and have a higher mortality rate due to their immunosenescence and the presence of multiple comorbidities^[1, 2]. To better understand the prevalence of lower respiratory tract infections (LRTIs) in elderly patients, sputum samples from inpatients aged over 60 were collected and subjected to culturing.

Lower respiratory tract infections are common bacterial infections among hospitalized patients, with a mortality rate of up to 3-5% in adults, particularly the elderly^[3, 4], these infections can be further complicated by the emergence of the novel coronavirus. Elderly patients with multiple underlying diseases and decreased immune function are more vulnerable to the new coronavirus infection, which is often accompanied by lower respiratory tract bacterial infection.

This study aimed to analyze the distribution of sputum bacterial culture pathogens in hospitalized elderly LRTI patients and the effect of the novel coronavirus on these pathogens. The results of this study will provide valuable insight into the prevalence in elderly LRTI patients and the impact of the novel coronavirus on these infections. This information can be used to inform clinical diagnosis and treatment strategies for elderly LRTI patients.

This retrospective study included 163 elderly LRTI patients admitted to the hospital between October 2022 and January 2023, including 129 males and 34 females aged 60-95 years old (see Table 1 for more details). All patients underwent routine bacterial culture, isolation and identification of pathogenic bacteria from sputum specimens, and RT-PCR method was used to determine the coronavirus nucleic acid. This study was approved by the Medical Ethics Committee of Fuding Hospital.

Materials and Methods

Bacterial isolation and identification were conducted according to the third edition of the National Guide for Clinical Laboratory Procedures. Bacterial analyzers and identification cards were used for the isolation and identification of pathogens. Before the patient received anti-infective therapy upon admission, an oropharyngeal swab was tested for coronavirus nucleic acid, and sputum, suction sputum, tracheal secretions, and deep tracheal secretions were also obtained and immediately sent to the laboratory for bacterial culture.

The laboratory conducted a preliminary screening by microscopy, Gram staining and low-power observation of single-field squamous epithelial cells less than 10 and more than 25 neutrophils were considered qualified sputum specimens. Qualified sputum specimens were inoculated on Blood agar plates and cultured in a 35°C incubator for 24-48 hours to isolate and purify the dominant bacteria and make an identification. Microorganisms were identified performing a VITEK 2 identification system.

The control strains used: *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212 and *Pseudomonas aeruginosa* ATCC 27853 were all obtained from the Fujian Provincial Inspection Center. The coronavirus nucleic acid test was performed by RT-PCR, and the reagents, positive and negative control reagents, automatic nucleic acid extractor, and fluorescent PCR instrument were all provided by Xi'an Tianlong Gene Co., Ltd. Ct values (cycle threshold values) less than 40 were judged as positive results.

Data processing was performed using the SPSS version 22.0 software (SPSS Inc., Chicago, IL, United States), and the count data was expressed as percentages. The Chi-square test (χ^2) or Fisher's exact test was used for inter-group comparison. Fisher's exact test was applied as numbers in one or more categories were <5 . Testing of data for normal distribution was performed by means of Kolmogorov-Smirnov test. For metric data that had passed the normality test, the median and quartiles (P25-P75) were used to represent the data. Mann-Whitney U test (non-parametric test) was used for data comparison. In all tests, a $P < 0.05$ was considered statistically significant.

Results

A total of 163 hospitalized elderly patients were included in this study, including 84 patients in the COVID-19 group and 79 in the CNT group. The age of the patients in the two groups was tested by Kolmogorov-Sminov test, with the results of COVID-19 group $Z = 0.086$, $P = 0.162$ and CNT group $Z = 0.162$, $P < 0.001$. The data showed a non-normal distribution, and statistical analysis was performed by Mann-Whitney U test (non-parametric test). Chi-square test was used to compare the gender between the two groups. The test results of age and gender were shown in Table 1, and there was no statistically significant difference ($P > 0.05$).

Among 163 hospitalized elderly patients with sputum samples, 195 strains of bacteria were isolated, including 22 Gram-positive bacteria (11.3%) and 178 Gram-negative bacteria (88.7%). The top 10 pathogenic bacteria were *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Stenotrophomonas maltophilia*, *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenza*, *Enterobacter cloacae*, and *Enterobacter aerogenes*. accounting for 30.3%, 19.0%, 12.8%, 7.7%, 7.2%, 6.7%, 4.6%, 3.1%, 2.1%, and 1.5%, respectively, and the remaining bacteria accounted for 6.0%. See Table 2 and Figure 1.

Single bacteria infection occurred in 163 cases (82.2%, 134/163) of hospitalized elderly patients, and mixed infection with two bacteria occurred in 25 cases (16.0%, 26/163), and mixed infection with three bacteria occurred in 3 cases (1.8%, 3/163).

The distribution of bacteria in COVID-19 group (98 strains) and CNT group (97 strains) was analyzed. Except for *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*, there was no statistical difference in the distribution of other strains. The composition ratio of *Acinetobacter baumannii* in the COVID-19 group (7.1%) was lower than that in the CNT group (18.6%), the difference was statistically significant ($P = 0.017$); the composition ratio of *Stenotrophomonas maltophilia* in the COVID-19 group (12.2%) was higher than that in the CNT group (3.1%), the difference was statistically significant ($P = 0.016$). See Table

Discussion and Conclusion

The novel coronavirus has been found to have membrane glycoprotein, spike protein, nucleocapsid protein, envelope protein and coagulase^[5]. The spike glycoprotein on the surface of the virus plays a major role in its attachment and entry into host cells, and the infection can lead to lethal damage in the lungs, heart, kidneys, circulatory system, gastrointestinal tract and nervous system tissues^[6]. Elderly people are particularly

vulnerable to the virus due to their weakened immune systems, and evidence suggests that a large number of hospitalized patients during the COVID-19 pandemic had mixed bacterial infections and secondary bacterial infections, which were a major cause of higher mortality in elderly patients [7]. When the novel coronavirus invades the lungs, it causes damage to the lung cells and tissues, which attracts neutrophils and macrophages to the infected site and promotes inflammation, and eventually leads to bacterial adhesion and invasion into the cells and proliferation [8]. Therefore, it is essential to identify the bacterial pathogens of LRTIs in the elderly.

The results of this study showed that *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacteroides fragilis*, *Escherichia coli*, *Stenotrophomonas maltophilia*, *Staphylococcus aureus*, and *Streptococcus pneumoniae* were the main pathogenic bacteria in the sputum specimens of 163 hospitalized elderly patients in this study. This is consistent with similar studies [9], which showed that the common bacteria identified in respiratory cultures, even the sputum culture results of elderly patients with pulmonary infections, were mostly Gram-negative bacteria, mainly including *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacteroides fragilis*, etc.; the Gram-positive bacteria infected included *Streptococcus pneumoniae*, *Staphylococcus aureus*, etc. *Klebsiella pneumoniae* is a Gram-negative bacteria with a thick capsule, mostly distributed in the human respiratory and gastrointestinal tracts, and is a common pathogen for elderly respiratory infections. SAIDK et al. [10] conducted a screening for combined microbial infection in 301 COVID-19 patients, and the main microorganisms detected were *Klebsiella pneumoniae* (37%, 48/301), *Pseudomonas aeruginosa* (8.5%, 11/301), and *Escherichia coli* (18.6%, 24/301).

The opportunistic Gram-negative bacillus *Stenotrophomonas maltophilia* is known to infect mostly elderly patients. According to one study, individuals over the age of 60 were more prone to *S. maltophilia* infection, which could be attributed to immunosuppression [11]. In recent years, *S. maltophilia* has been relatively stable in third place among non-fermenting Gram-negative bacteria, after *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, according to the CHINET monitoring service [12]. Patients with severely impaired or weakened immune functions were more susceptible to serious consequences when infected with *S. maltophilia*, suggesting that the respiratory tract was the main site of colonization and infection of *S. maltophilia*, which may have been associated with its ability to form biofilms and colonize the respiratory tract of hospitalized patients [13]. Recently, *S. maltophilia* was reported as one of the secondary bacterial infections in ICU patients with COVID-19 [9], which is similar to what was found in this study: the infection rate of *S. maltophilia* was higher in the COVID-19 group than in the CNT group.

Acinetobacter baumannii is a Gram-negative bacterium with strong vitality, and it is a major opportunistic pathogen that can cause double infection, especially in hospitalized patients with viral respiratory infection [14]. Recent studies have shown that the infection rate of *Acinetobacter baumannii* in COVID-19 patients varies widely in different regions. For example, Nanshan Chen et al. [15] reported that among 99 COVID-19 patients in Wuhan, only one was cultured with *Acinetobacter baumannii*, with an infection rate of 10.1% (1/99); another domestic report showed that among 1495 hospitalized COVID-19 patients in Wuhan, 102 (6.8%) had bacterial mixed infection, mainly *Acinetobacter baumannii* (35.8%), and nearly half (49.0%, 50/102) died during hospitalization [16]; Iranian scholars SHARIFIPOUR et al. [14] reported that 17 out of 19 elderly COVID-19 patients had *Acinetobacter baumannii* infection, with an infection rate of 89.5% (17/19); Brazilian researchers SILVADL et al. [17] reported that the infection rate of *Acinetobacter baumannii* was 32.8% (21/64); SAIDKB et al. in Saudi Arabia reported [10] that 34 of the 301 COVID-19 patients had drug-resistant *Acinetobacter baumannii* (26%, n=34).

The infection rate of *Acinetobacter baumannii* varies in different regions, and further research is needed to investigate the specific reasons. In the hospital environment, COVID-19 elderly LRTIs patients may face another threat to health, which is mixed bacterial infection and nosocomial secondary bacterial infection, especially the mixed infection and secondary infection of *Staphylococcus aureus* and *Acinetobacter baumannii*, which may seriously affect the clinical outcome of COVID-19 patients.

Whereas, This study has certain limitations, for it was solely focused on bacteria, not including fungi, mycoplasma, chlamydia, parasites and other viruses into the study of pathogens in elderly LRTIs patients;

The number of patients enrolled is small, which could result in a sample size bias, therefore large-scale clinical studies need to be conducted to investigate the incidence, prevalence, characteristics and microbiological distribution of COVID-19 complicated infections. As a result, a multicenter, prospective, longitudinal study is required to confirmed the research.

In conclusion, the current study has identified the main bacterial pathogens of elderly LRTIs patients, and has highlighted the importance of identifying and treating secondary bacterial infections in elderly patients with COVID-19. Furthermore, the findings of this study suggest that *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacteroides fragilis*, *Escherichia coli*, *Stenotrophomonas maltophilia*, *Staphylococcus aureus*, and *Streptococcus pneumoniae* are the main bacterial pathogens of elderly LRTIs patients, and that *Stenotrophomonas maltophilia* is an opportunistic pathogen that is particularly dangerous for elderly patients with weakened immune systems.

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Contributions

Shi-Yan Zhang, conceived and designed the project, analyzed and interpreted the data, and wrote the paper.

Jing Shi, designed the project and interpreted the data.

Ying Zhuo, analyzed the data and wrote the paper.

Tian-Qiang Wang, acquired and analyzed the data.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

Research data are not shared.

Table 1. Clinical parameters of COVID-19 group and CNT group [case (%)]

Items	CNT (n=79)	COVID-19 (n=84)	Mann-Whitney U / χ^2 test	P value
Age (years) (range)	(61-95)	(60-94)		
Age median (P_{25} - P_{75})	71.0 (66.0-79.0)	73.5 (67.0-79.0)	-0.723	0.470
Gender			1.800	0.180
Male	67(57.9)	62(56.3)		
Female	12(42.1)	22(43.7)		

Kolmogorov-Sminov test was carried out in the age of COVID-19 group and CNT group : COVID-19 (Z

=0.086, $P = 0.162$), CNT ($Z = 0.162$, $P < 0.001$). CNT: non-COVID control subjects.

Table 2. Species and composition of pathogenic bacteria in the studied subjects [n (%)]

Bacteria	CNT (n=97)	COVID-19 (n=98)	Two groups (n=195)
Gram-positive bacterium	12 (12.4)	10 (10.2)	22 (11.3)
<i>Streptococcus pneumoniae</i>	4 (4.1)	5 (5.1)	9 (4.6)
<i>Staphylococcus aureus</i>	8 (8.2)	5 (5.1)	13 (6.7)
Gram-negative bacterium	85 (87.6)	88 (89.8)	173 (88.7)
<i>Achromobacter denitrificans</i>	0 (0.0)	1 (1.0)	1 (0.5)
<i>Moraxella catarrhalis</i>	0 (0.0)	1 (1.0)	1 (0.5)
<i>Aeromonas hydrophila</i>	0 (0.0)	1 (1.0)	1 (0.5)
<i>Leclercia adecarboxylate</i>	1 (1.0)	0 (0.0)	1 (0.5)
<i>Raoultella ornithinolytica</i>	1 (1.0)	0 (0.0)	1 (0.5)
<i>Ralstonia pickettii</i>	1 (1.0)	0 (0.0)	1 (0.5)
<i>Klebsiella oxytoca</i>	1 (1.0)	1 (1.0)	2 (1.0)
<i>Serratia marcescens</i>	0 (0.0)	2 (0.0)	2 (1.0)
<i>Enterobacter aerogenes</i>	1 (1.0)	2 (3.0)	3 (1.5)
<i>Enterobacter cloacae</i>	3 (3.1)	1 (1.0)	4 (2.1)
<i>Haemophilus influenzae</i>	2 (2.1)	4 (4.1)	6 (3.1)
<i>Escherichia coli</i>	10 (10.3)	4 (4.1)	14 (7.2)
<i>Stenotrophomonas maltophilia</i>	3 (3.1)	12 (12.2)	15 (7.7)
<i>Acinetobacter baumannii</i>	18 (18.6)	7 (7.1)	25 (12.8)
<i>Pseudomonas aeruginosa</i>	15 (15.5)	22 (22.4)	37 (19.0)
<i>Klebsiella pneumoniae</i>	29 (29.9)	30 (30.6)	59 (30.3)

CNT: non-COVID control subjects.

Table 3. Comparison of the distribution of pathogenic bacteria between COVID-19 group and CNT group

Bacteria	CNT (n=97)	CNT (n=97)	COVID-19 (n=98)	χ^2	P value
<i>Stenotrophomonas maltophilia</i>	Yes	3 (3.1)	12 (12.2)	5.751	0.016
	No	94 (96.9)	86 (87.8)		
<i>Acinetobacter baumannii</i>	Yes	18 (18.6)	7 (7.1)	5.682	0.017
	No	79 (81.4)	91 (92.9)		
<i>Staphylococcus aureus</i>	Yes	8 (8.2)	5 (5.1)	0.775	0.379
	No	89 (91.8)	93 (94.9)		

Bacteria	CNT (n=97)	CNT (n=97)	COVID-19 (n=98)	χ^2	<i>P</i> value
<i>Haemophilus influenzae</i>	Yes	2 (2.1)	4 (4.1)	0.663	0.415
	No	95 (97.9)	94 (95.9)		
<i>Escherichia coli</i>	Yes	10 (10.3)	4 (4.1)	2.823	0.093
	No	87 (89.7)	94 (95.9)		
<i>Streptococcus pneumoniae</i>	Yes	4 (4.1)	5 (5.1)	0.105	0.745
	No	93 (95.9)	93 (94.9)		
<i>Klebsiella pneumoniae</i>	Yes	29 (29.9)	30 (30.6)	0.012	0.913
	No	68 (70.1)	68 (69.4)		
<i>Klebsiella oxytoca</i>	Yes	1 (1.0)	1 (1.0)	0.000	0.994
	No	96 (99.0)	97 (99.0)		
<i>Enterobacter cloacae</i>	Yes	3(3.1)	1 (1.0)	1.037	0.309
	No	94 (96.9)	97 (99.0)		
<i>Pseudomonas aeruginosa</i>	Yes	15 (15.5)	22 (22.4)	1.547	0.214
	No	82 (84.5)	76 (77.6)		
<i>Enterobacter aerogenes</i>	Yes	1 (1.0)	2 (2.0)	0.327	0.568
	No	96 (99.0)	96 (98.0)		
<i>Ralstonia pickettii</i>	Yes	1 (1.0)	0 (0.0)	1.010	0.315
	No	96 (99.0)	98 (100.0)		
<i>Moraxella catarrhalis</i>	Yes	0 (0.0)	1 (1.0)	0.990	0.320
	No	97 (100.0)	97 (99.0)		
<i>Raoultella ornithinolytica</i>	Yes	1 (1.0)	0 (0.0)	1.010	0.315
	No	96 (99.0)	98 (100.0)		
<i>Leclercia adecarboxylate</i>	Yes	1 (1.0)	0 (0.0)	1.010	0.315
	No	96 (99.0)	98 (100.0)		
<i>Serratia marcescens</i>	Yes	0 (0.0)	2 (1.0)	1.990	1.158
	No	97 (100.0)	96 (98.0)		
<i>Achromobacter denitrificans</i>	Yes	0 (0.0)	1 (1.0)	0.990	0.320
	No	97 (100.0)	97 (99.0)		
<i>Aeromonas hydrophila</i>	Yes	0 (0.0)	1 (1.0)	0.990	0.320
	No	97 (100.0)	97 (99.0)		

CNT: non-COVID control subjects.

Figure 1. The distribution of the top of 10 frequently isolated pathogens

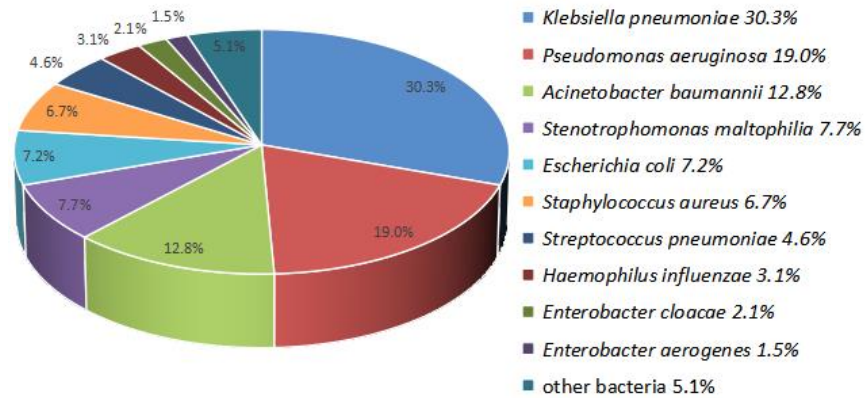


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