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Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Letter to the Editor

Antimicrobial stewardship in non-COVID-19 patients with fever and respiratory symptoms in outpatient settings: Lessons from the "dynamic zero-COVID policy" in mainland China



Dear Editor, We read with great interest the study by Kwok et al. published in the Journal of Infection,¹ in which the authors compared the antibiotic use in general outpatient settings unrelated to COVID-19 between the pre-pandemic and peri-pandemic periods. The result was consistent with studies conducted in Canada,² and Israel,³ indicating a significant decrease in community antibiotic use during the pandemic of COVID-19, especially in patients with respiratory tract infections. Unlike previous studies, Kwok et al. attributed the decline of antibiotic use in Hong Kong to its antibiotic stewardship instead of the impact of COVID-19 itself, as the suppress and lift strategy was adopted in Hong Kong during the study period.⁴ However, with different epidemic sizes and intervention policies, the trend of antibiotic use in COVID-19 unrelated patients in outpatient settings might be different, as the authors mentioned.¹

In mainland China, the government adopted the "dynamic zero-COVID policy", which is entirely different from other countries, aiming to diagnose and isolate COVID-19 cases and close contacts as soon as possible, eventually minimizing confirmed cases in each outbreak. According to this policy, physicians were recommended to order a chest computed tomography (CT) in addition to SARS-CoV-2 PCR, C-reactive protein (CRP) and complete blood count (CBC) test in patients with fever and respiratory symptoms if no contraindications were documented. Therefore, there might be a significantly increased proportion of patients receiving CRP tests and chest CT scans. We hypothesized that these recommended interventions could help reduce antibiotic use in non-COVID-19 febrile patients with respiratory symptoms, as they offered comprehensive information to clinicians.

To test the hypothesis, we conducted a retrospective study in the Wuhu Hospital of East China Normal University by including two cohorts of patients with fever and respiratory symptoms that were both treated in the outpatient service, the pre-pandemic cohort (1st May 2019 to 31st October 2019) and the peri-pandemic cohort (1st May 2021 to 31st October 2021). Outcomes were the rate of antibiotic use in the included cohorts and corresponding factors associated with antibiotic use. The hospital's ethics committee approved the study (No. 2021–17).

There were 4589 non-COVID-19 patients included in the study, with 1972 patients in the peri-pandemic cohort and 2617 patients in the pre-pandemic cohort. The median age was 30 (IQR 23–46) years, of 54.2% were female. Compared with patients in the pre-pandemic cohort, those in the peri-pandemic cohort had a shorter duration of fever when they visited the outpatient service (1 [IQR

0.1–5] day vs 2 [IQR 1–3] days, $p < 0.001$). The rate of chest CT scan (893/45.3% vs 106/4.1%, $p < 0.001$), CPR test (1189/60.3% vs 5/0.2%, $p < 0.001$) and CBC test (1763/89.4% vs 1661/63.5%, $p < 0.001$) were significantly higher than those in the pre-pandemic cohort. The rate of antibiotic use in the peri-pandemic cohort was lower (1321/67% vs. 1913/73.1%, $p < 0.001$) than that of pre-pandemic cohort, and also with fewer patients received combination (152/11.5% vs. 461/24.3%, $p < 0.001$) and intravenous antibiotic therapy (746/37.8% vs. 1362/52%, $p < 0.001$). The majority (3305/84.6%) of the included patients received antibiotics in the "watch" category and presented a significantly increased trend from the pre-pandemic period to the peri-pandemic period (77.2% to 96.8%) (Table 1).

Multivariable logistic regression was performed to assess the impact of chest CT scan and CRP test on antibiotic use in patients with fever and respiratory symptoms. The results indicated that only the peri-pandemic period was associated with the decreased rate of antibiotic use (OR 0.76, 95% CI 0.64–0.92, $p = 0.004$). Neither the performance of the chest CT scan nor the CRP test affected the rate of antibiotic use. However, in terms of combination antibiotic therapy, apart from the peri-pandemic period (OR 0.67, 95% CI 0.51–0.88, $p = 0.004$), the CRP test (OR 0.33, 95% CI 0.23–0.46, $p = 0.000$) was also associated with the decreased use of combination antibiotic therapy (Table 2).

The present study demonstrated a 6.1% decline in antibiotic use in non-COVID-19 febrile patients with respiratory symptoms in outpatient service in the peri-pandemic cohort, consistent with recently published studies.^{1–3} As a city with only one COVID-19 case reported during the study period, the impact of the COVID-19 cases on the rate of antibiotic use can be ignored. Therefore, we sought to explain such reduction as the interventions implemented during the peri-pandemic period under the "dynamic zero-COVID-19 policy" in mainland China. Previous studies have demonstrated well that CRP tests and chest CT scans reduced the rate of antibiotic use in acute respiratory tract infections.^{5,6} Interestingly, apart from the peri-pandemic period in this study, both the chest CT scan and CRP test were not associated with the decreased rate of antibiotic use in patients with fever and respiratory symptoms. Therefore, reducing antibiotic use in the peri-pandemic cohort might be primarily explained as the increased awareness of viral pathogens through the education of COVID-19. Moreover, unlike the CRP test in the present study, receiving a chest CT scan did not change any patterns of antibiotic use, indicating that the purpose of the prescription of antibiotics in the included cohorts was for upper respiratory tract infections rather than the suspected pneumonia.

There had two significant limitations in the present study. First, we did not consider the decreased incidence of other virus infections during the peri-pandemic period,⁷ which might cause imbalance between the two cohorts and diminish the real impact of the

Table 1

Characteristics and management of patients with fever and respiratory symptoms in the pre-pandemic and peri-pandemic period.

Variable	Pre-pandemic cohort n = 2617	Peri-pandemic cohort n = 1972	p value
Age	30 [25–46]	29 [22–46]	< 0.001
Gender (Female)	1494 (57.1%)	995 (50.5%)	< 0.001
T max, °C	38.5 [38–39]	38.3 [37.8–38.77]	< 0.001
Duration of fever, days	2 [1–3]	1 [0.5–1]	< 0.001
Tested CBC	1661 (63.5%)	1763 (89.4%)	< 0.001
Tested CRP	5 (0.2%)	1189 (60.3%)	< 0.001
Performed chest CT	106 (4.1%)	893 (45.3%)	< 0.001
Received antibiotics	1913 (73.1%)	1321 (67%)	< 0.001
Received combination antibiotics	461 (24.3%)	152 (11.5%)	< 0.001
Received antibiotics intravenously	1362 (52%)	746 (37.8%)	< 0.001
Category of antibiotics			
Access	554 (22.8%)	47 (3.2%)	< 0.001
Watch	1876 (77.2%)	1429 (96.8%)	< 0.001

Table 2

Multivariable logistic regression analyzing factors associated with antibiotic use in patients with fever and respiratory symptoms in the pre-pandemic and peri-pandemic period.

	Odds ratio	95% CI	p value
Receiving antibiotics			
Age	1.00	0.99–1.00	0.934
Peri-pandemic period	0.76	0.64–0.92	0.004
Tested CRP	1.01	0.83–1.22	0.911
Performed chest CT	0.93	0.78–1.11	0.438
Receiving combination antibiotic therapy			
Age	1.01	1.00–1.01	0.001
Peri-pandemic period	0.67	0.51–0.88	0.004
Tested CRP	0.33	0.23–0.46	0.000
Performed chest CT	1.14	0.84–1.52	0.396

interventions on antibiotic use. Second, most included patients did not have a precise diagnosis, which limited us to assess the effects of the interventions on overall antibiotic use rather than the rate of unnecessary antibiotic therapy in both cohorts.

In conclusion, from the perspective of antimicrobial stewardship, only adding CRP test and chest CT scan on fever patients with respiratory symptoms cannot reduce the rate of antibiotic use in outpatient settings in mainland China. Future antimicrobial stewardship programs should focus on managing upper respiratory tract infections appropriately by improving the procedure of diagnosis and etiology confirmation.

Funding

The study was supported by the High-level Talents Fund of Wuhu Municipal Government (2021–134).

Authors' contribution

Design of Study and Conceptualization: Lei Zha and Lingling Pan. Data Collection: Zhichu Ren, Yi Zou, Shirong Li, and Gang Yang. Data analysis: Lei Zha and Qiancheng Xu. Original Draft Construction: Gang Yang and Zhichu Ren. Draft Review and Scientific Revisions: Lei Zha and Lingling Pan. Final draft approval: all authors.

Availability of data and materials

Data are available on request.

Ethics approval

The study was approved by the ethics committee of the Wuhu Hospital of East China Normal University (No. 2021–17).

Declaration of Competing Interest

None to declare.

Acknowledgments

None.

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