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LETTER TO THE EDITOR

Bacterial coinfections contribute to severe COVID-19 in winter

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Dear Editor,

Although most cases of COVID-19 caused by SARS-CoV-2 Omicron variants are mild or asymptomatic worldwide, coinfection with SARS-CoV-2 and other respiratory pathogens may still aggravate the severity of the illness.[1,2] The current literature indicates that coinfection with COVID-19 could occur in 3.70%–9.7% of patients.[1,3,4] The proportion of bacterial, and other respiratory viral coinfections may range from 3.02% to 9.7% and 5.41% to 6.61%, respectively. However, these studies demonstrated that coinfections with respiratory pathogens are not common. Thus, antibacterial therapy and diagnostic tests are considered to be unnecessary upon admission for most patients hospitalized with COVID-19.[3,5]

Starting from December 2022, a new wave of COVID-19 epidemic has escalated and spread quickly across China. However, data on the prevalence of coinfection with respiratory pathogens during this wave of Omicron BA.5.2/BF7 are limited. To better describe the rates of coinfection observed during this winter, a retrospective study of electronic medical and laboratory records of 545 SARS-CoV-2-positive patients was performed in the time frame from December 2022 to January 2023. Coinfection with respiratory pathogens was identified in 21.47% of patients ($n = 117$), including 20.18% ($n = 110$) with bacteria and 1.28% ($n = 7$) with other respiratory viruses (Fig. 1a). The proportion of SARS-CoV-2–bacterial coinfections was higher than that in current publications.[1,3,4] Among these bacterial coinfections ($n = 110$), 54 patients had monobacterial infections and 56 patients had multiple mixed bacterial infection. Although *Pseudomonas aeruginosa*, *Klebsiella spp*., and *Staphylococcus aureus* were the most common coinfection pathogens, we determined that a relatively high proportion of patients with COVID-19 initially presented with *Haemophilus influenza* ($n = 50$, 45.45%), *Staphylococcus aureus* ($n = 48$, 43.64%), and/or *Streptococcus pneumonia* ($n = 33$, 30%) coinfection (Fig. 1b). In contrast to most previous studies, our analysis indicates that other respiratory viral coinfections were infrequent ($n = 7$), and all of these SARS-CoV-2 patients were coinfected with only one respiratory virus (Fig. 1c).

Further analysis of the data was performed to confirm the proportion of severe COVID-19 in patients with SARS-CoV-2 monoinfections or SARS-CoV-2–bacterial coinfections. We noticed that bacterial infections were associated with increased COVID-19 severity in patients with SARS-CoV-2 (31.82% vs 16.59%, $\chi2 = 12.829$, $P = 0.000341$) (Fig. 1d). We also observed that none of these viral coinfection patients had severe symptoms.

In summary, during this wave of Omicron BA.5.2/BF7 infection in China this winter, among all the inpatients and outpatients, over 20% of patients with SARS-CoV-2 had bacterial coinfections. And more than half of them had multiple mixed bacterial infections. Moreover, more than 30% of patients with bacterial coinfections were diagnosed with severe COVID-19. Hence, bacterial coinfections should be considered as critical risk factors influencing the mobility and severity of COVID-19. Interestingly, Massey et al. reported that, among the symptomatic patients of COVID-19, much higher proportion of bacterial coinfection was observed (55.4% *Staphylococcus aureus*, 19.4% *Moraxella catarrhalis*, and/or 3.8% *Klebsiella pneumoniae*),[6] due to the fact that only symptomatic patients were represented in the sample. This phenomenon might support our findings from another perspective. In addition, the bacterial types in coinfected patients were confirmed to be different from those in other reports.[5,6] The proportion of coinfections in SARS-CoV-2-infected patients and the types of bacteria involved vary between our study and other reports, which may be attributed to the different seasons and regions of specimen collection. Therefore, based on our current data, we suggest that early respiratory microbiological diagnostic tests are necessary for patients with COVID-19 symptoms, which will help us to find appropriate infection control measures and administer the appropriate antibacterial treatments.

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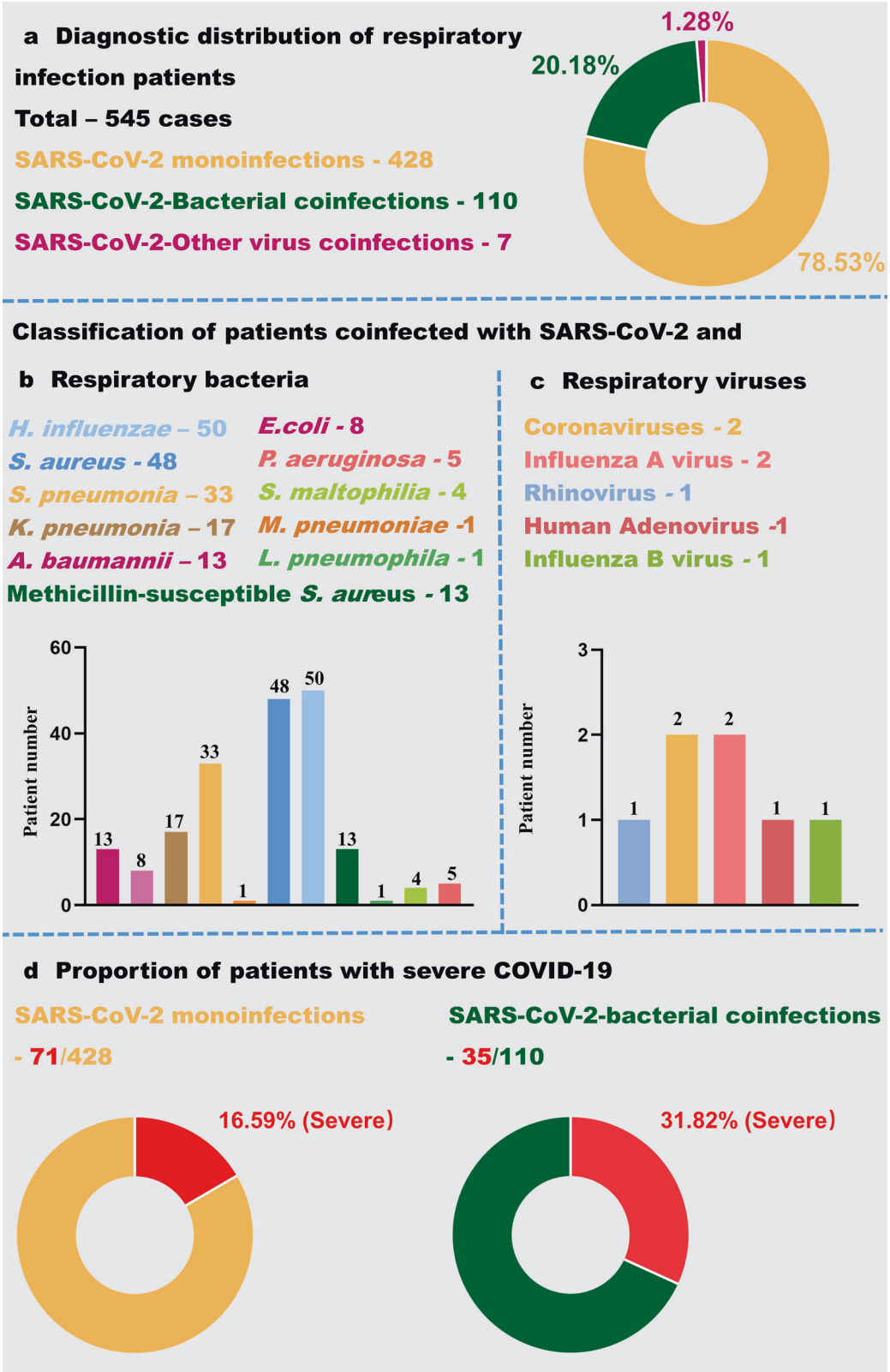

Fig. 1 Respiratory coinfections contribute to severe COVID-19. a Diagnostic distribution of respiratory infection patients with SARS-CoV-2 and other respiratory pathogens. Classification of patients coinfected with both SARS-COV-2 and (**b**) respiratory bacteria and (**c**) respiratory viruses. **d** Proportion of patients with severe COVID-19. A two-sided Pearson's χ^2 test or Fisher exact test was used to evaluate the differences between patients with SARS-CoV-2 monoinfections and those with SARS-CoV-2–bacterial coinfections. χ^2 test was used for those meeting the test conditions. $P < 0.05$ indicated statistically significant difference.

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AUTHOR CONTRIBUTIONS

K.L., Y.C., C.Z., H.F., and G.C. designed and supervised the study. L.Z., S.Yang, X.L., C.H., X.T., S.Q., S.Yu, Z.W., and M.G. performed and analyzed the experiments. C.Z., H.F., and G.C. recruited the COVID-19 individuals. L.Z., J.L., X.L., C.H., and S.Yang wrote the manuscript and all authors provide feedback.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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