LETTERS TO THE EDITOR

False-positive Legionella pneumophila antibodies in COVID-19 patients

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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_i) value $(30.6 \pm 4.8 \text{ vs. } 26.2 \pm 4.3, p < 0.05)$ and IgM titers $(2.1 \pm 2.8 \text{ vs. } 0.3 \pm 0.6, P < 0.05)$ 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.

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	Lp-IgM Negative	Lp-IgM Positive	
	n=9	n=14	P value :
Demographics			
Age, years	$60.4{\scriptstyle\pm}18.0$	$60.6 {\pm} 20.0$	0.981
Male, n (%)	6 (66.7)	10 (71.4)	0.809
Smoke, n (%)	2 (22.2)	2 (14.3)	0.624
Comorbidities, n (%)			
Hypertension	5 (55.6)	10 (71.4)	0.435
Diabetes	4 (44.4)	8 (57.1)	0.552
Heart disease	2 (22.2)	2 (14.3)	0.624
COPD	0 (0)	1 (7.1)	0.412
Lung cancer	0 (0)	1 (7.1)	0.412
Autoimmune diseases	1 (11.1)	3 (21.4)	0.524
APACHE II score	20.4±5.1	20.6±8.6	0.981
SOFA score	8.6±2.1	9.1±.5	0.587
Days from onset to icu admission	12.7 ± 7.4	12.8 ± 8.1	0.972
Days from onset to antibody detection	13.6±7.2	16.4±8.1	0.407
/lanagement, n (%)			
Corticosteroids	9 (100)	13 (92.9)	1.000
Dosage of Corticosteroids (mg)*	38±17	29±17	0.451
Tocilizumab	3 (33.3)	6 (42.9)	0.648
Invasive ventilation	9 (100)	14 (100)	1
Vasopressors	8 (88.9)	13 (92.9)	0.742
Renal replacement therapy	0 (0)	2 (14.3)	0.235
aboratory			
Ct value of ORF1ab	26.2±4.3	30.6±4.8	0.037
Ct value of N gene	26.5±4.5	30.5±4.8	0.063
hsCRP (mg/L)	35.2±32.8	105.4±88.4	0.034
B. IgM Titers of SARS-CoV-2 between T	wo Groups		
- 10 -	P<0.05	•	
SARS-COV-2 IgM titlers			

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 \pm 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 α 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_t* 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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