Review Article

The Association between Allergic Rhinitis and COVID-19: A Systematic Review and Meta-Analysis

Cong Xu,1,2,3 He Zhao,1,2,3 Yuwan Song,2,3 Jiamin Zhou,2,3 Ting Wu,2,3 Jingjing Qiu,2,3 Junxin Wang,2,3,4 Xicheng Song,2,3 and Yan Sun2,3

1The Second Medical College of Binzhou Medical University, Yantai 264000, Shandong, China
2Department of Otorhinolaryngology and Head and Neck Surgery, Yuhuangding Hospital Affiliated to Qingdao University, Yantai 264000, Shandong, China
3Shandong Provincial Clinical Research Center for Otorhinolaryngologic Diseases, Yantai 264000, Shandong, China
4Weifang Medical University, Weifang, Shandong, China

Correspondence should be addressed to Xicheng Song; drxchsong@163.com and Yan Sun; entsunyan@126.com

Received 16 June 2022; Revised 6 August 2022; Accepted 12 September 2022; Published 28 September 2022

Academic Editor: Dimitri Poddighe

Copyright © 2022 Cong Xu et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Objective. Previous studies have yielded conflicting results regarding the association of coronavirus disease 2019 (COVID-19) with allergic rhinitis (AR). Data on AR prevalence in COVID-19 patients are limited. Consequently, whether AR is a harmful or protective factor for COVID-19 patients remains controversial. Therefore, we analyzed the relationship between COVID-19 and AR. Methods. We systematically searched PubMed, Embase, Cochrane, and Web of Science databases for studies published between January 1, 2020 and January 11, 2022. We included studies reporting the epidemiological and clinical characteristics of COVID-19 and its incidence in patients with AR. We excluded letters, case reports, literature review articles, non-English language articles, and non-full-text articles. The raw data from these studies were pooled into a meta-analysis. Results. We analyzed the results of nine studies. The prevalence of AR in patients with COVID-19 was 0.13 (95% confidence interval [CI] 0.04–0.25), with an overall I² of 99.77%, P ≤ 0.0001. COVID-19 patients with AR are less prone to severe disease (odds ratio [OR] = 0.79, 95% CI, 0.52–1.18, P ≤ 0.0001) and hospitalization (OR = 0.23, 95% CI, 0.02–2.67, P ≤ 0.0001) than patients without AR. Conclusion. Our data suggest that allergic rhinitis is a protective factor in patients with COVID-19.

1. Introduction

In December 2019, a novel coronavirus disease (COVID-19) emerged in Wuhan, China, and spread rapidly, leading the World Health Organization (WHO) to declare a pandemic for the first time in over 10 years. COVID-19 is a highly contagious and sometimes fatal disease, causing over 435 million cases to date [1]. COVID-19 leads to high utilization of medical resources that include nucleic acid testing, hospitalization, and intensive care. Determining which clinical factors place patients at high or low risk for severe COVID-19 is of great significance and can aid clinical decision-making [2]. Allergic rhinitis (AR) is a common chronic disease and often occurs in conjunction with combined airway disease, with an incidence of about 16.7% [3]. Whether AR acts as an independent risk factor for COVID-19 infection, severity, and hospitalization remains controversial [4].

Limited evidence suggests that AR exerts a protective effect against COVID-19 infection [4] and may reduce its severity [5]. On the contrary, a national cohort study in Korea showed that AR increased COVID-19 susceptibility and severity [4]. It has also been argued that AR is COVID-19 susceptibility and severity [6]. Chhiba et al. [7] reported that AR was not associated with an increased risk of hospitalization in patients with COVID-19.

Consequent to the conflicting findings of the aforementioned report, the objective of this study was to evaluate whether AR is a significant risk factor for COVID-19 infection, severity, and hospitalization. Such a determination...
may indicate the value of a history of AR as a prognostic indicator to facilitate clinical decision-making.

2. Methods

2.1. Search Strategy and Selection Criteria. In this meta-analysis, we searched PubMed, Embase, Cochrane Library, and Web of Science databases for articles published from January 1, 2020 to January 11, 2022. The electronic search was conducted using the strategy as follows: (1) “COVID-19”, OR “SARS-CoV-2,” OR “coronavirus disease 2019”; and (2) “allergic rhinitis”, OR “rhinitis” OR “allergy” OR “atopic”. Additional articles were retrieved by screening the list of references included in the study. The literature search was limited to articles published in English. Studies investigating the epidemiological and clinical features of COVID-19 were eligible.

2.2. Exclusion Criteria. Three reviewers (Cong Xu, He Zhao, and Yuwan Song) excluded studies that did not describe AR and COVID-19; studies that did not evaluate potential epidemiologic relationships between AR and COVID-19, studies that explored associations between COVID-19 and allergic diseases (AR and asthma as a composite variable); and studies that assessed the relationship between COVID-19 and one symptom of AR (e.g., sneezing). Letters, case reports, literature review articles, non-English language and non-full-text articles (e.g., editorials or congressional summaries) were excluded. EndNote (version X9.0) was used to manage records and exclude duplicate records.

2.3. Data Extraction. Three reviewers (Cong Xu, He Zhao, and Yuwan Song) independently screened the titles and abstracts of potential studies. Conflicts were resolved through discussion. We then independently read full-text articles to identify studies that met the inclusion criteria and carefully reviewed the reference lists from all identified studies and reviews for inclusion. For each study, the following data were extracted: the name of the first author; the country in which the study was conducted; cohort size; numbers of participants in severe and nonsymptoms disease groups; and numbers of participants in the inpatient and noninpatient illness groups.

The quality of studies in each was evaluated using the Newcastle-Ottawa Scale (NOS) by three reviewers (Cong Xu, He Zhao, and Yuwan Song). A total score of ≥7 indicated a high-quality study, whereas a total score of <7 was considered a low-quality study. Five factors (risk of bias, imprecision, inconsistency, indirectness, and publication bias) may cause a rating of the quality of evidence [8].

We conducted a meta-analysis on the prevalence rate of allergic rhinitis in patients with COVID-19 and calculated the combined prevalence rate with a 95% confidence interval (CI). The odds ratio (OR) was used to describe the relationship between the number of critically ill patients and inpatients with COVID-19 (dependent variable) and antecedent AR (independent variable). Due to heterogeneity within and between studies, we used a random effects model to estimate AR prevalence and calculated pooled ORs using Stata data and the Review Manager (version 5.3) tools analysis tool. The random effects model was used to estimate the mean effect and its accuracy, as it would provide a conservative estimate of the 95% CI. We used forest plots to represent the data and tested for between-study heterogeneity using the $I^2$ statistic and $I^2$ values >50% to indicate significant heterogeneity. We defined severe COVID-19 as cases requiring mechanical ventilation, vital life support, requiring intensive care unit admission, or ending in death. Funnel plots were used to assess publication bias.

3. Results

The initial search yielded 2178 potentially relevant papers, of which 1110 duplicates, 87 reviews, 297 animal experiments, and seven meta-analyses were excluded in the first screening of titles and abstracts. A total of 666 articles were excluded after the title and abstract screening. 16 papers met the inclusion criteria. After a more careful full-text review, seven additional papers were excluded for having incomplete data. Consequently, nine studies were included (Figure 1).

The nine studies included a total of 294,622 patients. Two studies were from the USA, two were from China, one from Turkey, one from Britain, one from Iran, and one from South Korea. The controls were patients without AR. In terms of study design, two articles (Jianjun Ren and Amirhossein Darabi) were prospective cohort studies, and the others were retrospective observational studies (Table 1). Two (22.2%) articles each had total NOS scores of 6, 8, and 9 and three (33.3%) articles had a score of 7 (Table 2). In addition, these studies have excluded the effects of comorbidities, especially respiratory.

3.1. Prevalence of Allergic Rhinitis in Confirmed COVID-19 Cases. The nine studies included 3,341 patients with AR, and the authors reported a total of 27,196 COVID-19 cases. The combined prevalence of AR in COVID-19 patients was 0.13 (95% CI, 0.04–0.25) (Figure 2). There was a high level of heterogeneity among the included case series ($I^2 = 99.77%$; $P ≤ 0.00001$) (Figure 3).

3.2. Disease Severity and Hospitalization Rates among COVID-19 Patients with and without AR. COVID-19 cases were classified as severe or nonsymptoms in only four of the nine studies. Reports on four studies involving 2,484 patients with AR contained COVID-19 data. Only three of the nine articles (involving 1,906 patients with AR) detailed the number of patients hospitalized. The meta-analysis showed that patients with AR have a lower risk of severe COVID-19 than COVID-19 patients without AR (odds ratio [OR] = 0.79, 95% CI, 0.52–1.18, $P = 0.25$), which had less heterogeneity ($I^2 = 53%$; $P = 0.1$) (Figures 4 and 5). Moreover, patients hospitalized for COVID-19 were 0.23 times less likely to have comorbid AR (OR = 0.23, 95% CI, 0.02–2.67, $P = 0.24$) (Figures 6 and 7). There was a high degree of heterogeneity ($I^2 = 99%$; $P < 0.00001$).
2178 potentially relevant articles were identified by searching databases
- Pubmed (n = 619)
- Embase (n = 714)
- Cochrane (n = 129)
- Web of science (n = 716)

Duplicates (n = 1110)

1068 records after duplicates removed
- Reviews (n = 81)
- Meta-analysis (n = 7)
- Animal trial (n = 297)

683 records screened after reviews, meta-analysis and animal trial removed

Records excluded after title and abstract screening (n = 667)

16 Full-text articles assessed for eligibility

Full-text articles were excluded (n = 7)

Studies included (n = 9)

Figure 1: Flow diagram of study identification.

Table 1: Summary of findings table.

| Study             | Country       | Sample size | COVID-19 severe symptoms | COVID-19 hospitalization |
|-------------------|---------------|-------------|--------------------------|--------------------------|
|                   |               |             | AR | Non-AR |                   | AR | Non-AR |
| Jee et al. [9]    | China         | 219,959     | 103 (257) | 2073 (4352) |                |    |        |
| Hai et al. [6]    | China         | 1172        | 16 (119)   | 99 (973)     | 115 (1172)    | 1057 (1172) |
| Amirhossein D et al. [5] | Iran       | 400         | 5 (64)     | 63 (336)     | 5 (64)        | 59 (336)   |
| Ali [1]           | Turkey        | 250         | 21 (35)    | 104 (215)    | 68 (138)      | 57 (112)   |
| Jianjun et al. [4]| China         | 70557       | —           | —            | 126 (4915)    | 419 (10775) |
| Hui et al. [10]   | China         | 182         | —           | —            | —             | —          |
| Tuğba, Aksu. [11]| Ankara, Turkey| 235         | —           | —            | —             | —          |
| Anjeni et al. [2] | USA           | 2013        | —           | —            | —             | —          |
| Foster et al. [12]| USA           | 1013        | —           | —            | —             | —          |

Table 2: Newcastle-Ottawa Scale scores for the included articles.

| Study             | Selection | Comparability | Outcome | Total scores |
|-------------------|-----------|---------------|---------|--------------|
| Jee et al. [9]    | ★★★★★    | ★★            | ★★★★    | 9            |
| Hai et al. [6]    | ★★★★☆     | ★★            | ★★★★    | 7            |
| Amirhossein et al. [5] | ★★★★☆ | ★★            | ★★★★    | 7            |
| Ali [1]           | ★★★★☆     | ★★            | ★★★★    | 9            |
| Jianjun et al. [4]| ★★★★★    | ★★            | ★★★★    | 8            |
| Hui et al. [10]   | ★★★★☆     | ★★            | ★★★★    | 7            |
| Tuğba, Aksu. [11]| ★★★★☆     | ★★            | ★★★★    | 6            |
| Anjeni et al. [2] | ★★★★☆     | ★★            | ★★★★    | 8            |
| Foster et al. [12]| ★★★★☆     | ★★            | ★★★★    | 6            |
Figure 2: Meta-analysis of AR in COVID-19 cases of stay forest plot.

Figure 3: Meta-analysis of AR in COVID-19 cases of stay funnel plot.
4. Discussion

Our pooled analysis of published studies to date indicates that AR is considered comorbidity associated with reducing severity and hospitalization rates for COVID-19 patients. The nasal cavity expression of ACE2 is abundant in patients with COVID-19 and acts as the cellular receptor that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) uses to enter host cells [13]. Furthermore, SARS-CoV-2 dissemination also relies on the cellular serine protease TMPRSS2, which is also essential for the transmission of several clinically relevant viruses that include other beta-coronaviruses and the influenza A virus [14–17]. Kimura et al. [18] demonstrated that TMPRSS2 was elevated...
in the nasal and airway epithelial cells of AR patients, suggesting that AR patients are more susceptible to infection. Hoffmann et al. showed that host cell entry of SARS-CoV-2 can be partially blocked by a clinically proven inhibitor of TMPRSS2, which is employed by SARS-CoV-2 for S protein priming [14, 19]. However, according to the report, ACE2 plays a critical role in the development of COVID-19 and consequent lung injury [14, 20]. Some case studies have identified risk factors for serious illness, such as age, gender, hypertension, and diabetes, which can reduce ACE2 expression in vivo [21–24]. Nasal epithelial cells from participants with AR demonstrate lower ACE2 expression than healthy individuals [6, 18]. Cat allergens can significantly reduce ACE2 mRNA expression in nasal brush samples from adult patients with AR caused by cat hypersensitivity. ACE2 gene expression was decreased in nasal and bronchial epithelial cells of AR patients, which reduces susceptibility to infection [6, 18]. Taken together, the results of these studies may provide a convincing physiological explanation of our finding that allergic rhinitis is a protective factor in patients with COVID-19.

Some studies suggest that AR drugs protect against the development of severe COVID-19 and patients taking these drugs are no more prone to SARS-CoV-2 infection [25–27]. This may be one reason that patients with AR and COVID-19 have milder pneumonia symptoms.

Histamine H1 receptor (H1 receptor) antagonists have immediate effects on sneezing and sniffle, which are used widely in the treatment of AR. Recently, many studies have shown that H1 receptor antagonists have direct antiviral activity against SARS-CoV-2 by interfering with the early steps of viral replication or by binding ACE2 [25, 28–30]. Patients taking these drugs had a significantly lower risk of SARS-CoV-2 infection [31]. In addition, treatment with H1 receptor antagonists and azithromycin prevented deterioration of lung inflammation in elderly patients with SARS-CoV-2 infection [32].

Montelukast, a cysteinyl leukotriene 1 receptor antagonist, may act as an antiviral agent by modulating innate and adaptive immunity [33]. It reduces mucus secretion from respiratory glands, affects lymphocyte activation and differentiation, and blocks the expression of inflammatory proteins in the lung by inhibiting type-2 T-helper (Th2) cytokines [interleukin (IL)-4, IL-5, and IL-13], especially in eosinophils [34, 35]. Levocetirizine, a third-generation antihistamine, and montelukast exhibit remarkable synergistic anti-inflammatory activity across a spectrum of signaling proteins, cell adhesion molecules, and leucocytes and eosinophil and neutrophil quantity and migration, which may prevent the progression of the disease from mild to moderate to severe and reduce both morbidity and mortality [36].

Th2 cytokine inhibitors reduce AR symptoms by inhibiting the production of Th2 cytokines, which are critically important in the pathogenesis of AR [37]. Poddighe and Kovzel considered that patients with COVID-19 taking such agents (omalizumab, anti–IL-5 biologics, and dupilumab) had milder or even no symptoms [38]. This finding is supported only by case reports and series; further studies, including those with case-control designs, are needed.

As with any meta-analysis, our study is susceptible to the limitations of the original studies, which may include design bias, selection bias, and residual confounding [39]. Due to these limitations, it is almost impossible to determine whether there were comorbidities other than allergic rhinitis in the COVID-19 patients. Advanced age, cardiovascular disease, and diabetes are associated with increased COVID-19 severity [23, 24]. In a systematic review of the nine articles, we found that only five had a positive comparison of outcomes between AR and non-AR patients. The results of our meta-analysis were heterogeneous in terms of sensitivity analysis, and a detailed analysis of forest plots showed that none of the included studies reported statistically significant differences between the two groups.
5. Conclusions
Our results suggest that COVID-19 incidence, severity, and risk of hospitalization are reduced in patients with AR. These findings strongly suggest that AR can be regarded as a protective factor and prognostic indicator in patients with COVID-19. This association may enhance our understanding of COVID-19 pathogenesis and provide a novel indicator for clinical decision support. Larger studies are needed to confirm these findings.

Data Availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest
The authors declare that they have no conflicts of interest.

Authors’ Contributions
Xicheng Song and Yan Sun conceived and designed this study. Cong Xu, He Zhao, and Yuwan Song defined the search strategy and performed the literature search and also contributed to the writing of the manuscript. Jiamin Zhou, Wu Ting, Jingjing Qiu, and Junxin Wang assessed the significance and feasibility of the article and reviewed and revised the manuscript according to the editorial board’s comments. All of the authors read and approved the final version of this paper. Cong Xu, He Zhao and Yuwan Song contributed equally to this work.

References
[1] A. Guvey, “How does allergic rhinitis impact the severity of COVID-19?: a case-control study,” European Archives of Oto-Rhino-Laryngology, vol. 278, no. 11, pp. 4367–4371, 2021.
[2] A. Keswani, K. Dhana, J. A. Rosenthal, D. Moore, and M. Mahdavinia, “Atopy is predictive of a decreased need for hospitalization for coronavirus disease 2019,” Annals of Allergy, Asthma, & Immunology, vol. 125, no. 4, pp. 479–481, 2020.
[3] M. D. Seidman, R. K. Gurgel, S. Y. Lin et al., “Clinical practice guideline: allergic rhinitis,” Otolaryngology - Head and Neck Surgery, vol. 152, pp. S1–S43, 2015.
[4] J. Ren, W. Pang, Y. Luo et al., “Impact of allergic rhinitis and asthma on COVID-19 infection, hospitalization, and mortality,” Journal of Allergy and Clinical Immunology: In Practice, vol. 10, no. 1, pp. 124–133, 2022.
[5] A. Darabi, M. Delghanfard, S. Jozan et al., “Investigating the association between allergic diseases and COVID-19 in 400 Iranian patients,” Allergologia et Immunopathologia, vol. 49, no. 5, pp. 9–15, 2021.
[6] H. Wang, J. Song, Y. Yao et al., “Angiotensin-converting enzyme II expression and its implication in the association between COVID-19 and allergic rhinitis,” Allergy, vol. 76, no. 3, pp. 906–910, 2021.
[7] K. D. Chhiba, G. B. Patel, T. H. T. Vu et al., “Prevalence and characterization of asthma in hospitalized and nonhospitalized patients with COVID-19,” The Journal of Allergy and Clinical Immunology, vol. 146, no. 2, 2020.
[8] G. Guyatt, A. D. Oxman, E. A. Akili et al., “GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables,” Journal of Clinical Epidemiology, vol. 64, no. 4, pp. 383–394, 2011.
[9] J. M. Yang, H. Y. Koh, S. Y. Moon et al., “Allergic disorders and susceptibility to and severity of COVID-19: a nationwide cohort study,” The Journal of Allergy and Clinical Immunology, vol. 146, no. 4, pp. 790–798, 2020.
[10] H. Du, X. Dong, J. J. Zhang et al., “Clinical characteristics of 182 pediatric COVID-19 patients with different severities and allergic status,” Allergy, vol. 76, no. 2, pp. 510–532, 2021.
[11] T. Naziroglu and K. Aksu, “Rare atopy in COVID-19 patients or COVID-19 famine in atopic patients?” Dermatologic Therapy, vol. 34, no. 1, Article ID e14581, 2021.
[12] K. J. Foster, E. Jauregui, B. Tajudeen, F. Bishehsari, and M. Mahdavinia, “Smell loss is a prognostic factor for lower severity of coronavirus disease 2019,” Annals of Allergy, Asthma, and Immunology, vol. 125, no. 4, pp. 481–483, 2020.
[13] A. C. Walls, Y. J. Park, M. A. Tortorici, A. Wall, A. T. McGuire, and D. Veesler, “Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein,” Cell, vol. 183, no. 6, p. 1735, 2020.
[14] M. Hoffmann, H. Kleine-Weber, S. Schroeder et al., “SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor,” Cell, vol. 181, no. 2, 2020.
[15] X. Y. Ge, J. L. Li, X. L. Yang et al., “Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor,” Nature, vol. 503, no. 7477, pp. 535–538, 2013.
[16] I. Glowacka, S. Bertram, M. A. Muller et al., “Evidence that TMPRSS2 activates the severe acute respiratory syndrome coronavirus spike protein for membrane fusion and reduces viral control by the humoral immune response,” Journal of Virology, vol. 85, no. 9, pp. 4122–4134, 2011.
[17] N. Iwata-Yoshikawa, T. Okamura, Y. Shimizu, H. Hasegawa, M. Takeda, and N. Nagata, “TMPRSS2 contributes to virus spread and immunopathology in the airways of murine models after coronavirus infection,” Journal of Virology, vol. 93, no. 6, 2019.
[18] H. Kimura, D. Francisco, M. Conway et al., “Type 2 inflammation modulates ACE2 and TMPRSS2 in airway epithelial cells,” The Journal of Allergy and Clinical Immunology, vol. 146, no. 1, p. 80, 2020.
[19] M. Kawase, K. Shirato, L. van der Hoek, F. Taguchi, and S. Matsuyama, “Simultaneous treatment of human bronchial epithelial cells with serine and cysteine protease inhibitors prevents severe acute respiratory syndrome coronavirus entry,” Journal of Virology, vol. 86, no. 12, pp. 6537–6545, 2012.
[20] J. Song, M. Zeng, H. Wang et al., “Distinct effects of asthma and COPD comorbidity on disease expression and outcome in patients with COVID-19,” Allergy, vol. 76, no. 2, pp. 483–496, 2021.
[21] W. J. Guan, Z. Y. Ni, Y. Hu et al., “Clinical characteristics of coronavirus disease 2019 in China,” New England Journal of Medicine, vol. 382, no. 18, pp. 1708–1720, 2020.
[22] A. Fernandez-Atucha, A. Izagirre, A. B. Fraile-Bermudez et al., “Sex differences in the aging pattern of renin-angiotensin system serum peptidases,” Biology of Sex Differences, vol. 8, no. 1, p. 5, 2017.
[23] Y. Li, W. Zhou, L. Yang, and R. You, “Physiological and pathological regulation of ACE2, the SARS-CoV-2 receptor,” Pharmacological Research, vol. 157, Article ID 104833, 2020.
[24] C. Wu, X. Chen, Y. Cai et al., “Risk factors associated with acute respiratory distress syndrome and death in patients with COVID-19,” The Journal of Allergy and Clinical Immunology, vol. 146, no. 2, 2020.
coronavirus disease 2019 pneumonia in Wuhan, China,” 
*JAMA Internal Medicine*, vol. 180, no. 7, pp. 934–943, 2020.

[25] L. R. Reznikov, M. H. Norris, R. Vashisht et al., “Identification of antiviral antihistamines for COVID-19 repurposing,” *Biochemical and Biophysical Research Communications*, vol. 538, pp. 173–179, 2021.

[26] M. Lommatzsch, P. Stoll, and J. C. Virchow, “COVID-19 in a patient with severe asthma treated with Omalizumab,” *Allergy*, vol. 75, no. 10, pp. 2705–2708, 2020.

[27] D. C. Copertino, R. R. R. Duarte, T. R. Powell, M. Mulder Rougvie, and D. F. Nixon, “Montelukast drug activity and potential against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),” *Journal of Medical Virology*, vol. 93, no. 1, pp. 187–189, 2021.

[28] B. Ellinger, D. Bojkova, A. Zaliani et al., “A SARS-CoV-2 cytopathicity dataset generated by high-content screening of a large drug repurposing collection,” *Scientific Data*, vol. 8, no. 1, p. 70, 2021.

[29] Y. Hou, S. Ge, X. Li, C. Wang, H. He, and L. He, “Testing of the inhibitory effects of loratadine and desloratadine on SARS-CoV-2 spike pseudotyped virus viropexis,” *Chemico-Biological Interactions*, vol. 338, Article ID 109420, 2021.

[30] S. Ge, X. Wang, Y. Hou, Y. Lv, C. Wang, and H. He, “Repositioning of histamine H1 receptor antagonist: doxepin inhibits viropexis of SARS-CoV-2 Spike pseudovirus by blocking ACE2,” *European Journal of Pharmacology*, vol. 896, Article ID 173897, 2021.

[31] A. Vila-Corcoles, O. Ochoa-Gondar, E. M. Satue-Gracia et al., “Influence of prior comorbidities and chronic medications use on the risk of COVID-19 in adults: a population-based cohort study in Tarragona, Spain,” *BMJ Open*, vol. 10, no. 12, Article ID e041577, 2020.

[32] J. I. Morán Blanco, J. A. Alvarenga Bonilla, S. Homma, K. Suzuki, P. Fremont-Smith, and K. Villar Gomez de Las Heras, “Antihistamines and azithromycin as a treatment for COVID-19 on primary health care—a retrospective observational study in elderly patients,” *Pulmonary Pharmacology & Therapeutics*, vol. 67, Article ID 101989, 2021.

[33] C. Fidan and A. Aydogdu, “As a potential treatment of COVID-19: Montelukast,” *Medical Hypotheses*, vol. 142, Article ID 109828, 2020.

[34] A. Y. Wu, S. C. Chik, A. W. Chan, Z. Li, K. W. Tsang, and W. Li, “Anti-inflammatory effects of high-dose montelukast in an animal model of acute asthma,” *Clinical and Experimental Allergy*, vol. 33, no. 3, pp. 359–366, 2003.

[35] X. Qu, Y. Chen, and C. Yin, “Effect of montelukast on the expression of CD4(+)CD25(+) regulatory T cells in children with acute bronchial asthma,” *Experimental and Therapeutic Medicine*, vol. 16, no. 3, pp. 2381–2386, 2018.

[36] B. C. May and K. H. Gallivan, “Levocetirizine and montelukast in the COVID-19 treatment paradigm,” *International Immunopharmacology*, vol. 103, Article ID 108412, 2022.

[37] N. T. Orban, M. R. Jacobson, K. T. Nouri-Aria, S. R. Durham, and A. O. Eifan, “Repetitive nasal allergen challenge in allergic rhinitis: priming and Th2-type inflammation but no evidence of remodelling,” *Clinical and Experimental Allergy*, vol. 51, no. 2, pp. 329–338, 2021.

[38] D. Poddighe and E. Kovzel, “Impact of anti-type 2 inflammation biologic therapy on COVID-19 clinical course and outcome,” *Journal of Inflammation Research*, vol. 14, pp. 6845–6853, 2021.

[39] Y. Wang, G. Ao, X. Qi, and B. Xie, “The association between COVID-19 and asthma: a systematic review and meta-analysis,” *Clinical and Experimental Allergy*, vol. 50, no. 11, pp. 1274–1277, 2020.