# Prevalence and influence of COVID19 in asthma control and lung function in severe asthma patients under biological treatment

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**Palabras clave:** Asma, COVID19, Tratamiento biológico, Función pulmonar, Control.

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) targets the respiratory system through binding with angiotensin-converting enzyme 2 (ACE2) receptors in the alveolar epithelium [1, 2]. It is hypothesized that allergic sensitization in asthma is linked to lower expression of ACE2 receptors in upper and lower respiratory airways, suggesting a protective effect [3]. Inhaled corticosteroids might yield a protective effect against the coronavirus disease 2019 (COVID-19) [4]. There is controversial evidence about the impact of asthma and its medication on the clinical course of COVID-19 [5] and little information about pulmonary function and control after COVID-19 in asthmatics. The aim of our retrospective study was to determine the prevalence and severity of COVID-19 in severe asthma [6] adult patients under biological treatment (*bt*) followed at a multidisciplinary severe asthma unit in a tertiary hospital (homogeneous sample) and to evaluate if there was any difference in the allergic phenotype. Pulmonary function test (PFT) and asthma control before and after COVID-19 were analyzed. After approval of the local ethics committee and informed consent signature, data was obtained from electronic medical records from March to December 2020. SPSS Statistics V25 program was used. Quantitative parameters were expressed as median, minimum and maximum values (*mmv*) and qualitative parameters as frequencies and percentage.

132 patients were included with a median age of 55 years old (*yo*) (17-87); 66% female. 43% current or former smokers with a median pack-year index (*pyi*) of 13 and a median body mass index (BMI) of 28 kg/m$^2$ (19-49). Comorbidities: hypertension (34%), diabetes mellitus (15%), gastroesophageal reflux (54%), sleep apnea hypopnea syndrome (22%), bronchiectasis (32%), alpha-1 antitrypsin deficiency (8%), chronic rhinosinusitis with polyposis (39%), aspirin intolerance (29%) and bronchopulmonary aspergillosis (8%). 17 patients (13%) had cardiovascular diseases, being the most frequent arrhythmias (7) and cardiomyopathies (5). All asthmatics were T2 phenotype [6]: 67 (51%) eosinophilic, 22 (17%) allergic and 43 (32%) eosinophilic and allergic. *BT*: 51 omalizumab (38.6%), 43 (32.6%) mepolizumab, 29 (22%) benralizumab, 3 (2.2%) reslizumab, 4 (3%) dupilumab, 1 (0.8%) omalizumab + mepolizumab and 1 (0.8%) omalizumab + benralizumab. 10 patients (8%) were corticodependent. Spirometric values (median [*mmv*]): forced vital capacity (FVC) 2980 milliliters (ml) (1330-6530), %FVC 98% (48-155), forced expiratory volume in the first second (FEV1) 2040ml (880-5420), %FEV1 79% (28-159), %FEV1/FVC 68% (39-91). Asthma Control Test (ACT) score (median [*mmv*]): 20 (6-25).

Among the 132 patients, 19 (14.39%) had COVID-19 (9 eosinophilic, 4 allergic and 6 eosinophilic and allergic) with compatible symptoms. *BT*: 10 mepolizumab, 4 benralizumab and 5 omalizumab. Only 1 patient was corticodependent. COVID-19 diagnosis was confirmed by 6 real-time polymerase chain reaction tests (Cobas 6800 SARS-COV-2 [Roche] and TaqPath COVID-19 kit [Thermo Fisher Scientific]), 2 antigenic tests (Panbio™ COVID-19 [Abbot Diagnostic]) and 3 antibody tests (Chemiluminescent micro-particle immunoassay for qualitative detection of immunoglobulin [Ig] G against SARS-CoV-2. Abbott Laboratories). The

 
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remaining cases (8) were diagnosed based on clinical, radiological and/or analytical evaluation considering the pandemic epidemiological context between March and May 2020 [7] with a negative post-disease (≥ 4 months) IgG against SARS-CoV-2 determination. Duration of antibody rises is unknown and there is insufficient data to estimate sensitivity of antibodies tests beyond 35 days post-symptom onset [8].

COVID-19 patients median age was 56*yo* (23-67), 58% female, 63% current or former smokers with a median *pyi* of 14.5 and a median BMI of 28.23 kg/m$^2$ (22-49). Six of them (31.58%) required hospital admission, 4 pneumonias and 2 infections without pneumonia (admitted to have a closer follow up because of comorbidities). The remaining cases were managed as outpatients, 11 infections and 2 pneumonias without acute respiratory failure (*arf*) who signed their voluntary discharge. Five (83%) hospital-admitted patients versus (vs) 9 (69%) outpatients had a BMI > 25 kg/m$^2$. Five (83%) hospital-admitted patients vs 13 (100%) outpatients had ≥ 1 comorbidities. Among the 6 hospitalized patients, 2 had *arf* treated with supplemental oxygen (*sO2*), 5 required systemic corticosteroid (SC) and only one received remdesivir. No acute respiratory distress syndrome (ARDS), admission to intensive care unit (ICU), neither deaths were reported. Among the 13 outpatients, only 3 (23%, all infections) were treated with SC.

Ten COVID-19 patients (15.38%) had an allergic profile of whom 4 (40%) required hospital admission (3 pneumonias, 1 infection). The remaining 6 outpatients had infection. Among hospital-admitted patients, 2 had *arf* treated with *sO2*, 3 required SC and only one received remdesivir. No ARDS, admission to ICU, neither deaths were reported.

Our results showed a COVID-19 prevalence of 14.39% of whom 31.58% required hospital admission. Rial et al [7] reported a prevalence of 6.4% (with 22.9% hospitalized) and Eger et al [9] of 1.4% (with 77.8% hospitalized) in adult severe asthma patients under *bt*. Probably, our study showed a greater COVID-19 prevalence due to area location differences and a longer follow-up period (10 months versus 4 months [7] and +/- 6 weeks [9]).

Although the theoretical protective effect of allergic sensitization [3], COVID-19 prevalence in our patients with allergic profile (15.38%) was similar to global population.

Eger et al [9] considered ≥ 1 comorbidities and obesity risk factors for severe COVID-19 [9]. However, our results would not support that ≥ 1 comorbidities predisposed for severe COVID-19 (100% outpatients vs 83% *hap*) while a BMI > 25 kg/m$^2$ (69% outpatients vs 83% *hap*) could be a hallmark of a more severe disease.

After COVID-19, we found a better ACT score but no differences in PFT (Table 1). A better ACT score after COVID-19 could be explained by an improvement in treatment adherence (probably due to fear to exacerbations), hygienic care, mask use and social lockdown.

Our study has the limitations of being retrospective and the small sample size so it was not possible to make comparisons between different sub-phenotypes and *bt*. However, to our knowledge, this is the first report to analyze the COVID-19 prevalence according to the allergic phenotype and to explore PFT and asthma control after COVID-19.

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Table 1. Pulmonary function test and asthma control test score before and after COVID-19 in all population included and in severe asthma patients with an allergic profile.

| Parameter | All population included | | Asthmatics with an allergic profile | |
|---|---|---|---|---|
| | Pre – COVID-19 Median (min-max) | Post – COVID-19 Median (min-max) | Pre – COVID-19 Median (min-max) | Post – COVID-19 Median (min-max) |
| FVC (ml) | 3120 (2280-5290) | 3280 (2090-5110) | 3120 (2400-4360) | 3265 (2090-4700) |
| FVC% | 99 (71-122) | 108 (62-126) | 100 (71-120) | 103 (62-126) |
| FEV1 (ml) | 2370 (1130-3480) | 2530 (1080-3570) | 2395 (1180-3410) | 2575 (1090-3570) |
| FEV1% | 88 (44-110) | 88 (41-116) | 89 (44-110) | 94 (41-116) |
| FEV1/FVC | 70 (48-86) | 72 (39-86) | 77.61 (48-86) | 78 (52-86) |
| ACT | 19 (8-25) | 22 (8-25) | 19 (8-25) | 22 (8-24) |

ACT: asthma control test, COVID-19: coronavirus disease 2019, FEV1: forced expiratory volume in the first second, FVC: forced vital capacity, max: maximum, min: minimum, ml: milliliters.





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