Presenting characteristics, comorbidities, and outcomes of patients coinfected with COVID-19 and *Mycoplasma pneumoniae* in the USA

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Abstract
Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) is spreading at a rapid pace, and the World Health Organization declared it as pandemic on 11 March 2020. *Mycoplasma pneumoniae* is an "atypical" bacterial pathogen commonly known to cause respiratory illness in humans. The coinfection from SARS-CoV-2 and mycoplasma pneumonia is rarely reported in the literature to the best of our knowledge. We present a study in which 6 of 350 patients confirmed with COVID-19 were also diagnosed with *M. pneumoniae* infection. In this study, we described the clinical characteristics of patients with coinfection. Common symptoms at the onset of illness included fever (six [100%] patients); five (83.3%) patients had a cough, shortness of breath, and fatigue. The other symptoms were myalgia (66.6%), gastrointestinal symptoms (33.3%-50%), and altered mental status (16.7%). The laboratory parameters include lymphopenia, elevated erythrocyte sedimentation rate, C-reactive protein, lactate dehydrogenase, interleukin-6, serum ferritin, and D-dimer in all six (100%) patients. The chest X-ray at presentation showed bilateral infiltrates in all the patients (100%). We also described electrocardiogram findings, complications, and treatment during hospitalization in detail. One patient died during the hospital course.

KEYWORDS
coronavirus, epidemiology, immune responses, interleukin, pandemics, pathogenesis, respiratory tract, SARS coronavirus, virus classification

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) has infected more than 2.4 million people and resulted in more than 170,000 deaths worldwide caused by severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2).1 COVID-19 was declared as a global pandemic by the World Health Organization.2 COVID-19 can be associated with other organisms causing pneumonia. The symptoms caused by COVID-19 are like the other common respiratory pathogens, and it is essential to identify them and treat them appropriately. Patients who have COVID-19 can also get rarely coinfected with other respiratory pathogens. Coinfection of both COVID-19 and influenza has been described.3,4

*Mycoplasma pneumoniae* pneumonia is commonly seen in younger adults and is the common reason for atypical pneumonia.5
The coinfection from SARS-CoV-2 and mycoplasma pneumonia is rarely reported in the literature.6,7 The goal of this study is to provide a detailed description of the clinical characteristics, relevant laboratory associations, treatments, and complications in such coinfection that have never been described before.

2 | METHODS

2.1 | Patients

The present study is a retrospective cohort review of all consecutive COVID-19 patients who were admitted to a community teaching hospital between 1 March and 15 April 2020. The institutional review board of Interfaith Medical Center, Brooklyn, New York, approved the study protocol with patient consent exemption. The patients who were coinfected both with COVID-19 and M. pneumoniae were a total of 6 among 350 patients.

2.2 | Data collection

Subject data were extracted from electronic medical records, and the data was deidentified for analysis. The following data was collected—patient’s demographic information, pertinent clinical data including medical comorbidities, laboratory data, chest X-ray, electrocardiogram (EKG). The mycoplasma diagnosis was made based on the serologies (enzyme-linked immunosorbent assay), and COVID-19 diagnosis was made based on polymerase chain reaction (PCR).

2.3 | Outcome assessment

We are discussing the patient’s clinical characteristics, comorbidities, complications, and clinical outcomes of patients presenting with COVID-19 and M. pneumonia.

2.4 | Statistical analysis

The statistical package for social sciences (SPSS) software (IBM SPSS, version 25) was used for statistical analysis was performed using. Frequencies and percentages were used to summarize categorical and continuous variables. The descriptive values were expressed as mean ± standard deviation (SD).

3 | RESULTS

3.1 | Clinical characteristics

Our study found that 6 patients were coinfected with COVID-19 and mycoplasma among 350 patients infected with COVID-19, with an incidence rate of 1.7%. Among the 350 patients, 30 patients (8.5%) were Hispanics, 10 (2.8%) were Caucasians, 5 (1.5%) were Asians (1.5%), and 305 (87.1%) were African-Americans. The clinical characteristics of the coinfected patients were listed in Table 1. The age range of these patients was from 39 to 68 years (mean age ± SD = 57 ± 10.6 years). Among the six patients, four were females and two were males. All the patients were African-Americans except for one Hispanic female. Among the comorbidities, hypertension was present in the majority (five patients—83.3%) and congestive heart failure in half (three patients—50%) of the patients. One-third (two patients—33.3%) of the patients had diabetes, hyperlipidemia, and bronchial asthma. Only one patient (16.7%) had a history of malignancy and one patient with end-stage renal disease (ESRD). The body mass index ranged from 22.6 to 40.7 (mean ± SD = 28 ± 6.5). One-third of the patients (two patients—33.3%) are active smokers, and one patient (16.7%) has a history of alcohol intake. Only one patient was taking Angiotensin-converting enzyme inhibitors on admission. The majority of the patients had hypertension, five of them were African-Americans and one of them was morbidly obese.

All the patients had a fever (100%). Cough, shortness of breath, and fatigue were present in the majority (five patients—83.3%). Two-thirds (four patients—66.6%) had myalgias, half of them (three patients—50%) had nausea, and one-third (two patients—33.3%) had diarrhea and vomiting. Only one patient (16.7%) had altered mental status. The length of the stay ranged from 5 to 11 days, and one patient expired on the fifth day of admission.

3.2 | Vital signs, EKG, and chest X-ray at presentation

The vital signs, EKG, and chest X-ray at presentation were summarized in Table 2. The temperature ranged from 99.8°F to 103.1°F. The respiratory rate ranged from 18 to 22 breaths per minute. 83.3% of the patients were hypoxic, with one patient needing mechanical ventilation, one patient needing nonrebreather, and three patients needing oxygen delivery by nasal cannula, and two among them needed high flow.

Bilateral infiltrates were present in all the patients on a chest X-ray at presentation (100%), as shown in Figure 1. Two patients (33.3%) has prolonged QT interval on EKG (QTc males 431-450; females 451-470). There were no new ST-T segment changes in any of these patients.

3.3 | Laboratory parameters for all the patients

The laboratory parameters for all the patients were summarized in Table 3.

White cell count was elevated in two patients (33.3%), while all the patients had lymphopenia, and neutrophils were elevated in the majority of the patients (five patients—83.3%). All the patients had a normal platelet count. Out of six patients, only one patient had anemia of chronic disease due to a history of ESRD at admission (16.6%). As there was no drop in hemoglobin/hematocrit for all the
**TABLE 1** Clinical characteristics of patients infected with COVID-19 and *Mycoplasma pneumoniae*

| Characteristics                                | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | N (%)
|------------------------------------------------|--------|--------|--------|--------|--------|--------|------
| Age                                            | 39     | 54     | 68     | 60     | 67     | 54     | NA
| Sex                                            | Female | Female | Male   | Female | Female | Male   | NA
| Body mass index                                | 26.8   | 23.5   | 22.6   | 28.3   | 40.7   | 26     | NA
| Ethnicity                                      |        |        |        |        |        |        |      
| African-American                               | Yes    | Yes    | Yes    | Yes    | NA     | Yes    | 83.3 |
| Hispanic                                       | NA     | NA     | NA     | NA     | Yes    | NA     | 16.7 |
| Comorbidities                                  |        |        |        |        |        |        |      
| Hypertension                                   | No     | Yes    | Yes    | Yes    | Yes    | Yes    | 83.3 |
| Diabetes                                       | No     | Yes    | No     | No     | No     | Yes    | 33.3 |
| Congestive heart failure                       | No     | Yes    | Yes    | No     | Yes    | No     | 50   |
| Bronchial asthma                               | No     | No     | Yes    | No     | No     | Yes    | 33.3 |
| Current smoker                                 | Yes    | No     | Yes    | No     | No     | No     | 33.3 |
| Coronary artery disease                        | No     | No     | No     | Yes    | No     | 16.7   |
| Alcohol use                                    | Yes    | No     | No     | No     | No     | No     | 16.7 |
| Hyperlipidemia                                 | No     | No     | Yes    | No     | No     | Yes    | 33.3 |
| End-stage renal disease                        | No     | No     | No     | No     | No     | Yes    | 16.7 |
| H/o of malignancy                              | No     | No     | No     | No     | No     | Yes    | 16.7 |
| Clinical presentation                          |        |        |        |        |        |        |      
| Cough                                          | Yes    | Yes    | Yes    | Yes    | No     | Yes    | 83.3 |
| Myalgia                                        | Yes    | No     | Yes    | Yes    | No     | Yes    | 66.6 |
| Fever                                          | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    | 100  |
| Shortness of breath                            | Yes    | Yes    | Yes    | Yes    | Yes    | No     | 83.3 |
| Nausea                                         | Yes    | Yes    | No     | Yes    | No     | No     | 50   |
| Vomiting                                       | Yes    | No     | No     | Yes    | No     | 33.3   |
| Diarrhea                                       | No     | Yes    | No     | No     | No     | No     | 33.3 |
| Fatigue                                        | Yes    | Yes    | Yes    | Yes    | No     | Yes    | 83.3 |
| Altered mental status                          | No     | No     | No     | No     | Yes    | No     | 16.7 |
| Length of stay, d                              | 9      | 8      | 11     | 10     | 5      | 5      |      |

Abbreviation: NA, not applicable.

**TABLE 2** Vital signs, electrocardiogram (EKG), and chest X-ray at presentation

| Vital Signs                        | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 |
|-----------------------------------|--------|--------|--------|--------|--------|--------|
| Temperature, °F                   | 102    | 101.5  | 99.8   | 100.9  | 102    | 103.1  |
| Respiratory rate                  | 18     | 20     | 22     | 20     | 22     | 18     |
| Systolic blood pressure, mm Hg    | 108    | 135    | 133    | 138    | 105    | 91     |
| Diastolic blood pressure, mm Hg   | 75     | 73     | 82     | 70     | 59     | 53     |
| Oxygen saturation                 | 95     | 95     | 96     | 95     | 100    | 95     |
| Oxygen delivery method            | Room air | Nasal cannula | High-flow nasal cannula | High-flow nasal cannula | Mechanical ventilation | Nonrebreather |
| Unilateral infiltrate             | No     | No     | No     | No     | No     | No     |
| Bilateral infiltrate              | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    |
| EKG                               |        |        |        |        |        |        |
| PR interval, ms (120-200)         | 146    | 150    | 154    | 158    | 174    | 162    |
| QTc interval, ms (males, 431-450; females, 451-470) | 401    | 510    | 430    | 474    | 500    | 455    |
| New ST-T wave changes             | No     | No     | No     | No     | No     | No     |
patients during the entire hospital course, cold agglutinin test was not performed. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), lactate dehydrogenase (LDH), interleukin-6 (IL-6) serum ferritin, and D-dimer was elevated in all the patients.

Troponin levels were elevated in the majority (five patients—83.3%), ranged from 0.01 to peak level of 2.21 ng/mL. Brain natriuretic peptide was elevated in half (three patients—50%) of the patients, ranged from 10 to 1335 pg/mL. The fibrinogen level was elevated in the majority (five patients—83.3%) and ranged from 368 to 660 mg/dL. The procalcitonin levels ranged from 0.12 to 2.37 mmol/L, which were elevated in a third of patients (two patients—33.3%). The lactic acid was elevated in one-third of patients (two patients 33.3%) and ranged from 0.9 to 3.5 mmol/L. The aspartate aminotransferase was elevated in four patients (66.6%), while alanine aminotransferase was elevated in only one patient (16.6%). The blood urea nitrogen (BUN) and creatinine were elevated in two-thirds of the patients (four patients—66.6%). The peak BUN level was 74.8 mg/dL, and peak creatinine level was 2.02 mg/dL. Potassium and magnesium levels were normal in all the patients. Prothrombin time/activated partial thromboplastin time were within normal limits.

All the patients were tested positive for SARS-CoV-2 by PCR. M. pneumoniae immunoglobulin M (IgM) and immunoglobulin G (IgG) were elevated in all the patients ranged from 909 to 1737 U/mL and 657 to 955 U/mL, respectively. All the patients were tested negative for both influenza A and B by PCR and urine Legionella Pneumophila antigen. Sputum, urine, and blood cultures were negative for all patients.

3.4 | In-hospital complications

The complications that occurred during the hospital course were summarized in Table 4. Only one patient (16.7%) required intensive care unit (ICU) stay and developed acute respiratory distress syndrome needing mechanical ventilation, developed shock needing vasopressor support, eventually leading to multiorgan failure and death. The acute cardiac injury was present in the majority (five patients—83.3%), and two-thirds (four patients—66.6%) developed acute kidney injury.

The medications used for the treatment of patients were listed in Table 5. All the patients received ceftriaxone for pneumonia, zinc, and vitamin C. About half of them (three patients—50%) received azithromycin or doxycycline with no overlap. Hydroxychloroquine was given to two patients (33.3%), and steroids were given to two patients (33.3%). The patient who died was treated with ceftriaxone, azithromycin, and steroids, but did not receive hydroxychloroquine.

4 | DISCUSSION

The novel coronavirus SARS-CoV-2 causes fever, cough, and shortness of breath and is spreading at an unrelenting pace daily. The United States has the highest number of patients infected, and mortality than any other country in the world. SARS-CoV-2 has spike (S) protein that utilizes membrane-bound angiotensin-converting enzyme 2 aided by serine proteases to gain entry into the human cell and cause infection.
### TABLE 3  Laboratory parameters for all the patients

| Parameters          | Reference range | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | N (%) abnormal |
|---------------------|-----------------|--------|--------|--------|--------|--------|--------|----------------|
| White cell count    | 4.5-11 (10^3/µL) | 4.2    | 3.7    | 5.6    | 6.2    | 13.4   | 12.9   | 33.3           |
| Hemoglobin          | Female: 11-15 g/dL; male: 13-17 g/dL | 13.6   | 12.1   | 13.6   | 12.5   | 12     | 9.8    | 16.6           |
| Platelet count      | 130-400 (10^3/µL) | 161    | 271    | 141    | 249    | 140    | 228    | 0              |
| Lymphocytes         | 22-48 (%)       | 6.4    | 16     | 8.5    | 6.5    | 3.5    | 4.5    | 100            |
| Neutrophils         | 40-70 (%)       | 75.6   | 57.9   | 75     | 88     | 90     | 91.3   | 83.3           |
| ESR                 | 0-20 mm/h       | 53     | 103    | 65     | 102    | 39     | 120    | 100            |
| CRP                 | 0-10 mg/L       | 108    | 46     | 56     | 144    | 146    | 114    | 100            |
| LDH                 | 125-220 U/L     | 500    | 778    | 345    | 390    | 1408   | 474    | 100            |
| Troponin I          | 0.00-0.03 ng/mL | 0.06   | 0.09   | 0.4    | 0.01   | 2.21   | 0.1    | 83.3           |
| BNP                 | 10-100 pg/mL    | 41     | 265    | 1335   | 10     | 567    | 35     | 50             |
| IL-6                | 0.0-15.5 pg/mL  | 300    | 54.6   | 245    | 346    | 74.5   | 200    | 100            |
| Serum ferritin      | 30-400 ng/mL    | 1200   | 810    | 1535   | 469    | 2920   | 3052   | 100            |
| D-dimer             | 0-500 ng/mL     | 1095   | 2032   | 4625   | 1445   | 3862   | 1592   | 100            |
| Fibrinogen          | 193-507 mg/dL   | 542    | 660    | 546    | 650    | 567    | 368    | 83.3           |
| PCT                 | 0.5-1.9 mmol/L  | 0.57   | 0.37   | 0.65   | 0.12   | 2.37   | 2.2    | 33.3           |
| AST                 | 5-34 U/L        | 37     | 29     | 44     | 35     | 229    | 20     | 66.6           |
| ALT                 | 10-55 U/L       | 26     | 12     | 16     | 27     | 106    | 20     | 16.7           |
| Lactic acid         | 0.5-1.9 mmol/L  | 2.1    | 1.5    | 1.8    | 1.2    | 3.5    | 0.9    | 33.3           |
| BUN                 | 9.8-20.1 mg/dL  | 6.7    | 39.7   | 38.5   | 10.9   | 40.7   | 74.8   | 66.6           |
| Creatinine          | 0.57-1.11 mg/dL | 0.79   | 2.02   | 1.51   | 0.75   | 1.85   | 1.24   | 66.6           |
| SARS-COV-2          | PCR Positive    | Positive | Positive | Positive | Positive | Positive | Positive | NA             |
| Influenza           | Type A Ag/Ab; type b Ag/Ab PCR Negative | Negative | Negative | Negative | Negative | Negative | Negative | NA             |
| Urine legionella Ag | Negative        | Negative | Negative | Negative | Negative | Negative | Negative | NA             |
| Mycoplasma pneumonia IgM | <770 U/mL | 1261 | 1075 | 1389 | 1167 | 1737 | 909 | NA |
| Mycoplasma pneumonia IgG | <100 U/mL | 816 | 955 | 725 | 707 | 806 | 657 | NA |

Abbreviations: Ab, antibody; Ag, antigen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IgG, immunoglobulin G; IgM, immunoglobulin M; IL-6, interleukin-6; LDH, lactate dehydrogenase; NA, not applicable; PCR, polymerase chain reaction; PCT, procalcitonin; SARS-COV-2, severe acute respiratory syndrome-coronavirus 2.

### TABLE 4  Complications of the patients

| Complications | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | N (%) abnormal |
|---------------|--------|--------|--------|--------|--------|--------|----------------|
| ARDS          | No     | No     | No     | No     | No     | Yes    | No             | 16.7           |
| Shock         | No     | No     | No     | No     | No     | Yes    | No             | 16.7           |
| Acute cardiac injury | Yes   | Yes    | Yes    | No     | Yes    | Yes    | Yes            | 83.3           |
| Acute liver failure | No    | No     | No     | No     | No     | Yes    | No             | 16.7           |
| Acute kidney injury | No    | Yes    | Yes    | No     | Yes    | Yes    | Yes            | 66.6           |
| Mechanical ventilation | No    | No     | No     | No     | No     | Yes    | No             | 16.7           |
| Death         | No     | No     | No     | No     | No     | Yes    | No             | 16.7           |
| ICU stay      | No     | No     | No     | No     | No     | Yes    | No             | 16.7           |

Abbreviations: ARDS, acute respiratory distress syndrome; ICU, intensive care unit.
SARS-CoV-2 can circulate in the environment with other microorganisms and can change with disease patterns. The influenza epidemic in Wuhan, China, was interfered with by COVID-19 emergence. In a study analyzing two centers in China, the coinfection pattern differed significantly, and a large proportion of patients in Quindao had other seasonal respiratory pathogens in patients with COVID-19 compared to Wuhan. The coinfection rate was 23.3% with mycoplasma pneumonia and COVID-19 in Quindao, China. SARS-CoV-2 is another zoonotic beta coronavirus that has close genetic homology with SARS-CoV-2. Mycoplasma coinfection with SARS-CoV has been detected on the serological assay but was not detected on the respiratory specimen PCR, thus limiting the incidence of coinfection.

Mycoplasma pneumonia is one of the important causes of respiratory tract infections in adults and children and confers 4% to 8% of community-acquired bacterial pneumonia. The number of cases can increase in epidemics and close clusters. The infection can range in severity from mild to life-threatening. An annual estimation of 2 million cases results from this infection leading to 100,000 hospitalizations of adults in the United States. The infections tend to be more common in summers but can occur in any climate. The symptoms of COVID-19 and M. pneumoniae pneumonia are similar with fever, cough, and shortness of breath.

All the patients in this study had both COVID-19 PCR and mycoplasma serologies positive. All the inflammatory markers were elevated, including IL-6, CRP, ESR, and serum ferritin, LDH, D-dimer that have been consistent with prior reported COVID-19. All the patients had lymphopenia, which is typical of viral infections. Most of the patients had elevated troponin I levels, which signifies acute cardiac injury. Bilateral infiltrates were present in all the patients on a chest X-ray at presentation.

Fan et al reported a case of a 36-year-old male in Singapore who had coinfection with mycoplasma and COVID-19. The patient had severe lymphopenia, and moderate thrombocytopenia needed ICU admission and ventilator support. The patient also had cold agglutinin titer of 1:8 and mycoplasma pneumonia antibody titer of 1:160, no hemolysis, or significant anemia was noted, and the direct agglutinin test was negative. Xu et al discussed a 49-year-old female patient who had coinfection SARS-COV-2 and mycoplasma. The patient presented with productive cough and chest congestion but no fever. Computed tomography of the chest showed bilateral ground-glass opacities in lower lobes and patchy shadows in the right upper lobe. The patient test positive for COVID-19 and mycoplasma and was treated with lopinavir/ritonavir, peramivir, interferon-α2b (anti-virals) as well as cefonicid sodium, azithromycin, and moxifloxacin (antibiotics). The patient fully recovered and was discharged from the hospital.

The diagnostic method of choice for mycoplasma pneumonia is nucleic acid amplification tests like PCR and multiplex assays because they have high sensitivity and specificity compared to serologies and culture. Serological tests can be used when molecular tests are not available or as an adjunct to the molecular tests. A single high IgM titer or a fourfold rise in IgG titers are used for serological diagnosis as in our patients.

There is no effective proven therapy for COVID-19 as of now, and supportive care is a vital aspect of care. Many treatment strategies have been utilized like hydroxychloroquine, remdesivir, azithromycin, lopinavir/ritonavir, and tocilizumab. The first-line therapies for M. pneumoniae are macrolides, tetracyclines, and fluoroquinolones. Fortunately, the majority of the patients responded well to the treatment and were discharged from the hospital.

### 5 CONCLUSION

The COVID-19 pneumonia is a serious condition and can be associated with the common respiratory pathogens. This can be dangerous and can result in protracted respiratory symptoms, prolonged ICU stay, morbidity, and mortality if not detected and treated appropriately. The physicians should screen for the common respiratory pathogens with appropriate diagnostic tests.

### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

### AUTHOR CONTRIBUTIONS

VG, PRG, MAM, and NR were involved in data collection, review, and preparation of the manuscript. VMK, MB, SN, and SA were involved in the analysis of data and final review of the manuscript.
preparation of tables. All the authors reviewed the manuscript and agreed with the findings and interpretation.

ETHICS STATEMENT
The institutional review board of Interfaith Medical Center, Brooklyn, New York, approved the study protocol with patient consent exemption.

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