Co-Infection with Common Respiratory Pathogens and SARS-CoV-2 in Patients with COVID-19 Pneumonia and Laboratory Biochemistry Findings: A Retrospective Cross-Sectional Study of 78 Patients from a Single Center in China

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Background: This retrospective study aimed to investigate co-infections with common respiratory pathogens and SARS-CoV-2 and laboratory biochemistry findings in patients with COVID-19 in the Zhuzhou area of China, in order to provide a reference for the disease assessment and clinical treatment of COVID-19.

Material/Methods: The clinical data of COVID-19 patients admitted to the hospital of Zhuzhou City from January 28 to March 15, 2020, as well as laboratory test results for respiratory pathogens and biochemical indicators, were collected to conduct correlation analyses. All patients were diagnosed based on fluorescence-based PCR assay for SARS-CoV-2.

Results: Eleven of the 78 patients (14.1%) were co-infected with other respiratory pathogens, among which Mycoplasma pneumoniae (n=5, 45.5%) and respiratory syncytial virus (n=4, 36.4%) were the most frequent. There were 8 patients co-infected with 1 other pathogen and 3 patients co-infected with 2 other pathogens. Compared with mono-infected COVID-19 patients, patients with co-infections had significantly higher levels of procalcitonin (P=0.002).

Conclusions: The findings showed that Mycoplasma pneumonia and respiratory syncytial virus were the most common co-infections in patients with COVID-19 pneumonia. Increased levels of PCT in patients with COVID-19 pneumonia were associated with co-infection.

MeSH Keywords: Coinfection • COVID-19 • Mycoplasma pneumonia • Respiratory Syncytial Viruses • SARS Virus

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/929783
Background

Coronavirus disease 2019 (COVID-19) is a new infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is transmitted through respiratory droplets and physical contact, with a high level of susceptibility in humans [1]. The main manifestations of COVID-19 are fever, fatigue, and dry cough, and most patients have a good prognosis. Individuals with COVID-19 tend to have mild symptoms that can be easily overlooked in the early stages, while severely ill patients rapidly develop acute respiratory distress syndrome and sepsis, which can lead to death from multiple organ failure [2,3]. SARS-CoV-2 is a positive-sense, single-stranded ribonucleic acid virus belonging to the genus Betacoronavirus [4]. It shares 78% and 50% nucleotide homologies with severe acute respiratory syndrome coronavirus (SARS-CoV, which has previously caused large epidemics in China) and Middle East respiratory syndrome coronavirus, respectively [5]. However, SARS-CoV-2 is more contagious and is capable of spreading over much wider distances [6]. SARS-CoV-2 has currently spread across more than 200 countries worldwide and COVID-19 has been declared a pandemic. As of November 6th, 2020, there have been more than 48 million confirmed cases and 1,226,813 deaths reported worldwide.

Despite the high transmissibility of SARS-CoV-2, the vast majority of infected individuals are either mildly ill with mild clinical symptoms and no imaging manifestation of pneumonia or moderately ill with a fever and respiratory symptoms and imaging manifestations of pneumonia, while about 20% of those infected progress to severe illness [2,3,6]. In the Northern Hemisphere, the COVID-19 outbreak occurred during the high-incidence season of other respiratory infections, such as influenza, viral pneumonia, and community-acquired pneumonia. Many individuals with SARS-CoV-2 infection have co-infection with other respiratory pathogens [7,8], which complicates the diagnosis and treatment of COVID-19. Hence, the differentiation between SARS-CoV-2 mono-infection and SARS-CoV-2 co-infection with other pathogens is of great importance to clinical management. To this end, we investigated co-infections among hospitalized COVID-19 patients. This retrospective study investigated co-infections with common respiratory pathogens and SARS-CoV-2 and laboratory biochemistry findings in patients with COVID-19 pneumonia to provide a reference for the disease assessment and clinical treatment of COVID-19. Our study shows that Mycoplasma pneumoniae (M. pneumoniae) and respiratory syncytial virus (RSV) were the most common pathways affecting COVID-19 patients, and elevated procalcitonin levels in COVID-19 patients may be a sign of the presence of infection with other respiratory tract pathogens.

Material and Methods

Research participants

The study was approved by the Ethics Committee of Zhuzhou Central Hospital in 2020 (No. 2020216). All data used were obtained from the electronic medical record system and the paper medical record system. In order not to disturb the patients, we applied to the Ethics Committee for exemption from informed consent and obtained approval.

We performed a retrospective analysis of the clinical data of 78 consecutive COVID-19 patients who were admitted to the People’s Hospital of Lukou District in China, the designated hospital for the isolation and treatment of COVID-19 patients in Zhuzhou City, between January 28 and March 15, 2020. Those patients consisted of 41 men and 37 women with an average age of 47.7±17.2 years.

Reagents and instruments

SARS-CoV-2 infection was confirmed using the 2019-nCoV Nucleic Acid Detection Kit (fluorescence-based PCR assay) and fully automated nucleic acid extraction instrument (Sansure Biotech, Inc., Changsha, China) [9,10]. We used immunoglobulin M antibody detection kits for 9 other respiratory pathogens (Legionella pneumophila, Coxiella burnetii, influenza A virus, influenza B virus, M. pneumoniae, Chlamydia pneumoniae, RSV, adenoviruses, and human parainfluenza virus) (Autobio Diagnostics Co., Ltd., Zhengzhou, China); a SYSMEXN 1000 fully automated hematology analyzer and its supporting reagents (Sysmex Corporation, Hyogo, Japan); a CS2000 fully automated coagulation analyzer and its supporting reagents (Sysmex Corporation, Hyogo, Japan); a Hitachi 7180 fully automated biochemical analyzer and its supporting reagents (Maccura Biotechnology Co., Ltd., Sichuan, China); and FS-301, a Finecare fully automated immunofluorescence quantitative test system (Guangzhou Wanfu Biotechnology Co., Ltd., Guangzhou, China).

Diagnostic methods and clinical severity classification

According to the criteria outlined in the Diagnosis and Treatment Protocol for COVID-19 (Trial Version 7) issued by the General Office of the National Health Commission on February 18, 2020 [10], we collected the clinical data of patients whose specimens (such as sputum, oropharyngeal swabs, and lower respiratory tract secretions) tested positive for SARS-CoV-2 nucleic acid via real-time fluorescence-based polymerase chain reaction (RT-PCR) assay. All 78 patients with COVID-19 in our hospital were tested for respiratory pathogens. If the patient was infected with COVID-19 and other respiratory pathogens, we diagnosed co-infection. If the patient was infected with COVID-19 but was not infected with other...
respiratory pathogens, we diagnosed mono-infection. The 78 patients were divided into mildly ill (8 patients), moderately ill (59 patients), severely ill (9 patients), and critically ill (2 patients) groups. The mildly ill group comprised patients who had mild clinical symptoms and showed no imaging manifestation of pneumonia. The moderately ill group comprised patients who had a fever and respiratory symptoms and showed imaging manifestations of pneumonia. The severely ill group comprised patients who met any of the following criteria: RDS with a respiratory rate of ≥30 breaths/min, blood oxygen saturation levels (SpO2) ≤93% at rest, or partial pressure of oxygen (PaO2)/fraction of inspired oxygen (FiO2) in arterial blood ≤300 mmHg. The critically ill group comprised patients who met any of the following criteria: the need for mechanical ventilation due to respiratory failure, shock, or the need for monitoring and treatment in the Intensive Care Unit (ICU) due to failures of other organs.

Statistical methods

Descriptive analyses of the variables produced data expressed as the median and interquartile range (IQR), mean±standard deviation, or number (%), as appropriate. For comparisons between experimental groups, statistical data that met the assumption of homogeneity of variance (P>0.05) were subject to two-sample t tests, while statistical data that violated the assumption of homogeneity of variance were subject to two-sample non-parametric tests. Categorical variables are expressed as frequencies and compared between groups using the chi-squared test. The binary logistical regression analysis was performed for multivariate analysis. P values <0.05 were considered statistically significant. All data were summarized by SPSS version 26 (IBM, Armonk, NY).

Results

Comparisons of clinical characteristics between co-infected and mono-infected COVID-19 patients

The 78 consecutive COVID-19 patients consisted of 41 men (52.6%) and 37 women (47.4%), ranging in age from 3 years to 88 years, with an average age of 47.7±17.2 years. There were 8 mildly ill patients (10.3%), 59 moderately ill patients (75.6%), and 11 severely/critically ill patients (14.1%). There were no statistically significant differences between the 2 groups in patient characteristics such as age, sex, epidemiological history, comorbidities, onset time, clinical symptom, physical examination, computerized tomography scan result, severity classification, and length of stay (P>0.05) (Table 1).

Co-infections in COVID-19 patients

Eleven out of those 78 COVID-19 patients (14.1%) were co-infected with other respiratory pathogens, comprising 6 men and 5 women, with an average age of 42.7±14.9 years. According to the clinical severity classification, those co-infected patients comprised 2 mildly ill patients, 7 moderately ill patients, and 2 severely/critically ill patients. Among the co-infecting pathogens, M. pneumonia (45.5%) and RSV (36.4%) accounted for the highest rates of co-infection. There were 8 COVID-19 patients (72.7%) co-infected with 1 other pathogen, which included M. pneumonia (3 patients), RSV (3 patients), influenza B virus (1 patient), and adenoviruses (1 patient), while the remaining 3 COVID-19 patients (27.3%) were co-infected with 2 other pathogens, which included M. pneumonia and C. pneumoniae (1 patient), M. pneumoniae and RSV (1 patient), and C. pneumoniae and L. pneumophila (1 patient). Almost all co-infected patients had unilateral or bilateral pulmonary lesions, with the exception of 1 moderately ill, influenza B virus-co-infected patient who showed no obvious lung abnormalities (Table 1). One of the severely ill patients was co-infected with M. pneumoniae and RSV and had underlying cardiovascular diseases, while the other severely ill patient was co-infected with adenoviruses and had hypertension and diabetes as underlying diseases. Other co-infected patients did not have any underlying disease.

Comparisons of laboratory test results between co-infected and mono-infected COVID-19 patients

The comparisons of laboratory test indicators between mono-infected COVID-19 patients and COVID-19 patients co-infected with other respiratory pathogens revealed that the co-infection group had no significantly lower levels of lactate dehydrogenase (LDH), creatine kinase (CK), and C-reactive protein (CRP) than in the mono-infection group (P 0.318, 0.692, 0.362, respectively). For inflammatory markers, there were 4 co-infected patients (36.4%) and 4 mono-infected patients (6.0%) with increased levels of procalcitonin (PCT), which differed significantly between the 2 groups of patients (P=0.002). Multivariate analysis also showed significant differences in the level of PCT between the 2 groups (P=0.003, OR=0.038,95%CI (0.004–0.341)). On the contrary, there were no statistically significant differences in other laboratory test results between the 2 groups of patients (Tables 2, 3).

Discussion

SARS-CoV-2 that has invaded the human body is highly contagious, with a long incubation period, and has clinical manifestations that are similar to other respiratory infections [11]. The outbreak of COVID-19 occurred during the high-incidence...
|                         | Total | Monoinfection group | Coinfection group | P value |
|-------------------------|-------|---------------------|-------------------|---------|
| **Patients (n)**        | 78    | 67                  | 11                | –       |
| **Sex**                 |       |                     |                   |         |
| Male                    | 41    | 35 (52.6%)          | 6 (54.5%)         | 0.887   |
| Female                  | 37    | 32 (47.8%)          | 5 (45.5%)         |         |
| **Age (years)**         |       |                     |                   |         |
|                         | 47.7±17.2 | 48.5±17.5 | 42.7±14.9 | 0.252   |
| **Age stratification (n)** |       |                     |                   | 0.832   |
| ≤20                     | 5    | 4 (6.0%)            | 1 (9.1%)          |         |
| 21–40                   | 24   | 20 (29.9%)          | 4 (36.4%)         |         |
| 41–60                   | 28   | 24 (35.8%)          | 4 (36.4%)         |         |
| >60                     | 21   | 19 (28.4%)          | 2 (18.2%)         |         |
| **Epidemiological history (positive, n)** | 66 | 68 | 8 | 0.377 |
| **Symptom**             |       |                     |                   |         |
| Fever                   | 56   | 47 (70.1%)          | 9 (81.8%)         | 0.425   |
| Cough                   | 62   | 53 (79.1%)          | 9 (81.8%)         | 0.836   |
| Expectoration           | 39   | 34 (50.7%)          | 5 (45.5%)         | 0.745   |
| Fatigue                 | 56   | 47 (71.8%)          | 9 (81.8%)         | 0.425   |
| Shortness of breath     | 25   | 23 (34.3%)          | 2 (18.2%)         | 0.288   |
| Chest tightness         | 7    | 6 (9.0%)            | 1 (9.1%)          | 0.988   |
| Chest pain              | 3    | 2 (3.0%)            | 1 (9.1%)          | 0.370   |
| Diarrhea                | 13   | 12 (17.9%)          | 1 (9.1%)          | 0.467   |
| Muscular soreness       | 18   | 16 (23.9%)          | 2 (18.2%)         | 0.678   |
| **Physical examination**|       |                     |                   |         |
| Body temperature (°C)   | 37.3 (36.7–38.5) | 37.4 (36.7–38.5) | 37.3 (36.8–39.1) | 0.714   |
| Blood oxygen saturation level (%) | 98.0 (96.0–98.0) | 98.0 (96.0–98.0) | 98.0 (95.5–98.0) | 0.749   |
| Pulse rate (beats/min)  | 88.2±10.8 | 87.6±11.1 | 92.0±8.3 | 0.588   |
| Respiratory rate (breaths/min) | 20 (20–20) | 20 (20–20) | 20 (20–25) | 0.921   |
| CT scan result          | 78   | 67 (100.0%)         | 11 (100.0%)       | 0.467   |
| No obvious abnormalities | 13   | 12 (17.9%)          | 1 (9.1%)          |         |
| **Chronic disease**     |       |                     |                   |         |
| Diabetes                | 8    | 7 (10.4%)           | 1 (9.1%)          | 0.891   |
| Cardiovascular and cerebrovascular diseases | 19 | 17 (25.4%) | 2 (18.2%) | 0.607   |
| Chronic obstructive pulmonary disease (COPD) | 6 | 6 (9.0%) | 0 (0.0%) | 0.586   |
| Chronic liver disease   | 6    | 5 (7.5%)            | 1 (9.1%)          | 1.000   |

Table 1. Comparisons of clinical characteristics between co-infected and mono-infected COVID-19 patients with univariate analysis.
Table 1 continued. Comparisons of clinical characteristics between co-infected and mono-infected COVID-19 patients with univariate analysis.

| Clinical severity classification           | Total | Monoinfection group | Coinfection group | P value |
|-------------------------------------------|-------|---------------------|-------------------|---------|
| Mildly group                              |       |                     |                   | 0.555   |
| 8 (10.3%)                                 | 6 (9.0%) | 2 (18.2%)          |                   |         |
| Moderately group                          | 59 (75.6%) | 52 (77.6%) | 7 (63.6%)       |         |
| Severely/critically group                 | 11 (14.1%) | 9 (13.4%) | 2 (18.2%)       |         |
| Onset time (days)                         | 4.0 (2.0–6.0) | 4.0 (2.8–7.0) | 3.0 (1.5–4.0) | 0.173   |
| length of stay (days)                     | 13 (11–20) | 14 (10–21) | 13 (12–14)     | 0.205   |

Quantitative variables are expressed as median (interquartile range) or mean±standard deviation; categorical variables are expressed as frequencies (percentages); CT – computerized tomography.

Table 2. Comparisons of laboratory test results between co-infected and mono-infected COVID-19 patients with univariate analysis.

| Patients (n) | Total | Monoinfection group | Coinfection group | p-Value |
|--------------|-------|---------------------|-------------------|---------|
| WBC (10^9/L) | 4.97 (3.70–6.27) | 5.01 (3.74–6.84) | 3.78 (2.69–5.61) | 0.329   |
| RBC (10^12/L)| 4.38±0.63         | 4.40±0.65         | 4.27±0.50         | 0.631   |
| PLT (10^9/L) | 196 (165–247)     | 200 (171–248)     | 176 (133–262)    | 0.518   |
| Hemoglobin (g/L) | 135 (121–152) | 135 (121–153) | 132 (121–144) | 0.858   |
| NEU (10^9/L) | 2.82 (2.03–4.59) | 2.93 (2.14–4.60) | 1.75 (1.36–4.75) | 0.46    |
| LYM (10^9/L) | 1.32 (0.93–1.82) | 1.32 (1.03–1.89) | 1.05 (0.63–1.62) | 0.248   |
| MON (10^9/L) | 0.38 (0.28–0.46) | 0.38 (0.28–0.46) | 0.26 (0.23–0.45) | 0.392   |
| PT (s)       | 12.9 (12.6–13.7) | 12.9 (12.4–13.6) | 13.7 (12.9–15.0) | 0.129   |
| TT (s)       | 30.7 (28.2–32.9) | 30.7 (28.2–32.5) | 30.2 (27.8–36.1) | 0.816   |
| Fg (g/L)     | 3.33 (2.40–4.52) | 3.33 (2.50–4.52) | 3.01 (2.13–5.43) | 0.308   |
| TP (g/L)     | 65.7±6.3          | 66.0±6.6          | 63.7±3.3         | 0.455   |
| D-D (ug/ml)  | 0.31 (0.22–0.51) | 0.32 (0.22–0.52) | 0.28 (0.19–0.76) | 0.432   |
| ALT (U/L)    | 20.0 (14.0–38.0) | 19.5 (14.8–40.8) | 22.0 (13.5–27.0) | 0.937   |
| AST (U/L)    | 25.0 (21.0–31.0) | 25.0 (20.8–31.0) | 23.0 (21.0–32.0) | 0.790   |
| TP (g/L)     | 65.7±6.3          | 66.0±6.6          | 63.7±3.3         | 0.455   |
| Alb (g/L)    | 39.8±5.5          | 40.1±5.2          | 37.6±6.9         | 0.401   |
| Gld (g/L)    | 25.7±4.7          | 25.7±4.6          | 25.7±4.4         | 0.999   |
| DBIL (umol/L)| 3.02 (2.19–4.43) | 3.04 (2.20–4.54) | 2.73 (1.91–4.25) | 0.736   |
| γ-GT (U/L)   | 21.50 (13.75–38.25) | 22.00 (14.00–38.75) | 18.50 (10.75–32.25) | 0.438   |
| ALP (U/L)    | 59 (49–69)        | 59 (49–69)        | 57 (47–71)       | 0.704   |
| LDH (U/L)    | 194.0 (168.0–244.0) | 194.5 (168.0–244.8) | 177.0 (158.5–226.5) | 0.318   |
| CK (U/L)     | 81 (50–103)       | 81 (53–105)       | 54 (35–126)      | 0.278   |
| CK-Mb (U/L)  | 11 (8–16)         | 11 (8–16)         | 10 (9–17)        | 0.692   |
| Cre (µmol/L) | 72.0 (60.0–86.3)  | 76.0 (63.0–88.8)  | 66.0 (53.0–71.3) | 0.145   |
season of other respiratory infections, and patients are prone to co-infection with SARS-CoV-2 and other respiratory pathogens. As described in previous studies [12,13], co-infection of COVID-19 with other pathogens may lead to high rates of ICU stay and mortality.

Our study shows that *M. pneumoniae* and RSV were the most common pathogens affecting COVID-19 patients, and elevated procalcitonin levels in COVID-19 patients may be a sign of the presence of infection with other respiratory tract pathogens. In this study, 11 out of those 78 COVID-19 patients (14.1%) in the Zhuzhou area were co-infected with other respiratory pathogens, among which *M. pneumonia* (45.5%) and RSV (36.4%) accounted for the highest rates of co-infection, followed by *C. pneumoniae* (18.2%), influenza B virus (9.1%), adenoviruses (9.1%), and *Legionella* (9.1%). Co-infections with coronaviruses and other respiratory pathogens are more commonly seen in case reports, such as SARS patients co-infected by *Mycoplasma* [14] and *Chlamydia* and in COVID-19 patients co-infected by influenza A virus [7] or *Legionella* [8], but there have been few comprehensive studies on co-infections. Kim et al. [15] found that 24 out of 116 SARS-CoV-2-positive patients (20.7%) in northern California (USA) were co-infected with at least 1 other pathogen, and the most common co-infecting pathogens were rhinovirus/enterovirus, RSV, and other members of the *Coronaviridae* family. Richardson et al. [16] reported that the rate of co-infection with other pathogens was 2.1% among 5700 COVID-19 patients in New York City. Hazra et al. [17] also reported that at least 1 respiratory pathogen combined with SARS-CoV-2 occurred in 3.3% of detected specimens. These studies suggested that there are relatively great differences in the number and types of co-infecting respiratory pathogens in COVID-19 patients across countries and regions.

The dynamic profiling of cardiac enzymes is an important clinical diagnostic indicator for cardiac injury in COVID-19 patients.

### Table 2. Comparisons of laboratory test results between co-infected and mono-infected COVID-19 patients with univariate analysis.

|                  | Total                        | Monoinfection group | Coinfection group | p-Value |
|------------------|------------------------------|---------------------|-------------------|---------|
| Urea (mmol/L)    | 3.85 (2.90–4.40)             | 3.95 (2.90–4.73)    | 3.65 (2.95–4.25)  | 0.481   |
| UA (umol/L)      | 273.0 (211.5–348.3)          | 209.5 (212.3–354.3) | 207.5 (182.5–281.8)| 0.121   |
| TC               | 3.88 (3.38–4.39)             | 3.88 (3.37–4.46)    | 3.88 (3.41–4.34)  | 0.986   |
| TG               | 1.27 (0.96–1.69)             | 1.31 (0.98–1.70)    | 1.01 (0.74–1.50)  | 0.125   |
| LDL              | 1.17±0.21                    | 1.16±0.21           | 1.24±0.21         | 0.248   |
| CRP >10 mg/L     | 31 (39.7%)                   | 28 (41.8%)          | 2 (3.3%)          | 0.362   |
| PCT >0.1 ng/mL   | 8 (10.3%)                    | 4 (6.0%)            | 4 (36.4%)         | 0.002*  |

Table 2. Comparisons of laboratory test results between co-infected and mono-infected COVID-19 patients with univariate analysis.

Quantitative variables are expressed as median (interquartile range) or mean±standard deviation; categorical variables are expressed as frequencies (percentages). APTT – activate partial thromboplastin time; ALB – albumin; ALT – alanine transaminase; AST – aspartate aminotransferase; ALP – alkaline phosphatase; CK – creatine kinase; CK-MB – creatine kinase isoenzyme-MB; Cre – creatinine; CRP – C-reactive protein; DBIL – direct bilirubin; D-D – D-dimer; Fg – fibrinogen; Glb – globulin; g-GT – g-glutamyl transferase; HDL – high density lipoprotein; Hgb – hemoglobin; LDH – lactate dehydrogenase; LDL – low density lipoprotein; LYM – lymphocyte; MON – mononuclear cell; NEU – neutrophil; PCT – procalcitonin; PT – prothrombin time; PLT – platelet; RBC – red blood cell; TT – thrombin time; TP – total protein; TBIL – total bilirubin; TC – total cholesterol; TG – triglyceride; Urea – urea nitrogen; UA – uric acid; WBC – white blood cell.

### Table 3. Risk factors between co-infected and mono-infected COVID-19 patients with multivariate analysis.

|                  | P value | OR   | 95% CI      |
|------------------|---------|------|-------------|
| Sex              | 0.512   | 1.711| (0.344–8.512)|
| Age stratification | 0.146   | 0.460| (0.161–1.312)|
| Fatigue          | 0.052   | 0.187| (0.034–1.017)|
| Clinical severity classification | 0.849   | 0.842| (0.144–4.920)|
| Onset time(days) | 0.075   | 0.653| (0.409–1.044)|
| PCT >0.1 ng/mL   | 0.003   | 0.038| (0.004–0.341)|

Table 3. Risk factors between co-infected and mono-infected COVID-19 patients with multivariate analysis.

Age stratification includes: ≤20, 21–40, 41–60, >60. PCT – procalcitonin; OR – odds ratio.
Our study showed that co-infected COVID-19 patients had lower levels of LDH and CK than mono-infected patients in the early stages, indicating that co-infection does not aggravate myocardial injury in COVID-19 patients. This may be associated with cardiomyocyte damages caused directly by viral entry via the angiotensin-converting enzyme 2 (ACE2) receptor [20]. ACE2 receptors are ubiquitous in the human body, and co-infecting pathogens can affect the ACE2-related signaling pathways. Our results are consistent with the previously reported findings [21] showing no difference in the rate of co-infections among mildly, moderately, and severely ill COVID-19 patients. CRP and PCT play vital roles in the diagnosis and treatment of infectious diseases. The production of PCT is mainly triggered by bacterial toxins and inflammatory cytokines, while its activation and production are inhibited by the large amount of INF-γ produced during viral infections [22]. Our study found that the patients with co-infection were significantly more likely to have elevated PCT levels than those with mono-infection, suggesting greater severity of inflammatory responses in co-infected patients.

COVID-19 patients were treated with anti-inflammatory therapy according to the inflammatory index and clinical experience. Combination therapy with antiviral and antibiotic agents was recommended for definite COVID-19 patients and suspected COVID-19 patients [23,24]. In this study, 52 of 78 cases (66.7%) were treated with a single antibiotic (21 cases with levofloxacin, 22 cases with moxifloxacin, 5 cases with levofloxacin converted to moxifloxacin, 1 case from piperacillin sulbactam to moxifloxacin, 1 case to piperacillin tazobactam, 2 cases from levofloxacin/moxifloxacin to linezolid), and 7 cases (9.0%) with combined antibiotics (1 case of meropenem combined with vancomycin, 1 case of meropenem with linezolid, 2 cases of moxifloxacin with meropenem, 1 case of levofloxacin with cefoperazone sulbactam, 1 case of moxifloxacin combined with cefoperazone sulbactam, and 1 case of levofloxacin with piperacillin sulbactam). All 78 cases of infection were well controlled, and neither secondary infection nor adverse events occurred. According to the experience in the treatment of respiratory tract pathogens, quinolones such as levofloxacin or moxifloxacin are the first choice in the treatment of respiratory tract pathogens. Then, the curative effect of antibiotics should be further evaluated according to the development of the disease, inflammatory indicators, and etiological results, and the antibiotics needed further are selected according to the antibiotics sensitivity test. In the specific clinical work, the past medical history of patients, especially infection susceptibility factors, needs to be well considered.

Due to the situation of epidemic control in China, the number of COVID-19 patients in our area is limited. At the same time, as our hospital is the local designated treatment hospital, all patients in the region are treated there. These conditions may have prevented us from finding more differences between the co-infection and mono-infection groups. Large sample and multicenter studies in other regions are still needed. In addition, this study was conducted in the early stage of the epidemic, and the patient diagnosis and treatment process and hospital-related work flow were not yet perfect, so the clinical data were not comprehensive. More comprehensive research is needed to assess the influence of other conditions on infection.

Conclusions

The findings showed that *M. pneumoniae* and RSV were the most common co-infections in patients with COVID-19 pneumonia. Increased levels of PCT in patients with COVID-19 pneumonia were associated with co-infection.

Acknowledgements

We wish to thank all our colleagues who participated in this project for providing timely help, especially all doctors on the first-line of managing COVID-19.

Conflicts of interest

None.
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