The Impact Of COVID-19 on Asthma Control and Lung Function in Patients with Severe Asthma

Impacto do COVID-19 no Controlo da Asma e da Função Pulmonar em Doentes com Asma Grave.

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ABSTRACT

INTRODUCTION: Severe asthma affects approximately 4%-5% of asthmatic patients and increases susceptibility to respiratory infections, including SARS-CoV-2. The impact of COVID-19 on severe asthma remains unclear.

We aimed to evaluate the effects of SARS-CoV-2 infection on asthma control, quality of life, and lung function.

METHODS: A retrospective study of 114 severe asthma patients followed in our severe asthma unit from March 2020 to July 2022. We compared pre- and post-COVID-19 scores of the Asthma Control Test (ACT), Control of Allergic Rhinitis and Asthma Test (CARAT), Mini Asthma Quality of Life Questionnaire (mini-AQLQ) and lung function. Statistical analysis was performed using SPSS 25 (p <0.05).

RESULTS: Among 49 infected patients, ACT scores significantly decreased (p = 0.002). CARAT, mini-AQLQ, and lung function showed no significant differences.

CONCLUSION: SARS-CoV-2 infection negatively impacted asthma control, with a significant decrease in ACT scores. Further studies are needed to clarify long-term effects.

KEYWORDS: Antibodies, Monoclonal, Humanized; Asthma; Biological Products; COVID-19; SARS-CoV-2

RESUMO

INTRODUÇÃO: A asma grave afeta aproximadamente 4%-5% dos doentes asmáticos, aumentando a suscetibilidade a infeções respiratórias, nomeadamente ao SARS-CoV-2. No entanto, o impacto da COVID-19 na asma grave não está bem estabelecido.

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O nosso objetivo foi avaliar o impacto da infeção SARS-CoV-2 no controlo da asma, na qualidade de vida e na função pulmonar.

MÉTODOS: Estudo retrospetivo que incluiu 114 doentes com asma grave seguidos na nossa consulta de Imunoalergologia entre março de 2020 e julho de 2022. Compararam-se os valores pré e pós-COVID-19 do *Asthma Control Test* (ACT), Control of Allergic Rhinitis and Asthma Test (CARAT), *Mini Asthma Quality of Life Questionnaire* (mini-AQLQ) e da função pulmonar. A análise estatística foi realizada com SPSS 25 (p <0,05 significativo).

RESULTADOS: Dos 49 doentes infetados por SARS-CoV-2, verificou-se uma diminuição significativa dos valores de ACT (p = 0,002). O CARAT, o mini-AQLQ e a função pulmonar não apresentaram diferenças significativas.

CONCLUSÃO: Este estudo demonstrou que a infeção por SARS-CoV-2 teve um impacto negativo no controlo da asma, com uma diminuição significativa nos valores de ACT. No entanto, são necessários mais estudos para estabelecer os possíveis efeitos a longo prazo.

PALAVRAS-CHAVE: Anticorpos Monoclonais Humanizados; Asma; Biológicos; COVID-19; SARS-CoV-2

INTRODUCTION

Almost 4%-5% of the asthmatic patients are classified as having the severe asthma phenotype. The main goals of asthma management are symptom control and reduction of exacerbations, achieved through both maintenance and reliever treatments. Asthma also accounts for nearly 50% of the total costs associated with the disease and is frequently linked to various comorbidities. Patients with poor baseline disease control are more susceptible to exacerbations triggered by respiratory infections, including viral infections. In maintenance therapy, adherence and correct inhaler techniques are crucial for therapeutic success. Patients with poor baseline control are predisposed to the occurrence of exacerbations due to respiratory infections.[1]

Asthma evaluation questionnaires are simple, fast and low-cost instruments to accurately assess compliance with asthma treatment, including disease control and impact on quality of life. These tools provide, with good reproducibility and responsiveness, cut-off values to identify, among other factors, uncontrolled asthma and its impact on quality of life.[2-4]

Depending on its severity, SARS-CoV-2 infection can negatively affect the control of chronic diseases. Regarding asthma, data on the impact of COVID-19 in patients with severe asthma remain limited. The association between asthma and COVID-19 is inconsistent.[5] Current literature suggests that the prevalence of asthma among patients hospitalized with COVID-19 is similar to that observed in the general population. Additionally, different asthma endotypes are associated with varying clinical outcomes, with the T2-inflammatory profile appearing to have a protective effect.[6]

Regarding severe asthma and COVID-19 correlation, studies are scarce; however, it seems like severe Asthma is not an independent risk factor for mortality and severity of SARS-CoV-2 infection. Also, biological therapy does not seem to increase disease severity.[7,8] However, patients with poor disease baseline control have an increased risk of developing severe disease.

Recent evidence suggests that the lungs are the primary organ affected by COVID-19. These findings raise concerns about the evaluation of lung injury for discharged patients.[9]

We aim to investigate the effects of COVID-19 on Asthma control, quality of life and lung function.

MATERIAL AND METHODS

The retrospective study included 114 patients followed in our allergology outpatient clinic. We reviewed clinical files from March 2020 to July 2022, and compared Asthma Control Test (ACT), Control of Allergic Rhinitis and Asthma (CARAT) and Mini Asthma Quality of Life Questionnaire (mini-AQLQ) before and after COVID-19. Lung function was also assessed and compared pre- and post-COVID-19. Disease severity was classified based on hospitalization, need for oxygen therapy, or systemic corticosteroids. SPSS 25 for Windows was used to do statistical analysis. Non-parametric tests (sign test) were conducted with a significance level set at $p < 0.05$.

We analyzed the following variables: demographic characteristics, Asthma control test (ACT), Control of Allergic Rhinitis and Asthma Test (CARAT), SARS-CoV-2 infection, lung function (FEV1: Forced expiratory volume during 1st second; FVC: forced vital capacity; FEV1/FVC: Tiffeneau index; MEF: maximum expiratory flow; RV: residual volume; TLC: total lung capacity; DLCO: diffusing capacity of the lungs for carbon monoxide; FeNO: fractional exhaled nitric oxide)

DISCUSSION

In our department, 114 patients with severe asthma are under follow-up, the majority

of whom are female (r (n = 81.71%), median age 58 years old (min. 15 years old, max. 84 years old). Forty--nine out of 114 patients had SARS-CoV-2 infection, 35 of them were female, median age of 58 years (Figs. 1 and 2).

Of the 49 infected patients with SARS-CoV-2, 47 were under monoclonal antibody therapy: 25 was under omalizumab, 14 under mepolizumab, 5 under benralizumab and 3 under dupilumab. Additionally, 43% of these patients self-administered their treatment at home (n = 20) (Fig. 3).

Towards disease severity, 27 out of 49 patients were classified as having mild disease, 20 patients were classified as having moderate disease and 2 patients were classified has having severe disease. Disease severity was assessed accordingly Portuguese national health authority norm: 1) mild disease: mild symptoms without evidence of pneumonia or hypoxemia; 2) moderate disease: fever 3 or more days, dyspnea but SpO2≥ 90 % without supplemental oxygen therapy, without hemodynamic instability; 3) severe disease: pneumonia; SpO2<90% without supplemental oxygen therapy, hemodynamic instability[10] (Fig. 4).

We did not find any relationship between disease severity and gender (*p*-value 0.480): female (18 mild, moderate 16, severe 1); male gender (mild 9, moderate 4, severe 1) (Fig. 5).

We also investigated whether there was any relationship between disease severity and the type of biologic (eosinophil depleting or not) as eosinopenia has been reported to be present in patients with COVID-19.[11] To investigate this, we divided the patients into two groups: anti-IL5 monoclonal antibodies (mepolizumab/benralizumab) *versus* non-anti-IL 5 monoclonal antibodies (omalizumab/dupilumab). No statistically significant relationship was found between disease severity and type of monoclonal antibody (*p* = 0.372).

Asthma's control was assessed using ACT and CARAT, while quality of life was evaluated using the Mini-A-QLQ. The median ACT score before COVID-19 was 22 points, compared to 20 points after COVID-19 (*p*-value

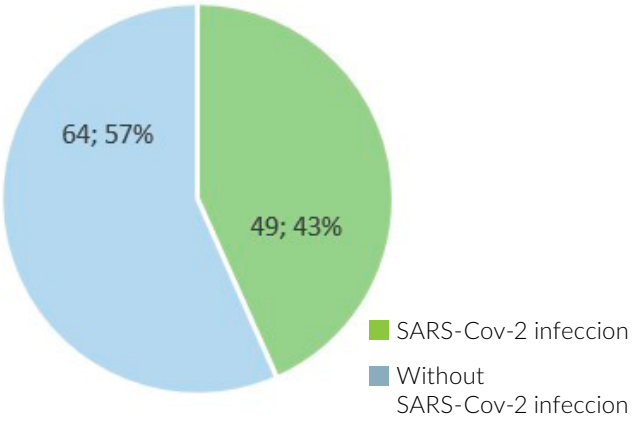

FIGURE 1. SARS-CoV-2 infectione coronal).

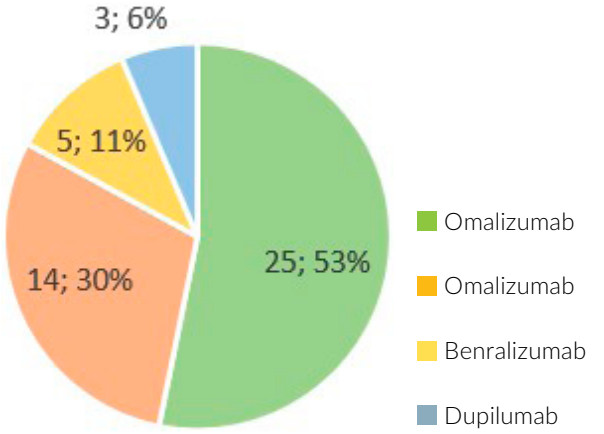

FIGURE 3. Gender distribuction in patiens with COVID-19

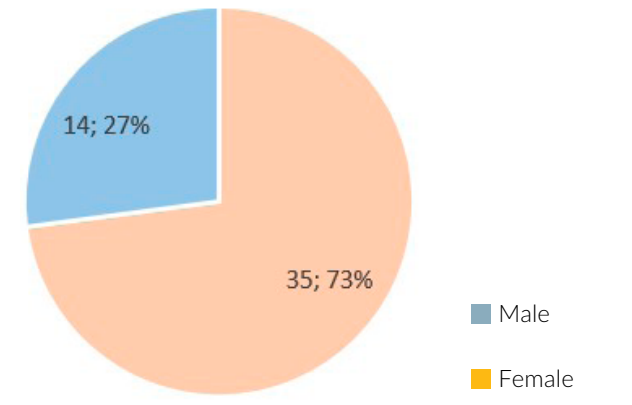

FIGURE 2. Gender distribuction in patiens with COVID-19

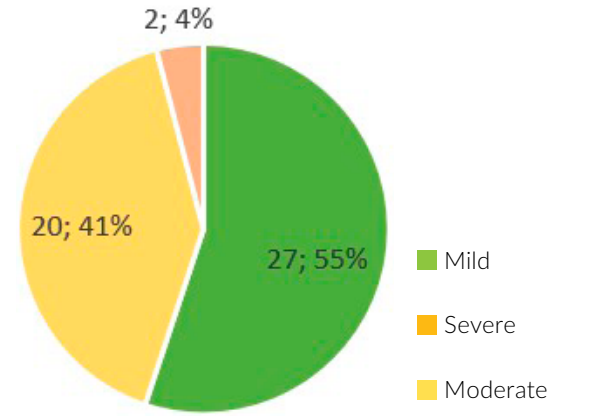

FIGURE 4. Disease severity (COVID-19)

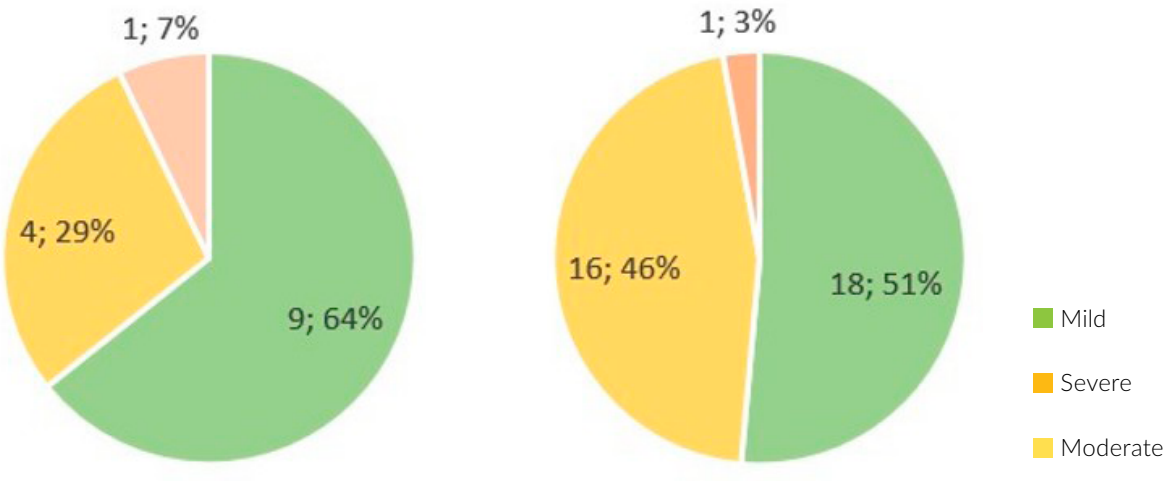

FIGURE 5. Disease severity. A- disease severity male gender; B- disease severity female gende

0.002). The Control of Allergic Rhinitis and Asthma Test (CARAT) was also assessed pre- and post-COVID-19; the median CARAT score before COVID-19 was 21 points, and 19 points after COVID-19 (p-value 0.054). We also did not find a statistically significant difference (*p*-value 0.949) between mini-AQLQ before[5,6] and after COVID-19 median score (5.0) (Table 1).

Regarding lung function, pulmonary function tests were only available for 21 of the 49 patients with SARS-CoV-2 infection. No statistically significant difference was found in lung function values before and after COVID-19 (Table 1).

FeNO value seems to increase after COVID-19, however, at the time of this study,

there were insufficient data to establish a relationship. Additionally, FeNO values were unavailable for most patients due to hospital limitations, which prevented comparisons with current values. In the future, we hope to gather more data to draw definitive conclusions.

As of the date of data analysis, only 2 patients had been reinfected with SARS-CoV-2; therefore, only the presence of an infection was considered, with the first infection being analyzed in these cases. In the future, it would be interesting to complete this analysis with the missing lung function values to determine if there are any statistically significant changes. It would be helpful to understand the impact of SARS-CoV-2 reinfection on both asthma control and lung function.

CONCLUSION

SARS-COV-2 infection was found to negatively impact asthma's control and quality of life, as evidenced by a decrease in ACT, CARAT and mini-AQLQ scores. However, the difference was only statistically significant for the ACT.

TABLE 1. Evaluated variables before and after covid-19. A- lung function; B- Patient reported outcomes

Lung function test variables	Median before COVID-19	Median after COVID-19	*p*-value
FEV1 (L)	1.81	2.02	1
FEV1 %	80	80	0.383
FVC (L)	2.2	3.13	0.664
FVC%	104	104	0.503
FEV1/FVC	63.16	64.65	1
MEF (L/s)	1.01	1.03	1
MEF %	33	34	1
RV(L)	2.28	2.21	0.664
RV%	125.5	119	0.503
TLC (L)	5.48	5.39	1
TLC %	109	108	1
DLCO (mL/min/mmHg)	7.95	6.81	0.219
DLCO %	93.64	94.3	1
FeNO (ppb)	11	22.5	N/A

Patient Reported outcomes	before COVID-19	after COVID-19	*p*-value
ACT	22	20	0.002
CARAT	21	19	0.054
Mini-AQLQ	5.6	5	0.949

Regarding lung function, no significant changes were observed between the variables assessed before and after COVID-19. It is important to note that only half of the patients underwent lung function testing after COVID-19, and conclusions may vary due to missing data. Additionally, beyond measures to prevent exposure to SARS-CoV-2 and vaccination, adherence to and optimization of maintenance therapy are crucial for ensuring effective asthma control. Further studies with a larger sample size, including patients without a severe

asthma phenotype, are needed to gain a deeper understanding of this potential correlation."

CONTRIBUTORSHIP STATEMENT/ DECLARAÇÃO DE CONTRIBUIÇÃO

MG, JS - Conceptualization, formal analysis, research, methodology, visualisation, writing the original draft, revision and editing.

SM, AC, ARP - Formal analysis, research, methodology, visualisation, writing the original draft, revision and editing.

AM, CL - Resources, Supervision, revision and editing.

All the authors approved the final version to be published.

MG, JS - Conceptualização, análise formal, investigação, metodologia, visualização, redação do rascunho original, revisão e edição.

SM, AC, ARP - Análise formal, investigação, metodologia, visualização, redação do rascunho original, revisão e edição.

AM, CL - Recursos, Supervisão, revisão e edição.

Todos os autores aprovaram a versão final a ser publicada

RESPONSABILIDADES ÉTICAS

CONFLITOS DE INTERESSE: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

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PROTECTION OF HUMAN AND ANIMAL SUBJECTS: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2024).

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