

# Clinical features and etiology of patients with community-acquired pneumonia in southern China

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## Research article

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# Abstract

**Background:** The aim of this study was to investigate the clinical features and etiology in patients with community-acquired pneumonia (CAP) in southern China. **Methods:** A total of 342 patients who presented community-acquired pneumonia (CAP) from January 2019 to December 2019 were enrolled in this study. The respiratory pathogens in nine test and loop-mediated isothermal amplification (LAMP) detection were used to identify pathogens.

**Results:** The mean age of this study population was  $60.89 \pm 18.87$  years. The total incidences of CAP were more prevalent in males (60.5%, 207/342) than females (39.5%, 135/342), and the percentage was 65.8% (225/342) CAP patients in summer and autumn. The main causative pathogens were identified in 96/342 (28.1 %) patients. Of these, 14 (14.6 %) were MP infection, the most frequently isolated microorganism. Bacterial infection in the single infection was present in 47 (47/96, 49.0%). Mixed infections were demonstrated in 26 (26/96, 27.1%). MRSA infection was close to patients with systemic diseases ( $P = 0.001$ ). Factors that were associated with systemic disease was the age  $>65$  (OR 5.555, 95%CI 3.402-9.071,  $P < 0.001$ ).

**Conclusions:** MP is common organisms isolated in community-acquired pneumonia. The year of above 65, the count of WBC and mixed pathogens infections may be associated with an increased risk of CAP patients with systemic disease.

## Background

Community-acquired pneumonia (CAP) is a common clinical disease that ranked as the fifth leading cause of mortality global[1]. It is reported that there are about 3.2 million people die from CAP each year globally, surpassing other infectious diseases, such as tuberculosis, HIV and malaria[2]. A prospective multicenter study in Asia reported that the mortality rate of CAP in Asia was as high as 7.3%[3]. Several factors are associated with the risk of CAP mortality, including inflammatory response, cardiovascular complications, and etiology[4–6]. Some studies identified age and male sex increases the incidence of CAP[7, 8]. Identification the etiology of CAP patients remains challenging, 30–65% of patients do not have a certain pathogen isolated[9]. *Streptococcus pneumoniae*(*S. pneumoniae*) is the most frequently identified CAP pathogen[10]. The etiology of a large number of CAP patients is triggered by bacterial and viral microorganisms, 20–50% of CAP cases are cause by bacterial pathogens[11, 12]. Viral CAP pathogens such as Influenza, respiratory syncytial virus are the most common[13]. CAP also has impact on national economic development for high consumption rates of therapy in both inpatient and outpatient. CAP patients have not been sufficiently evaluated, leading to almost all patients are treated empirically because of the lack of specific diagnostic methods to rapidly isolate the pathogen[14].

The bacterial culture and smear microscopy are the detection of bacterial pathogen most extensively used[15]. In recent years, loop-mediated isothermal amplification (LAMP) have become a useful

alternative to the effective detection of pathogenic microorganism. LAMP-based PCR is detection of thirteen common respiratory pathogens in patients with CAP[16, 17].

Microbial cause varies by host factors and geographic location. The aim of this study is to analyze the pathogens and clinical features of patients that were diagnosed of CAP in southern China.

## Methods

### Study patients

342 hospitalized patients with CAP were recruited from inpatient of Meizhou People's Hospital between January 2019 to December 2019. All participants age from 13 to 99 years old in this study. Patients were diagnosed as CAP if they met one of the following clinical characteristics: (1) typical characteristics of pneumonia, which were defined by a new infiltrate on a chest X-rays or computed tomography (CT) scan examined by radiologists. (2) one or more respiratory symptoms, including new cough, exacerbated cough with or without sputum production, fever ( $> 37.8\text{ }^{\circ}\text{C}$ ) or hypothermia ( $< 35.6\text{ }^{\circ}\text{C}$ )[18].

The study was approved by the ethics committee of Meizhou people's hospital and all participants signed an informed consent form. Severe immunodepression (severe hematological disease, HIV infection), use of immunosuppressive medications were excluded. The data of CAP patients of the clinical and laboratory testing were collected, analyzed, and compared.

### Microbiological diagnostic method

Two sensitivity analyses were performed, including nucleic acid detection of respiratory pathogenic bacteria in loop-mediated isothermal amplification (LAMP)-based and respiratory pathogens in nine test were chosen for pathogens identification of viruses, atypical microorganisms and bacteria. Respiratory pathogens in nine test : the serum of patients with extraction for its detection, respectively, *Adenovirus*, *Q thermicus*, *Chlamydia pneumonia*, *Influenza B virus*, *Legionella pneumophila*, *Influenza A virus*, *Mycoplasma pneumonia*, *Parainfluenza virus*, *Respiratory syncytial virus* were tested by indirect immunofluorescent assay. Loop-mediated isothermal amplification (LAMP): all sputum samples were performed by using the Universal Kit for Bacterial DNA Extraction Kit (CapitalBio, Chengdu, China) according to the manufacturer's recommended protocol for DNA extraction and examined by PCR for respectively detection of *Acinetobacter baumannii*(*A. baumannii*), *Methicillin-resistant staphylococcus*(*MRSA*), *Streptococcus pneumoniae*(*S.pneumoniae*), *Staphylococcus aureus*(*S.aureus*), *Escherichia coli*(*E.coli*), *Klebsiella pneumoniae*(*K. pneumoniae*), *Pseudomonas aeruginosa*(*P. aeruginosa*), *Stenotrophomonas maltophilia*(*S. maltophilia*), *Haemophilus influenzae*(*H. influenzae*), *Legionella pneumophila*(*L. pneumophila*), *Mycoplasma pneumoniae*(*MP*), *Chlamydia pneumonia*(*CP*), *Mycobacterium tuberculosis complex*(*MTBC*). PCR procedure:  $37\text{ }^{\circ}\text{C}$  for 3 minutes and  $65\text{ }^{\circ}\text{C}$  for 47 minutes. Detection of amplified products by viewing the real-time imaging system (CapitalBio Technology, Beijing, China) and pathogen nucleic acid detection software were used to analyze results.

# Statistical analysis

SPSS 21.0 software (SPSS Inc., Chicago, USA) was used for statistical analyses of the data. Descriptive data are presented as frequencies (percentages). Categorical variables were compared with the Pearson Chi-square test. Two-group comparisons of continuous variables were compared with independent samples t-test. The level of statistically significant was  $P \leq 0.05$ .

## Results

### Study population and clinical characteristics

In Table 1, of the 342 patients with CAP, 207 patients (60.5%) were male and 135 patients (39.5%) were female. The average age of study population was 60.89, including 197 cases were nonelderly with a mean age of 48.38 ( $\leq 65$  years), and 145 cases were elderly with a mean age of 77.90 ( $\geq 65$  years). A total of 169 patients (49.42%) had at least 1 systemic diseases disease, including coronary artery disease, cerebral infarction, diabetes, hypertension. Laboratory parameters of the white blood cell (WBC) counts ( $> 9.5 \times 10^9$  cells/L) was found in 145 cases (42.4%). Summer and autumn have more patients with CAP (108/342, 31.6%; 117/342, 34.2%) in this study.

Table 1  
The clinical characteristics of the study population

Items	N (%)
Total	342
Gender	
Male	207 (60.5)
Female	135 (39.5)
Age (years), mean $\pm$ SD	60.89 $\pm$ 18.87
$\leq$ 65	197 (57.6)
$>$ 65	145 (42.4)
Clinical symptom	
Fever	171 (50)
Cough	311 (90.9)
Expectoration	279 (81.6)
Chest pain	19 (5.6)
Smoking	82 (24)
Drinking	57 (16.7)
WBC ( $> 9.5 \times 10^9$ cells/L)	145 (42.4)
D-dimer (mean $\pm$ SD)	1.77 $\pm$ 1.48
Systemic diseases	
Coronary artery disease	70 (20.5)
Cerebral infarction	45 (13.2)
Diabetes	46 (13.5)
Hypertension	89 (26)
Seasons	
Spring (3–5)	43 (12.6)
Summer (6–8)	108 (31.6)
Autumn (9–11)	117 (34.2)

SD: standard deviation, WBC: white blood cell

Items	N (%)
Winter (12 - 2)	74 (21.6)
SD: standard deviation, WBC: white blood cell	

## Pathogens

In 96/342 (28.1%) patients the etiology of CAP was identified. Pathogen detection showed that single infection was found in 70 patients (72.9%), the most frequently isolated microorganism was MP (14/96, 14.6%), followed by MRSA (12/96, 12.5%), fungus as a group (9/96, 9.4%), K. pneumonia (7/96, 7.3%), P. aeruginosa (6/96, 6.3%). Bacterial infection in the single infection was present in 47 (47/96, 49.0%). Mixed infections were demonstrated in 26 (26/96, 27.1%). Table 2 shows the number of every causal microorganisms.

Table 2  
The etiological analysis of identified in patients with CAP

Pathogen	Cases (%)
<i>Single infection</i>	
<i>P. aeruginosa</i>	6 (6.3)
<i>S. maltophilia</i>	1 (1.0)
<i>L. pneumophila</i>	2 (2.1)
<i>A. baumannii</i>	3 (3.1)
<i>E. coli</i>	4 (4.2)
<i>K. pneumoniae</i>	7 (7.3)
<i>S. pneumoniae</i>	3 (3.1)
MTBC	4 (4.2)
<i>S. aureus</i>	3 (3.1)
<i>H. influenzae</i>	4 (4.2)
MRSA	12 (12.5)
Fungus	9 (9.4)
MP	14 (14.6)
<i>Multiple pathogens</i>	
MP + Flu B	1 (1.0)
MP + Flu B + <i>E. coli</i>	1 (1.0)
MP + <i>S. aureus</i>	1 (1.0)
MP + MRSA + <i>K. pneumoniae</i>	1 (1.0)
MP + <i>K. pneumoniae</i> + <i>A. baumannii</i>	1 (1.0)
MRSA + <i>E. coli</i> + <i>A. baumannii</i>	1 (1.0)
MRSA + <i>S. maltophilia</i> + <i>L. pneumophila</i>	1 (1.0)
<i>S. aureus</i> + MRSA + <i>P. aeruginosa</i>	1 (1.0)

*P. aeruginosa*: *Pseudomonas aeruginosa*, *S. maltophilia*: *Stenotrophomonas maltophilia*, *L. pneumophila*: *Legionella pneumophila*, *A. baumannii*: *Acinetobacter baumannii*, *E. coli*: *Escherichia coli*, *K. pneumoniae*: *Klebsiella pneumoniae*, *S. pneumoniae*: *Streptococcus pneumoniae*, MTBC: *Mycobacterium tuberculosis complex*, *S. aureus*: *Staphylococcus aureus*, *H. influenzae*: *Haemophilus influenzae*, MRSA: *Methicillin-resistant staphylococcus*, MP: *Mycoplasma pneumoniae*, Flu B: *Influenza B virus*, Flu A: *Influenza A virus*

Pathogen	Cases (%)
<i>Adenovirus + S. aureus + MRSA + P. aeruginosa + A. baumannii</i>	1 (1.0)
<i>MRSA + P. aeruginosa</i>	2 (2.1)
<i>MRSA + L. pneumophila</i>	1 (1.0)
<i>MRSA + MTBC</i>	1 (1.0)
<i>MRSA + K. pneumoniae</i>	1 (1.0)
<i>MRSA + E. coli</i>	1 (1.0)
<i>H. influenzae + L. pneumophila</i>	1 (1.0)
<i>S. aureus + MRSA</i>	1 (1.0)
<i>Adenovirus + S. aureus + MRSA</i>	1 (1.0)
<i>S. pneumoniae + P. aeruginosa</i>	1 (1.0)
<i>S. pneumoniae + MRSA</i>	1 (1.0)
<i>K. pneumoniae + A. baumannii</i>	1 (1.0)
<i>E. coli + H. influenzae</i>	1 (1.0)
<i>E. coli + K. pneumoniae</i>	1 (1.0)
<i>E. coli + A. baumannii</i>	1 (1.0)
Total	96
<i>P. aeruginosa: Pseudomonas aeruginosa, S. maltophilia: Stenotrophomonas maltophilia, L. pneumophila: Legionella pneumophila, A. baumannii: Acinetobacter baumannii, E. coli: Escherichia coli, K. pneumonia: Klebsiella pneumonia, S. pneumoniae: Streptococcus pneumonia, MTBC: Mycobacterium tuberculosis complex, S. aureus: Staphylococcus aureus, H. influenza: Haemophilus influenza, MRSA: Methicillin-resistant staphylococcus, MP: Mycoplasma pneumonia, Flu B: Influenza B virus, Flu A: Influenza A virus</i>	

## Microbial Etiology According To Systemic Diseases

We divided all patients into two groups according to the systemic diseases (shown in Table 3): systemic diseases group (169 cases), non-systemic diseases group (173 cases), MRSA infection was the most common in patients with systemic diseases ( $P = 0.001$ ). MP infection in non-systemic diseases group was identified in 10 (52.63%) of the 19 patients, while there was no significant difference between systemic diseases group and non-systemic diseases group ( $P = 0.854$ ). In addition, there were 9 cases with systemic diseases group infected by *P. aeruginosa* ( $P = 0.029$ ).

Table 3  
Effects of systemic disease on the distribution of 342 CAP pathogens

Pathogen	Systemic diseases N = 169	Non-systemic diseases N = 173	$\chi^2$	<i>P</i>
<i>MRSA</i>	21	5	11.067	0.001
<i>MP</i>	9	10	0.034	0.854
<i>K. pneumoniae</i>	8	3	2.471	0.116
<i>P. aeruginosa</i>	9	2	4.774	0.029
<i>E. coli</i>	5	3	0.561	0.454
<i>fungus</i>	5	4	0.139	0.709
<i>A. baumannii</i>	4	3	0.171	0.679
<i>S. aureus</i>	6	2	2.145	0.143

*MRSA: Methicillin-resistant staphylococcus, MP: Mycoplasma pneumonia, K. pneumoniae: Klebsiella pneumoniae, P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli, A. baumannii: Acinetobacter baumannii, S. aureus: Staphylococcus aureus*

## Microbial Etiology In Age Groups

We divided all patients into two groups according to the age (shown in Table 4):  $\leq 65$  years group (197 cases),  $\geq 65$  years group (145 cases). There was no significant difference that the two frequently detected pathogens were MRSA ( $P = 0.101$ ) and MP ( $P = 0.614$ ) between  $\leq 65$  years group and  $\geq 65$  years group. For CAP in patients above 65 years of age, 8 patients were caused by *K. pneumoniae* infection compared to  $\leq 65$  years, 3 patients had *K. pneumoniae* infection ( $P = 0.039$ ). Microbial etiology by age group is shown in Table 4.

Table 4  
Effect of age on the distribution of 342 CAP pathogens

Pathogen	≤ 65 y (N = 197)	≥65 y (N = 145)	χ <sup>2</sup>	P
<i>MRSA</i>	11	15	2.695	0.101
<i>MP</i>	12	7	0.254	0.614
<i>K. pneumoniae</i>	3	8	4.281	0.039
<i>P. aeruginosa</i>	4	7	2.099	0.147
<i>E. coli</i>	4	4	0.194	0.660
<i>fungus</i>	3	6	2.229	0.135
<i>A. baumannii</i>	5	3	0.08	0.777
<i>S. aureus</i>	3	5	1.355	0.244

*MRSA: Methicillin-resistant staphylococcus, MP: Mycoplasma pneumonia, K. pneumonia: Klebsiella pneumonia, P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli, A. baumannii: Acinetobacter baumannii, S. aureus: Staphylococcus aureus*

## Logistic Regression Analysis

In multivariable logistic regression analysis, > 65 years but not gender, was found to be significant risk factors for the patients with CAP associated with systemic disease ( $p < 0.001$ ). Moreover, multiple pathogens and the counts of WBC were identified as independent risk factor for patients with CAP associated with systemic disease (OR 2.894, 95% CI 1.015–8.253,  $P = 0.047$ ; OR 1.067, 95% CI 1.009–1.127,  $P = 0.022$ ). No significant interaction was found between gender and smoking ( $P = 0.398$ ,  $P = 0.654$ ). Table 5 shows all ORs and 95% CIs.

Table 5  
Multivariable logistic regression analysis of the patients with CAP associated with systemic disease

	OR	95% CI	P
Gender	1.265	0.734–2.179	0.398
> 65	5.555	3.402–9.071	< 0.001
Smoking	1.153	0.619–2.146	0.654
Multiple pathogens	2.894	1.015–8.253	0.047
WBC	1.067	1.009–1.127	0.022
WBC: white blood cell			

## Discussion

CAP is a predominant threat to public health worldwide. In this study of 342 hospitalized CAP patients, 28.1% CAP cases were identified the etiology, lower than other regions is reported[9]. Maybe some patients included in this study were treated before go to the hospital. Furthermore, some patients may have received prior antibiotics that were consistent with the guidelines, but that failed. The potential bacterial may be obscured for patients use of antibiotics prior because of comorbidities[19]. Previous studies showed that etiology remains unknown in the most of cases, indicating that identification of a precise pathogen diagnosis for CAP patients is challenging[20].

The characteristics of CAP pathogens distribution in different regions are different, and with the passage of time, population distribution, seasonal alternation, the use of antibiotic and other factors, the anti-infection should be based on accurate diagnosis of pathogens, but due to the precise etiology testing has not been achieved in most patients, and there is currently no consistent antibiotic treatment plan[21]. In addition, alcoholism, smoking, chronic obstructive pulmonary disease (COPD), immunodeficiency, tumors, diabetes, cerebrovascular diseases and others have become risk factors of CAP, and the increase of age is closely related to the severity of CAP, which should be attached great importance to the prevention of CAP[22]. MP was the most frequently identified pathogens in our study. MP is a prokaryotic pleuropneumonia-like microorganism between bacteria and viruses that contains DNA and RNA and lacks the cell wall. Gram staining is negative, the diameter is 50–300 nm, the structure is simple, and it has various shapes such as sphere, rod, and filament that can pass through the bacteria filter. It is spread through close contact with infected patients with an incubation period of 1–3 weeks. It occurs more frequently in summer and autumn in the south, and more frequently in autumn and winter in the north. The prevalence of school-age children is 5–15 years old. It shows a downward trend after puberty and gradually disappears after adulthood. 25% of cases have extrapulmonary complications known as mucosal skin lesions[23].

MRSA was the most common bacterial etiology, followed by *K. pneumoniae* and *P. aeruginosa* in our identified cases. CAP caused by MRSA was the largest groups in our study group, with proportions of 11.5% and 15.6% in  $\leq 65$  years and  $\geq 65$  years, respectively. In addition, the percentages of bacterial pathogen infection with MRSA patients have systemic disease (21.9%) was relatively higher than patients without systemic disease group ( $P = 0.001$ ). MRSA is the most common bacterial pathogen infection that gives rise to a high burden of significant healthcare costs, morbidity, and mortality for patients every year[24–26]. The percentages of bacterial pathogen infection with *P. aeruginosa* tested positive made up 9.4% among patients with systemic disease group ( $P = 0.029$ ). We aimed to identify CAP patient characteristics associated with causative microorganisms in southern China. We found  $> 65$ , multiple pathogens and WBC are associated with a higher mortality rate; especially, above 65 years (OR 5.555, 95%CI 3.402–9.071,  $P < 0.001$ ) was close associated with increased CAP patients with systemic disease mortality. Our study found that age was similar to the findings of previous studies[27–29].

There are some limitations deserve consideration in our study. One was that we did not investigate a larger sample size from the same population due to the data collection limited to one year. Second, we used only two different assays for different pathogens but did not clarify the differences in detection performance between these microbiological techniques. Third, some of the individuals in this population self-medicated with antibiotics may not be generalized to CAPs. Therefore, further studies will be needed to confirm our findings.

## Conclusions

MP is common organisms isolated in community-acquired pneumonia. The year of above 65, the count of WBC and mixed pathogens infections may be associated with an increased risk of CAP patients with systemic disease.

## Abbreviations

*P. aeruginosa*: *Pseudomonas aeruginosa*, *S. maltophilia*: *Stenotrophomonas maltophilia*, *L. pneumophila*: *Legionella pneumophila*, *A. baumannii*: *Acinetobacter baumannii*, *E. coli*: *Escherichia coli*, *K. pneumonia*: *Klebsiella pneumonia*, *S. pneumoniae* : *Streptococcus pneumonia*, *MTBC*: *Mycobacterium tuberculosis complex*, *S. aureus*: *Staphylococcus aureus*, *H. influenza*: *Haemophilus influenza*, *MRSA*: *Methicillin-resistant staphylococcus*, *MP*: *Mycoplasma pneumonia*, *Flu B*: *Influenza B virus*, *Flu A*: *Influenza A virus*, *WBC*: white blood cell, *LAMP*: loop-mediated isothermal amplification, *OR*: Odds ratio.

## Declarations

### Ethics approval and consent to participate

The study was approved by the Ethics Committee of Meizhou People's Hospital, Meizhou Academy of Medical Sciences, Meizhou Hospital Affiliated to Sun Yat-sen University (NO: MPH-HEC 2018-A-10). Written informed consent was obtained from each patient in the study and participants are children (under 16 years old) from their parents or legal guardians.

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20180101). There was no role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

### **Availability of data and materials**

The datasets generated during the current study are not publicly available yet, due to privacy concerns and ongoing additional research. Data can be made available for peer review on reasonable request through contacting the corresponding author.

### **Authors' contributions**

ZZ conceived and designed the experiments; SL recruited subjects and collected clinical data. CG conducted the laboratory testing. XG, RW, ZZ helped to analyze the data. CG wrote the manuscript. All authors read and approved the final manuscript.

### **Consent for publication**

Not applicable.

### **Competing interests**

The authors declare that they have no competing interests.

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