Received: 9 August 2020 | Revised: 22 August 2020 | Accepted: 24 August 2020

DOI: 10.1002/jmv.26467

SHORT COMMUNICATION

JOURNAL OF MEDICAL VIROLOGY WILEY

Association of mortality and recent *Mycoplasma pneumoniae* infection in COVID-19 patients

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Abstract

To compare characteristics and outcomes of patients who had COVID-19 with *Mycoplasma pneumoniae* immunoglobulin M (IgM) antibodies to those without *M. pneumoniae* antibodies. We retrospectively reviewed cases admitted over a 4-week period between 17 March 2020 and 14 April 2020 to the Hoboken University Medical Center, NJ, USA. We compared the outcomes of COVID-19 patients who were positive for *M. pneumoniae* IgM with those who were negative for *M. pneumoniae* IgM. The primary outcome was mortality. The adjusted odds ratio was calculated after controlling for baseline differences. Of 139 patients admitted with COVID-19, 79 were positive for *M. pneumoniae* IgM. The mortality among those who were *M. pneumoniae* IgM positive was significantly higher (adjusted odds ratio: 2.28, 95% confidence interval: 1.03 to 5.03) compared with those who were *M. pneumoniae* IgM negative. Patients with coinfection (COVID-19 and mycoplasma) have higher mortality compared with patients with just COVID-19 disease.

KEYWORDS

mycoplasma IgM, outcome, SARS-CoV-2

1 | INTRODUCTION

1.1 | Mycoplasma

Pneumoniae affects 3%–10% of patients with respiratory tract diseases.[1] Laboratory and imaging findings of *Mycoplasma pneumoniae* infection mimic the features seen in the SARS-CoV-2 infection-induced coronavirus disease (COVID-19). These include hepatic transaminitis, normal leukocyte count, patchy pulmonary consolidation, and ground-glass opacities on computed tomography scans. Typical clinical features may be indistinguishable from COVID-19 disease and include pharyngitis; an intractable, nonproductive day-and-night cough; and dyspnea.[2] Fan et al.[3] described one case of *M. pneumoniae* and COVID-19 coinfection in a 36-year-old male. The authors concluded that COVID-19 coinfection with *M. pneumoniae* may exacerbate clinical symptoms, increase morbidity, and cause prolonged intensive care unit stays if undetected or untreated. Richardson et al.[4] described a case series of 5700 patients with COVID-19 admitted to intensive care units in New York in which only 1 patient had coinfection with *M. pneumoniae*. In another study, Easom et al.[5] reported one case of *M. pneumoniae* among 68 patients assessed for COVID-19 infection. However, we observed a different experience when patients were evaluated for viruses in nasopharyngeal swab who also underwent serological evaluation for *M. pneumoniae*. Our objective was to compare characteristics and outcomes of patients who had COVID-19 with coexistent positivity for *M. pneumoniae* immunoglobulin M (IgM) antibodies suggestive of recent infection with those who were negative for *M. pneumoniae* IgM.

2 | METHODS

We retrospectively reviewed all cases of respiratory illness admitted over a 4-week period between 17 March 2020 and 14 April 2020 to the Hoboken University Medical Center, NJ, USA, in which patients were investigated for SARS-CoV-2 infection. At our institute, patients were also investigated for other respiratory pathogens with testing for

influenza virus from the nasopharyngeal swab, and for recent mycoplasma infection by checking IgM. We collected baseline information on their comorbidities and clinical characteristics at admission. We compared the outcomes of those who were positive *M. pneumoniae* IgM (immunoassay: >950 U/ml for positive test; Quest Diagnostics) with those who were negative for *M. pneumoniae* IgM (immunoassay: <770 U/ml for negative test; Quest Diagnostics). Baseline characteristics and outcomes were compared using Student's *t*-test for continuous variables and χ^2 test for categorical variables. Odds ratios were calculated for mortality after adjusting for comorbidities and different baseline characteristics. Approval for retrospective chart review was obtained from the Hoboken University Medical Center, NJ, USA.

3 | RESULTS

Over a 4-week period, 347 patients were admitted to our institute with a clinical picture suggestive of atypical pneumonia/viral pneumonitis. Common presenting features were cough, dyspnea, fever, decreased appetite, and generalized malaise. Of these patients, 339 were investigated for SARS-CoV-2 via nasopharyngeal swab, of which 288 were positive for genome targets of SARS-CoV-2 by polymerase chain reaction (LabCorp or Quest Diagnostics). Of these 288 patients, 140 patients also had IgM testing done for *M. pneumoniae*: 79 (56.4%) were positive for *M. pneumoniae* IgM and 60 (43.6%) were negative. One patient was still admitted (negative *M. pneumoniae* IgM) at the time of preparation of this report.

Baseline characteristics of these 139 patients and their clinical courses and outcomes are compared in Table 1. Proportions of male patients and patients who had fever were higher in those with *M. pneumoniae* IgM positivity; however, proportions of patients with obesity and diabetes were lower in the same group. Overall, the rates of other comorbidities were lower in patients with *M. pneumoniae* IgM positivity. All patients received antibiotics coverage against *M. pneumoniae* in both groups. After adjustment for sex, diabetes, and body mass index > 30, the odds of mortality were higher in COVID-19 patients who were *M. pneumoniae* IgM positive compared with those who were negative; adjusted odds ratio: 2.28, 95% confidence interval: 1.03 to 5.03.

4 | DISCUSSION

In this single-center case series, we identified that, among patients with COVID-19, recent infection of *M. pneumoniae* was much more common than reported in the literature, with more than half of the

TABLE 1 Baseline characteristics and outcomes

Variables	SARS-CoV-2 infection and *Mycoplasma pneumoniae* IgM positive (*n* = 79)	SARS-CoV-2 infection but *M. pneumoniae* IgM negative (*n* = 60)	*P* Value
Characteristics			
Age in years, mean (*SD*)	62.3 (16.3)	62.2 (15.6)	.95
Male sex, *n* (%)	55 (69.6)	30 (50.0)	.02
Smoking, *n* (%)	14 (17.7)	12 (20.0)	.73
Hypertension, *n* (%)	35 (44.3)	35 (58.3)	.10
Coronary artery disease, *n* (%)	3 (3.8)	5 (8.3)	.26
Obesity (BMI > 30), *n* (%)	19 (24.1)	29 (48.3)	<.01
Diabetes, *n* (%)	23 (29.1)	31 (51.7)	.01
Chronic respiratory disease, *n* (%)	10 (12.7)	9 (15.0)	.69
Chronic kidney disease, *n* (%)	11 (13.9)	7 (11.7)	.69
Fever > 38°C, *n* (%)	51 (64.6)	45 (75.0)	.19
Course			
Invasive mechanical ventilation, *n* (%)	26 (32.9)	15 (25.0)	.31
Intensive care admission, *n* (%)	29 (36.7)	18 (30.0)	.41
Outcomes			
Renal replacement therapy, *n* (%)	9 (11.4)	3 (5.0)	.18
Death, *n* (%)[a]	38/79 (48.1)	17/60 (28.3)	.02

Abbreviations: BMI, body mass index; IgM, immunoglobulin M; *SD*, standard deviation.

[a]One patient in mycoplasma IgM negative group was still in hospital at the time of chart review.

patients positive for *M. pneumoniae* IgM. The rates of comorbidities were lower in patients with mycoplasma IgM positive. However, patients with COVID-19 and IgM positive had more than two times higher odds of mortality.

Due to a relatively low prevalence of *M. pneumoniae* infection and currently high prevalence of COVID-19-related pneumonia, it is possible that our rates differ from those reported in the literature because of the frequency of testing and type of testing.[4,5] We speculate that, the main difference between prior reports and our findings is the measurement of IgM versus the identification of *M. pneumoniae* via nasopharyngeal swab. However, we may have identified a predisposed population in whom the illness may be of higher severity. It is possible that compromised host status due to recent infection with *M. pneumoniae* may contribute to higher severity of illness associated with COVID-19. Recently, Gayam et al.[6] reported 6 of 350 (1.7%) patients had *M. pneumoniae* positive serology in their series in the USA. One of the six patient died who had multiorgan failure. *M. pneumoniae* infections in both acute and chronic conditions are associated with the induction of proinflammatory and other cytokines[7] such as interleukin-8 (IL-8), IL-6, IL-10, tumor necrosis factor-α, and IL-1β.[8] Severe deterioration of some COVID-19-infected patients has been closely related to the cytokine storm.[9] Coinfection or compromised host status may lead to greater severity of illness and increases in length of stay in hospital, time on a ventilator (and associated complications and procedures like tracheostomy and PEG), and, ultimately, morbidity and mortality. Whether or not a recent infection of *M. pneumoniae* and SARS-CoV-2 leads to an even more catastrophic cytokine storm than one individual infection needs to be determined. Untreated *M. pneumoniae* infections in patients with COVID-19 could result in extrapulmonary manifestations, an ominous prognostic factor.[2]

Clinical findings of our case series are interesting in the sense that there were lower rates of comorbidities, now well-known to be associated with mortality, in the group who had COVID-19 and mycoplasma IgM. This included nearly half the rate of obesity and diabetes and lower rates of smoking and hypertension compared with the group negative for IgM. This finding should be considered seriously with the fact that every patient, irrespective of their mycoplasma IgM status, received antibiotics for *M. pneumoniae*. This may have attenuated the mortality rate in the group with IgM positive status. Thus, we may have identified an important prognostic factor that may explain some of the deaths in relatively healthy individuals (lower comorbidity).

We would like to acknowledge some limitations of our report. First, this was a single-center experience. The findings need to be confirmed in reports from other centers. Second, we did not have enough information to investigate how recent infection with *M. pneumoniae* predisposes an individual to SARS-CoV-2 infection. Third, recent reports have indicated the presence of lupus anticoagulants in patients with COVID-19.[10] Whether or not the identification of IgM for *M. pneumoniae* in COVID-19 patients reflects the activation of some immunological pathway leading to positivity remains to be seen. Since 46% of our patients were not positive for IgM for *M. pneumoniae*, we feel that a true previous infection with *M. pneumoniae* may have predisposed these individuals to acquire COVID-19.

In conclusion, we report the unique findings of possible recent *M. pneumoniae* in patients with COVID-19 and higher odds of death among those who were IgM positive for *M. pneumoniae*. We propose that these findings deserve further investigation and clarification as to whether they are associated with higher severity of the disease. The current armamentarium for COVID-19 treatment includes macrolides in certain protocols; however, none of the protocols has provided a clear rationale for such cotreatment. Further research is warranted.

ACKNOWLEDGMENTS

The authors thank the staff of Hoboken University Medical Center for their relentless efforts in managing these patients. The authors also thank Jessica Yang for help with statistical analyses and Heather McDonald-Kinkaid for editing the manuscript.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Deepak Amin conceptualized the study, planned the study, and reviewed and revised manuscript. Kristin McKitish reviewed the protocol, collected data, and participated in drafting manuscript. Prakesh S. Shah reviewed protocol, analyzed data, reviewed, and revised manuscript. All authors approve final draft of the manuscript.

DATA AVAILABILITY STATEMENT

Data are available from authors upon reasonable request.

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How to cite this article: Amin D, McKitish K, Shah PS. Association of mortality and recent *Mycoplasma pneumoniae* infection in COVID-19 patients. *J Med Virol*. 2021;93:1180-1183. https://doi.org/10.1002/jmv.26467