INTRODUCTION

At the end of 2019, a novel coronavirus was identified in Wuhan, China, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has since spread around the world. The illness caused by this virus, coronavirus disease 2019 (COVID-19) has demonstrated huge variability in severity, from an asymptomatic or very mild respiratory illness to acute respiratory distress syndrome and multi-organ failure, with the severe form being more common in older patients and those with underlying comorbidities.[1] To date, it has infected more than 8 million people and resulted in more than 450 thousand deaths around the world according to the World Health Organization statistics.[2] Mycoplasma pneumoniae causes atypical bacterial pneumonia and is known to co-infect patients with viral pneumonias.

Methods: In this retrospective study, patients’ data of 580 inpatients with confirmed SARS-CoV-2 infection were reviewed retrospectively over a 3-month period which included the the first peak of COVID-19 infections in the UK. Results: Eight patients with COVID-19 and M. pneumoniae coinfection were identified – four males and four females. All patients were Caucasian, with an age range of 44–89 years. 37.5% of patients were hypertensive, whereas 25% had Type 2 diabetes mellitus. Dyspnea, cough, and pyrexia were found to be very common in these patients. Majority of the patients had abnormal C-reactive protein, lymphopenia, neutrophilia along with bilateral consolidation, and ground-glass opacities. Two patients required admission to intensive care, both of whom unfortunately died along with one patient receiving ward based care. Conclusion: Our confirmed the presence of co-infection with M. pneumoniae and describes the clinical features, investigation results, clinical course, and outcomes for these patients. Further research is needed to review the role of procalcitonin in excluding bacterial co-infection and to assess the impact of co-infection of patients with COVID-19 on morbidity and mortality.

KEY WORDS: Co-infection, coronavirus disease 2019, Mycoplasma pneumoniae, severe acute respiratory syndrome coronavirus 2
*Mycoplasma pneumoniae* is a very small bacterium in the class Mollicutes and is a well-recognized cause of atypical pneumonia and known to co-infect patients with viral pneumonia. We aim to review the clinical presentation, investigation results, management, and outcomes of COVID-19 inpatients coinfected with *M. pneumoniae*.

**METHODS**

Patients admitted to a National Health Service Trust based in Northern England with suspected COVID-19 and concerning clinical features were screened for atypical respiratory infections including *M. pneumoniae* using an antibody test. We have reviewed the mycoplasma titer all results of inpatients with confirmed SARS-CoV-2 over a 3-month period between March 1, 2020 and May 31, 2020.

Using a cutoff point of 100, particle agglutination test was used to confirm *M. pneumoniae* infection. Out of 580 patients with confirmed SARS CoV-2, 8 were found to be coinfected with *M. pneumoniae*.

We then retrospectively collected the data about these patients’ presentation, demographic details, investigation results, inpatient management, and outcome from the paper medical notes and electronic records.

**RESULTS**

A database with all patients admitted with the polymerase chain reaction (PCR) confirmed SARS-CoV-2 was screened for positive Mycoplasma antibody titers. We found eight patients with high IgG titers (defined as >100 in this study) along with a clinical suspicion of superadded bacterial infection. A total of 580 patients were admitted and treated in the hospital with confirmed COVID during this period. Out of these patients, an atypical respiratory screen was performed in 209 patients based on clinical suspicion, as demonstrated in Figure 1.

All eight patients were from the local area covered by the hospital and were white Caucasian (100%). The age range for these patients was from 44 to 89 years old. We had an equal male-to-female ratio, i.e., four male and four female patients. Although the mean age for females was 76.75 years old, it was significantly lower at 58.25 years old for male patients.

In terms of underlying comorbidities, 37.5% of the patients had hypertension while 25% had Type 2 diabetes. Twenty-five percent had underlying lung conditions such as chronic obstructive pulmonary disease, bronchiectasis, asthma, or lung nodules.

12.5% had chronic kidney disease. Twenty-five percent of the patients were current smokers, whereas 62.5% were nonsmokers. One patient (12.5%) was an ex-smoker.

Seventy-five percent of the patients presented with worsening dyspnea, whereas 37.5% had a cough. Twenty-five percent reported chest pain as a presenting complaint as well. Other symptoms such as myalgia and headache were reported in 25% of the patients. One patient had haemoptysis on presentation.

The mean systolic blood pressure on presentation was 139.6 mmHg. All of these patients were pyrexic (defined as temperature >38C for this study). 87.5% of the patients were found to be tachycardic on admission with a mean heart rate of 91.6 bpm. 62.5% of patients required oxygen while 75% had tachypnea at the time of admission.

All except one patient had normal hemoglobin while all the patients were lymphopenic on presentation (defined as count <1.5 for this study). Two patients had neutrophilia while high C-reactive protein (CRP) was seen in all patients with the mean being 140.5. Procalcitonin (PCT) was performed in five patients. Of these, 2 had high PCT on admission (defined as >0.5 in this study), whilst three patients had initial normal results followed by an increase in PCT value on repeat testing. Full admission blood results are shown in Table 1. Fifty percent of the patients were found to have acute kidney injury with one of them needing continuous venovenous hemofiltration.

62.5% of patients had bilateral consolidation while 25% had bilateral ground-glass opacities on chest X-ray.
TABLE 1: Blood test results on admission for eight patients with confirmed coronavirus disease 19 and Mycoplasma pneumoniae co-infection

| Case  | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 |
|-------|-------|--------|--------|--------|--------|--------|--------|
| Hemoglobin (115-160 g/L) | 124 | 128 | 158 | 134 | 109 | 128 | 113 | 88 |
| White cell count (4.0-12.0×10⁹/L) | 16.9 | 6.6 | 8.1 | 7.5 | 3.2 | 6.8 | 14 | 6.7 |
| Lymphocytes (1.5-4×10⁹/L) | 1.3 | 1.2 | 0.7 | 0.5 | 0.5 | 0.3 | 0.1 | 0.7 |
| Neutrophils (2.0-7.5×10⁹/L) | 13.7 | 4.7 | 7 | 6.1 | 2.5 | 6.3 | 12.2 | 5.2 |
| CRP (<10 mg/L) | 152 | 179 | 244.4 | 260 | 69.7 | 91.6 | 78.5 | 49.2 |
| Ferritin (22-275 μg/L) | 69 | 630 | 2627 | 1679 | 632 | - | 753 | - |
| Prolactin (<0.5 ng/mL) | - | - | 0.55 | 0.17 | 0.18 | 1.53 | 0.05 |
| Lactate dehydrogenase (125-243 U/L) | 319 | 259 | 551 | 658 | 282 | - | 792 | 396 |

CRP: C-reactive protein

In light of this and because of the difficulty excluding bacterial co-infection in patients admitted with suspected COVID-19, it has been common practice to treat these patients empirically with antibiotics and test for other respiratory pathogens in addition to SARS-CoV-2 PCR.

M. pneumoniae is a known cause of community-acquired pneumonia. The prevalence of M. pneumoniae in patients diagnosed with chest infection varies between 1.9% and more than 30% depending on the population and diagnostic tests used.⁹

Coinfection of M. pneumoniae with other viral respiratory pathogens is not uncommon. A retrospective analysis revealed that M. pneumoniae is the most common bacteria to co-infect patients with influenza A (H1N1) infection.¹⁰

SARS-CoV-2 coinfection with M. pneumoniae has been reported in a few case reports in China and Singapore.¹¹,¹² In addition, the rate and clinical characteristics of co-infection were reviewed in two retrospective cohort studies. A review of 350 patients with confirmed COVID-19 admitted to a community teaching hospital in the USA revealed six cases of coinfection with M. pneumoniae.¹³ This is significantly lower than the rate reported in a Chinese review by Quansheng et al., in which the reported prevalence of M. pneumoniae coinfection was 23% out of 68 cases diagnosed with SARS-CoV-2 infection.¹⁴ Both of these observational studies used serological evidence to confirm M. pneumoniae infection and did not rely on PCR of respiratory samples. The notable difference in the rate of M. pneumoniae co-infection between the American and Chinese studies could be related to the demographic variations across both populations.

In our study, patients who were discharged from the Accident and Emergency department were not included. All patients in our intensive care unit with COVID-19 were screened for M. pneumoniae; however, screening for atypical pathogens in patients with suspected and confirmed COVID-19 in the medical wards was based on the clinical suspicion of the treating physician. Therefore, the prevalence of coinfection we reported is subjected to a selection bias. Taking this into account, the prevalence of M. pneumoniae co-infection in our study was very similar to the American review. However, despite the similarities,
the majority of patients co-infected in the American study were African American in contrast to white Caucasian in our review.[13] This is possibly related to the difference in the population examined in both reviews.

The patients in our study were equally divided between males and females. All tested positive for SARS-CoV-2 PCR and *M. pneumoniae* serology. All of them had high CRP and were lymphopenic. D dimer, ferritin, troponin, and lactate dehydrogenase were not tested in all patients which makes it difficult to draw any conclusions. Chest X-ray was abnormal in all patients; main findings noted were bilateral ground-glass opacities and consolidation which have been described as common findings in COVID-19 patients.[15]

Most patients were treated with clarithromycin for 14 days in accordance with hospital policy for *M. pneumoniae* treatment. One patient received azithromycin instead of Clarithromycin because of drug-drug interaction and two patients received levofloxacin in addition to clarithromycin as shown in Figure 2.

The results of PCT in patients co-infected with *M. pneumoniae* were interesting. Three patients in our review had a PCT below the reference range despite having positive *M. pneumoniae* titer. This replicates the findings noted by Vijay in their cohort study.[13] These findings may question the efficacy of using PCT to help rule out bacterial coinfection in COVID-19 patients and trigger further research.

Half of the patients developed acute kidney injury; however, only one patient required renal replacement therapy. Unfortunately, two patients required admission to the intensive care unit and passed away.

Our study shed light on the presenting features, investigations results and outcomes of patients coinfected with *M. pneumoniae* and SARS-CoV-2. *M. pneumoniae* can cause severe community-acquired chest infections with a mortality of up to 30% reported in the literature. Antibiotics are available and required to treat the infection as it will presumptively improve the outcomes.[16]

Therefore, screening for atypical pathogens including *M. pneumoniae* is still justified despite the low co-infection rate reported in our study.

**CONCLUSION**

The COVID-19 pandemic has taken the medical fraternity by surprise and the response to this has been unprecedented. This is largely due to the highly infective and insidious ways that the virus spreads as well as the incidence of severe respiratory failure requiring intensive care support. Our review confirmed the presence of co-infection with *M. pneumoniae* and describes the clinical features, investigation results, clinical course, and outcomes for these patients. Further research is needed to review the role of PCT in excluding bacterial co-infection and to assess the impact of co-infection of patients with COVID-19 on morbidity and mortality. Future guideline development is warranted to clarify which patient populations with COVID-19 should be screened for *M. pneumoniae*.

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**Conflicts of interest**

There are no conflicts of interest.

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