

LETTERS TO THE EDITOR

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# False-positive *Legionella pneumophila* antibodies in COVID-19 patients

Shu-hua He<sup>1</sup>, Shan Li<sup>1</sup> and Li Weng<sup>1\*</sup> 

\*Correspondence:  
wengli@gmail.com

<sup>1</sup> Medical Intensive Care Unit, State Key Laboratory of Complex Severe and Rare Diseases, Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Sciences, 1 Shuai Fu Yuan, Beijing 100730, People's Republic of China

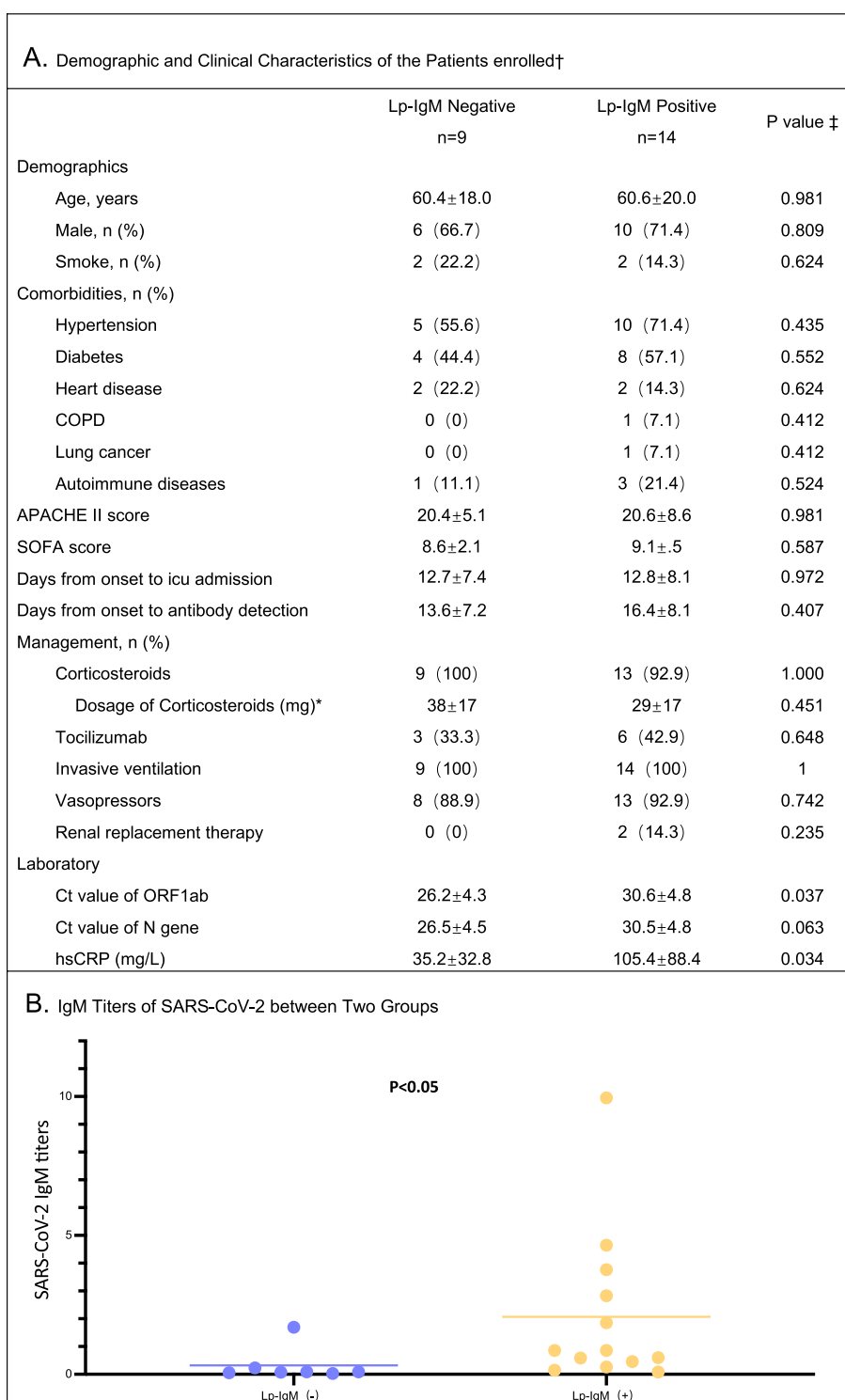
Dear Editor,

The number of patients with coronavirus disease 2019 (COVID-19) infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has increased in China since the reopening. From December 30, 2022, to January 30, 2023, a total of 23 critically ill patients with COVID-19 were consecutively admitted to a medical intensive care unit of Peking Union Medical College Hospital. We detected Immunoglobulin M (IgM) of *Legionella pneumophila* (LP) serological antibody test in 14 (14/23, 60.9%) patients. However, the subsequently confirmative investigation of both Polymerase chain reaction (PCR) (14/14, 100%) from bronchoalveolar fluid (BALF) and urine antigen test (12/12, 100%) for LP were negative.

As shown in Fig. 1A, the characteristics and managements were similar between LP-IgM positive and negative groups. Meanwhile, the PCR cycle threshold ( $C_t$ ) value ( $30.6 \pm 4.8$  vs.  $26.2 \pm 4.3$ ,  $p < 0.05$ ) and IgM titers ( $2.1 \pm 2.8$  vs.  $0.3 \pm 0.6$ ,  $P < 0.05$ ) of SARS-CoV-2 in LP-IgM positive group was higher than negative group (B).

Recent studies showed that the incidence of COVID-19 co-infection with LP ranged from 0.288–1.1% [1, 2] based on PCR from lower respiratory tract specimens or urine antigen testing, to 12.6–20% [3, 4] based on immune-fluorescence or ELISA serological antibody test. To our knowledge, our study was the first report to confirm false-positive LP-IgM in COVID-19, which was similar to the cross-immune responses in previous studies [5].

Considering the potential risk of false positive results in COVID-19 patients, we suggest avoiding the immediate testing of LP-IgM or diagnosing *Legionella pneumophila* infection. Similarly, we advise against the empirical use of antibiotics such as fluoroquinolones. Instead, we recommend testing respiratory secretions DNA or urine *Legionella pneumophila* antigen for accurate diagnosis and appropriate treatment. Given the decrease in the incidence of COVID-19, the disease has become a crucial differential diagnosis, highlighting the significance of identifying patients who are admitted to the ICU with COVID-19. Our findings suggest a high positivity rate of LP-IgM in COVID-19 patients, which could serve as a potential risk factor. Therefore, clinicians should consider conducting SARS-CoV-2 testing in LP-IgM-positive patients.



**Fig. 1** False-positive *Legionella pneumophila* antibodies in COVID-19 patients **A** shows the comparison of demographic and clinical characteristics of the enrolled patients between two groups. **B** shows the difference of IgM titers of SARS-CoV-2 between two groups. †Plus-minus values are means±standard deviation. ‡The categorical variables were compared using the Chi squared test or Fisher's exact test. The continuous variables were compared using the Mann-Whitney *U* test or *t* test. A two-sided  $\alpha$  of less than 0.05 was considered statistically significant. \*Patients who received corticosteroids on the day of LP-IgM testing (prednisone equivalent dose). *IgM* Immunoglobulin M, *LP* *Legionella pneumophila*, *APACHE* Acute Physiology and Chronic Health Evaluation, *COPD* Chronic obstructive pulmonary disease, *C<sub>t</sub>* cycle threshold, *hsCRP* High-sensitivity C-reactive protein

**Author contributions**

S-HH: Conceptualization, Methodology, Software, Investigation, Formal Analysis, Writing—Original Draft; SL: Resources, Supervision; LW: Conceptualization, Resources, Supervision, Writing—Review & Editing. All authors read and approved the final manuscript.

**Availability of data and materials**

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**Declarations****Ethics approval and consent to participate**

This study has been approved by the Ethics Committee of Peking Union Medical College Hospital(K23C0322).

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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