http://dx.doi.org/10.5588/ijtld.20.0608

LETTER

Impact of COVID-19 on patients with asthma

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Article submitted 7 August 2020. Final version accepted 24 August 2020.

Dear Editor,

Italy has been particularly affected by COVID-19, with over 253,118 cases and more than 35,418 deaths, and Lombardy (a region in North Italy) has the highest number of cases and deaths.[1] Because the airways and lung parenchyma are the main target of SARS-CoV-2, concern was raised regarding the outcome in patients with chronic respiratory diseases. In preliminary studies in China, asthma was underreported.[2] Subsequent data from Italy confirmed this; however, there have been contrasting data from other countries,[3–4] both in hospitalised patients and outpatients. Until now, asthma has been described as one of the comorbidities of COVID-19, but data regarding the prevalence of the disease in asthmatic patients are lacking.

We therefore conducted a survey to evaluate whether the virus affects patients with asthma. From 4 May to 21 May, a total of 122 patients with asthma, most of whom were referred to our Unit for disease management, were contacted over the phone by two independent researchers to assess the occurrence of COVID-19 and gather information regarding asthma control during the pandemic. Of the 122, 108 agreed to participate (see Table for patient characteristics). This study was approved by the institutional ethics committee of the Istituti Clinici Scientifici Maugeri, Pavia, Italy (2278 CE).

Most participants were female and never smokers with late onset asthma; half had severe asthma, mainly treated with monoclonal antibodies. Overall disease control, evaluated using an Asthma Control Test at the time of the survey, was good, with only 9.3% reporting one or more asthma exacerbations since the last visit. A subgroup of patients (55.6%) were evaluated at the time of the last visit for airway inflammation and more than half had eosinophilic airway inflammation. Almost all patients had received BCG, half had a flu vaccination and a quarter pneumococcal vaccination; 17.6% had all three. The median number of comorbidities was 2.5 (interquartile range 1-4), with cardiovascular diseases being the most common. During the pandemic, 40.7% patients experienced health problems, mainly cardiovascular and diabetes-related symptoms. Only one patient, a 57-year-old woman with severe asthma had COVID-19 confirmed with a positive test (0.9% of all the subjects, 1.6% of those with severe asthma). The patient reported asthenia, fever, migraine, arthralgia, anosmia, ageusia and dyspnoea, and was successfully treated at home by her general practitioner with hydroxychloroquine, azithromycin and methylprednisolone, and recovered in a month. Her asthma treatment before COVID-19 comprised high-dose inhaled corticosteroids (ICS) and long-acting beta-agonists (LABA). Another patient was tested for SARS-CoV-2 at onset of acute dyspnoea and cough, but with a negative result. Only one patient reported a SARS-CoV-2-infected relative. Two patients reported a change in inhalation therapy due to an increase in allergic symptoms. In Italy, in response to the COVID-19 pandemic, the government imposed a lockdown and movement of people was restricted. Three patients reported difficulties in accessing their asthma drugs during the lockdown period. Most of the subjects were retired, and among workers only a minority went out to work during the lockdown.

Asthma prevalence among hospitalised patients in Wuhan was low.[2] Other cohorts have reported a higher prevalence of patients with asthma: 25% of 19 consecutive COVID-19-positive deaths in a single hospital in Germany,[3] and 17% of all admitted COVID-19 patients in the USA, with higher prevalence (27%) among middle age subjects.[4] Among hospitalised patients with COVID-19 in Chicago, USA, 25.8% had asthma, and those younger than 65 years had a longer intubation time than patients without asthma. However, no indication regarding severity or asthma control was reported.[5] Chronic lung diseases (COPD, emphysema and asthma) were reported among the risk factors for COVID-19 with a high prevalence among hospitalised patients and ICU admissions.[4]

The prevalence of asthma in Italy is around 6.6%, and even for a small selected cohort, our data showed a low prevalence of COVID-19 in patients with asthma. It has been hypothesised that T2 inflammation, a characteristic of most patients with asthma, could counteract virus infection.[6] The majority of our patients were atopic, and most had an eosinophilic inflammatory pattern suggesting

a T2-driven disease. Angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) are SARS-Cov2 receptors. A low prevalence of COVID-19 in allergic patients with asthma could be due to a reduction in ACE2 gene expression, as occurred after a specific bronchial challenge.[7] ACE2 and TMPRSS2 are equally expressed in sputum cells of asthmatic and healthy individuals, with a higher expression in patients with asthma and diabetes.[8] Diabetes is one of the most common comorbidities in COVID-19 patients, but none of our patients with asthma as well as diabetes reported COVID-19 infection. Interestingly, independently from asthma mechanisms, ICS use was associated with lower expression of both SARS-CoV-2 receptors.[8] Furthermore, ICS can restore anti-viral capacity of immune cells of allergic people with asthma (usually defective for interferon production),[9] increasing their capacity to fight the virus.

Our respondents did not report an increase of asthma exacerbations during the survey period and their Asthma Control Test demonstrated good disease control. Alerts released by specialists, patient organisations and international societies advised patients with asthma to maintain adherence to their drugs, which may have increased patient compliance, favouring disease control and decreasing the risk of asthma exacerbation. The lockdown isolation may have also reduced pollen exposure in subjects sensitised to late winter/spring pollen, reducing airway inflammation and risk of exacerbations. Asthma exacerbations are often triggered by viral infections, particularly rhinovirus, which induces an increase in airway eosinophilic inflammation.[10] Patients infected by SARS-CoV-2 frequently presented a reduction in blood eosinophils,[2] not associated with a recruitment of eosinophils in the lung,[3] which could partly be responsible for the reduced capacity of the virus (compared to rhinovirus) to induce asthma exacerbations. Severe asthma has been indicated as a risk factor for COVID-19 mortality,[1] but only one of our patients with severe asthma reported COVID-19 and she was treated at home without severe respiratory complications.

As for the previous SARS-CoV, a positive association between air pollution and SARS-CoV-2 has been hypothesised.[11] Interviewed patients were living around Varese, Como and Milan areas, which have elevated air pollution levels and high COVID-19 incidence and prevalence. However, to date, no significant studies have presented data in support of this hypothesis. More than 80% had undergone BCG vaccination (as recommended in Italy for specific groups). BCG vaccination has been hypothesised to induce trained immunity that could increase monocyte ability to counteract infectious agents,[12] but there is no evidence to confirm this hypothesis.

In conclusion, our survey of a group of patients with asthma in Northern Italy demonstrated a low occurrence of SARS-CoV-2 infection and a low number of asthma exacerbations during this period. Most of the patients succeeded in following their asthma prescriptions despite the lockdown.

Conflicts of interest: none declared.

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Table. Characteristics of patients with asthma who responded to the survey

		n/N (%)
Baseline characteristics		
Age, years, median (range)		62 (19–85)
Male		37/108 (34.3)
Employed		45/108 (41.7)
Smoking history	Current	7/108 (6.5)
	Former	44/108 (40.7)
	Never	57/108 (52.8)
Asthma step (GINA)	Step 1	2/108 (1.9)
	Step 2	4/108 (3.7)
	Step 3	13/108 (12.0)
	Step 4	28/108 (25.9)
	Step 5	61/108 (56.5)
GINA Step 5 treatment	Azithromycin	2/108 (1.9)
	Monoclonal antibody	38/108 (35.2)
	Oral corticosteroids	18/108 (16.7)
FEV_1, l/s, median [IQR] Please provide unit. Added in legend		2.2 [1.6-3.0]
FEV_1 %, median [IQR]		86.0 [71.8-103]
FEV_1/FVC, median [IQR]		70.7 [64.3-78.1]
Induced sputum		62/108 (57.4)
Eosinophilic/neutrophilic/mixed-/pauci-granulocitic pattern, %		56.4/16.1/16.1/11.2
Atopy		67/108 (62.0)
Age of asthma onset, years, median [IQR]		43 [28-54]
Comorbidities	Cardiovascular disease	59/108 (54.6)
	Nasal polyposis	38/108 (35.2)
	Rhinitis	38/108 (35.2)
	Obstructive sleep apnoea	37/108 (34.3)
	Obesity	28/108 (25.9)
	Skeletal and muscular disease	27/108 (25.0)
	Gastroesophageal reflux	26/108 (24.1)
	Diabetes	16/108 (14.8)
	Anxiety and depression	10/108 (9.3)
	Kidney disease	4/108 (3.7)

Glaucoma	4/108 (3.7)
Oncological disease	4/108 (3.7)
BCG vaccination	88/108 (81.5)
Flu vaccination	55/108 (50.1)
Pneumococcal vaccination	26/108 (24.1)
History of previous TB	2/108 (1.9)
Results	
COVID-19 infection	1/108 (0.9)
Workers during the pandemic	12/108 (11.1)
Contact with COVID-19-positive relatives	1/108 (0.9)
Continuation of inhaled therapy for asthma	98/108 (90.7)
Change in inhalation therapy during the pandemic	2/108 (1.8)
Difficulty in obtaining inhaled therapy for asthma	3/108 (2.8)
Asthma exacerbations since the last control	10/108 (9.3)
Time elapsed since the last control, months, median [IQR]	100 [16.3-197.5]
Health problems during the pandemic	44/108 (40.7)
ACT score, median [IQR]	24 [21-25]

GINA = global initiative for asthma; FEV_1 = forced expiratory volume in first second; l/s= Litre/second; IQR = interquartile range; FVC = forced vital capacity; BCG = bacille Calmette-Guérin; ACT = Asthma Control Test.