

Correspondence

Asthmatic patients in COVID-19 outbreak: Few cases despite many cases



To the Editor:

We read with great interest the article “Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan” by Li et al,¹ one of the most detailed studies in terms of patients’ clinical characterization.

Interestingly, the reported asthma prevalence among patients with coronavirus disease 2019 (COVID-19) admitted to hospital was 0.9%, extremely lower than in the general population (6.4%): this is clearly unexpected because bronchial inflammation is associated with an increased susceptibility to viral infections.² It has been hypothesized that in the case of COVID-19, inhaled corticosteroid treatment could modulate that susceptibility,³ although at the moment the relationship between COVID-19 and asthma remains unclear.⁴ In this context, asthma prevalence in the general population and the impact of COVID-19 outbreak in a specific area may condition the proportion of affected patients with asthma.⁵ Furthermore, asthma has been not specifically reported or investigated as a risk factor.⁵

We revised the COVID-19 cases (Table I) admitted in the period between March 1 and April 30, 2020, to 2 major hospitals placed in Verona (Veneto region) and Brescia (Lombardia region), in the North-east of Italy, one of the most affected areas in Europe.⁶ Verona and Brescia are neighboring cities, and Brescia has a greater population density. This last aspect may have conditioned the deeply different impact of COVID-19 infection in the 2 cities in terms of total amount of infected subjects and patients needing hospitalization.⁷ Surprisingly, we observed that the *weight* of hospital admission due to COVID-19 in patients with asthma (confirmed diagnosis by National Health System exemption code) is very similar in Verona and Brescia (1.96% and 1.92%, respectively), as well as the prevalence in the general population in the 2 areas (6%). According to the prescribed inhaled treatment, 5 of 6 patients with asthma from Verona suffered from moderate asthma; the other one, together with 15 of 20 from Brescia, was affected by mild asthma and all reported an optimal adherence rate. The other 5 cases in Brescia were affected by mild-intermittent asthma. None of the subjects reported asthma exacerbation before the admission to hospital. Mild obesity, presence of nonsevere cardiovascular diseases, and active smoking habit characterized 14 (70%) of 20 patients with asthma in Brescia

Hospital, whereas in Verona 3 (50%) of 6 patients were affected by hypertension and another one by obesity and diabetes. In Verona, no one was a current smoker.

Similarly to the Wuhan report,¹ our observation, the first in the Italian population, highlights that the hospitalization rate due to COVID-19 in patients with asthma is extremely low, and consistent with the asthma prevalence in the general population, more than with the *size* of the viral outbreak. This finding supports the unexpected hypothesis that asthma itself cannot be considered a risk factor for susceptibility to COVID-19. Which is the missing link?

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TABLE I. Data related to the COVID-19 outbreak in Verona and Brescia, up to April 30, 2020

Epidemiological and COVID-19 related features of the study population	Brescia	Verona
Population	198,536	257,993
Population density (people per km ²)	2,197.77	1,296.99
People tested by swabs	216,526 (Lombardia region)	196,864 (Veneto region)
People positive to SARS-CoV-2	12,861	4,679
Patients admitted because of COVID-19, n (%)	1,043 (8.1% of positive cases)	305 (6.5% of positive cases)
Patients with asthma among patients admitted because of COVID-19, n (%)	20 (1.92%) 12 F, 8 M	6 (1.96%) 3 F, 3 M
	Age range: 41-77 y (mean, 61.5 y)	Age range: 55-79 y (mean, 69.3 y)
Prevalence of asthma in the general population	6.1%	6.0%

F, Female; M, male; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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Reply



To the Editor:

The article by Marco et al¹ titled “Asthmatic patients in COVID-19 outbreak: few cases despite many cases” discusses the prevalence of asthma in patients with coronavirus disease 2019 (COVID-19) in the Northeast of Italy. The low prevalence of asthma in patients with COVID-19 in Italy¹ was consistent with what we observed in our study,² but was much lower than those from the United States³ and Dublin.⁴ The reasons behind the regional difference in the prevalence of asthma with COVID-19 are worth discussion.

We searched PubMed and Medline database for articles published up to May 20, 2020, using the keywords “SARS-COV-2,” “COVID-19,” and “asthma.” As shown in Table 1,¹⁻⁷ the prevalence of asthma with COVID-19 in each country was listed as well as the prevalence of asthma in the general population of the corresponding region.

The studies from China, Italy, and Mexico confirmed the lower rates of asthma patients with COVID-19 when compared with the prevalence of asthma in the corresponding general population (0.9%, 1.92%, and 3.6%, compared with 6.4%, 6.1%, and 5.0%, respectively).^{1,2,5} However, recent data released from New York and Dublin indicated the high rates of asthma in COVID-19, which were similar or a little higher than the prevalence of asthma in the general population (9.0% and 8.8%, compared with 10.1% and 7%, respectively).^{3,4} The other 2 small cohorts from France and Australia also manifested the high rates of comorbidity of asthma in pediatric patients with COVID-19.^{6,7}

The reasons for the regional differences may partially be attributed to the variety in the strictness of prevention and control measures, the public awareness of self-protection, and the detection strategy of SARS-COV-2. However, we also notice that the risk of patients with asthma to COVID-19 in the regions with a low prevalence of asthma seems lower than that in regions with a high prevalence of asthma. The recent study suggested that T_H2 cytokine may decrease the expression of angiotensin-converting enzyme 2 (ACE2) in epithelial cells, but increase another SARS-COV-2 entry protein transmembrane protease serine 2 (TMPRSS2) gene expression. The regulation on the expressions of ACE2 and TMPRSS2 in T_H2-high patients with asthma differed from that in T_H2-low patients with asthma. Therefore, we may speculate that the difference in phenotype and genotype of asthma may contribute to the differential regulation of ACE2 and TMPRSS2 and be partially responsible for the variety in susceptibility of patients with asthma to COVID-19 among different regions.

The other concern is the various clinical characteristics of patients with asthma in the different regions; for example, high body mass index in patients with asthma is more common in the United States than in China and Italy. Obesity is related to an increased risk of COVID-19. Obese patients are also prone to have hypertension, which is a predisposing factor for COVID-19.

TABLE 1. Regional differences in the prevalence of asthma in patients with COVID-19

Country	Percentage of asthma with COVID-19 (n/n)	Prevalence of asthma in the general population	References
China	0.9% (5/548)	6.4%	Li et al ²
Italy	1.92% (20/1043)	6.1%	Caminati et al ¹
Mexico	3.6% (270/7497)	5.0%	Solís et al ⁵
USA	9.0% (479/5700)	10.1%	Richardson et al ³
Ireland	8.8% (17/193)	7.0%	Butler et al ⁴
France	8.5% (3/35)	11%	Belhadj et al ⁶
Australia	25% (1/4)	13.9%	Ibrahim et al ⁷

The different comorbidities with patients with asthma may also be one of the reasons for the regional differences in the prevalence of asthma in COVID-19.

Asthma is a disease with marked heterogeneity. It would be intriguing to investigate and understand how the heterogeneity of asthma is attributable to the variability in susceptibility and clinical course of asthma with COVID-19.

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Global lockdown, pollution, and respiratory allergic diseases: Are we in or are we out?



To the Editor:

We have read with great interest the work by Navel et al¹ about the impact of the current coronavirus disease 2019