

# Safety of Biologicals In Severe Asthma Patients Having COVID-19

Öner Özdemir<sup>1</sup>

<sup>1</sup>Sakarya Il Saglik Mudurlugu

February 6, 2023

## Safety of Biologicals In Severe Asthma Patients Having COVID-19

*Running title:* COVID-19, biologicals and severe asthma

Öner Özdemir<sup>1</sup>

<sup>1</sup> Division of Allergy and Immunology, Department of Pediatrics, Research and Training Hospital of Sakarya University Medical Faculty, Adapazarı, Sakarya, Türkiye.

**Correspondence:** Öner Özdemir, MD

Division of Allergy and Immunology Department of Pediatrics Faculty of Medicine, Sakarya University Research and Training Hospital of Sakarya University Adnan Menderes Cad., Sağlık Sok., No: 195 Adapazarı, Sakarya, Turkey. Tel: + 90-(264) -444 54 00 Fax: +90-(264) -275 91 92 E-mail: ozdemir\_oner@hotmail.com

### To the editor;

We have read the article titled ‘Safety of biologics in severe asthmatic patients with SARS-CoV-2 infection: A prospective study’ by Sara Manti et al. with great interest.<sup>1</sup> Since the literature data on the use of biologics in children are scarce, this study is very valuable. Although the results of this study on biologicals are somewhat consistent with the current literature, I have several questions/concerns about their experience with these patients.

In this study,<sup>1</sup> there are 21 patients (10 on therapy with omalizumab, 9 with dupilumab, and 2 with mepolizumab). Twenty out of 21 patients had a mild COVID-19 course, and no adverse outcome was observed. In this cohort of severe asthmatics treated with biologics,<sup>1</sup> hospitalization rate and/or poor outcome of SARS-CoV-2 cases and their COVID-19 course was found much lower and less severe when compared with other severe asthma registries (e.g. Dutch and Belgian Severe Asthma Registry (BSAR), etc.) reported as >65%.<sup>2-4</sup> How do the authors explain this discrepancy? It is not clear in the article.<sup>1</sup> May the effects of varying lockdown processes, different comorbidities, younger study groups, the doses of biologics, and utilization period of biologicals used in this study population also have a role?

Also, a detailed classification of the clinical spectrum of SARS-CoV-2 infection is given. Nevertheless, they do not mention how severe asthmatics are decided in the study. I could not be sure that it is classified according to the GINA or / other international guidelines. As far as I understand from the manuscript, a confirmed diagnosis of severe asthma seemed to be based on receiving therapy with one biological drug (monotherapy or in addition to nonbiologic therapy). Moreover, the authors, unfortunately, say that their ‘study design could appear as inappropriate therapeutic management of patients with severe asthma and SARS-CoV-2 infection’, according to the national guidelines. It is very hard to comprehend what exactly they mean.

Comorbidity of cystic fibrosis (71.45%) was detected in 15/21 of their patients.<sup>1</sup> This is a too-high ratio. Are their study group real cystic fibrosis patient groups rather than severe asthma patients? In normal circumstances, severe asthma patients do not have as much high comorbidity as cystic fibrosis. In the literature, poor outcomes (e.g., the risk for hospitalization or intubation) were also reported after SARS-CoV-2 infection in severe asthma patients on biologic therapy was associated with one or more comorbidity. Interestingly, there are no poor outcomes for such high comorbidity in their patients. How do the authors explain this contradiction?

Also, as a reader and pediatric allergists, we need to know these severe asthmatic patients' other laboratory and clinical parameters such as the use of inhaled corticosteroids as well as their type of asthma, e.g. eosinophilic or not, including total IgE, skin prick tests, specific IgE results. As mentioned in the article,<sup>1</sup> type 2 inflammation is usually known to control the expression of angiotensin-converting enzyme 2 (ACE2) receptor in human bronchial cells and affects the COVID-19 outcome. In the table of the article,<sup>1</sup> it is shown that the number of users of inhaled bronchodilators is 11/21 patients, and inhaled steroids is 9/21 patients. According to the international asthma guidelines (e.g. GINA, ATS, etc.), how a patient uses a biological product without taking even (high dose) inhaled corticosteroids?

As expected, treatment with biologics was not found to be associated with an increased risk of SARS-CoV-2 infection as well as exacerbation of asthma in their study group. However, a recent review of case reports and original articles by Poddighe et al.<sup>5</sup> showed that the rate of contracting SARS-CoV-2 infection in mepolizumab patients was more than in omalizumab. In this study, is there any difference in omalizumab and mepolizumab patients contracting SARS-CoV-2 infection? Additionally, in another study about biologics, among the 26 patients experiencing COVID-19 disease, most (16/26) had been receiving mepolizumab. Mepolizumab patients were mainly less allergic but more eosinopenic together with other risk factors/comorbidities.<sup>2</sup> Indeed, various cohorts showed that non-allergic asthma patients had a greater risk of SARS-CoV-2 test positivity than allergic asthma patients.<sup>6</sup>

Moreover, some studies indicate that high doses of inhaled corticosteroids and the chronic use of oral corticosteroids might be associated with a predisposition to COVID-19 and poor outcomes.<sup>7</sup> Is this one of the reasons that the authors did not see any poor outcomes in their patients?

I think that if these points are delineated, this valuable article would be more understandable and helpful to readers as well as to the literature.

**References** 1. Manti S, Giallongo A, Pecora G, Parisi GF, Papale M, Mulè E, Aloisio D, Rotolo N, Leonardi S. Safety of biologics in severe asthmatic patients with SARS-CoV-2 infection: A prospective study. *Pediatr Pulmonol.* 2023 Jan 2. doi: 10.1002/ppul.26298. Epub ahead of print. PMID: 36593591. 2. Papaioannou AI, Fouka E, Tzanakis N, Antoniou K, Samitas K, Zervas E, et al. SARS-CoV-2 infection in severe asthma patients treated with biologics. *J Allergy Clin Immunol Pract.* 2022; S2213-2198(22)00611-0. doi: 10.1016/j.jaip.2022.05.041.

3. Eger K, Hashimoto S, Braunstahl GJ, Brinke AT, Patberg KW, Beukert A, et al. Poor outcome of SARS-CoV-2 infection in patients with severe asthma on biologic therapy. *Respir Med.* 2020;177:106287. doi: 10.1016/j.rmed.2020.106287. 4. Hanon S, Brusselle G, Deschamphelire M, et al. COVID-19 and biologics in severe asthma: data from the Belgian severe asthma registry. *Eur Respir J.* 2020;56:2002857. 5. Poddighe D, Kovzel E. Impact of Anti-Type 2 Inflammation Biologic Therapy on COVID-19 Clinical Course and Outcome. *J Inflamm Res.* 2021;14:6845-6853. doi: 10.2147/JIR.S345665. 6. Yang JM, Koh HY, Moon SY, Yoo IK, Ha EK, You S, et al. Allergic disorders and susceptibility to and severity of COVID-19: a nationwide cohort study. *J Allergy Clin Immunol.* 2020;146(4):790–8. 7. Kong-Cardoso B, Ribeiro A, Aguiar R, Pité H, Morais-Almeida M. Understanding and Managing Severe Asthma in the Context of COVID-19. *Immunotargets Ther.* 2021; 10:419-430. doi: 10.2147/ITT.S342636.