
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

patient with lip dermatitis, received their second vaccination, with no recurrence of symptoms.

Two patients had symptoms consistent with anaphylaxis (within 30 minutes, developed hives, flushing, shortness of breath, feeling of impending doom) after dose 1. Neither received epinephrine. Both underwent successful desensitization procedures for their second dose (Table 1, footnote d).[2] Of the patients with a history of anaphylaxis unrelated to the vaccine, 18 received their second dose. Seven of them had symptoms, with 2 patients having hives and 5 with subjective shortness of breath or itching. None required epinephrine.

Twenty-two patients had subjective symptoms including shortness of breath, palpitations, feeling warm, or throat tightness after dose 1; 10 had a previous history of unrelated anaphylaxis. Because of the unclear symptom causation, the initial 6 patients were observed by an allergist for their second dose by means of either a graded vaccine challenge (10% and 90%) or direct challenge, and no patients had a reaction. The rest were instructed to get their second dose normally with no additional observation. Overall, 18 received their second dose. Eight (44%) had a recurrence of symptoms, but all were deemed to be less severe than the initial symptoms with no resultant anaphylaxis.

Subjective neurologic complaints of dizziness, vision changes, numbness, or tingling of mouth or extremities occurred in 10 patients after dose 1. The median onset was 30 minutes (range 15 minutes to 5 days) and duration of 14 hours (range 45 minutes to several weeks), with all symptoms resolved. Seven received their second dose and only 1 had a recurrence of symptoms. One patient with a history of COVID-19 infection causing loss of smell and taste had symptom recurrence after the initial Pfizer vaccine; it was recommended this patient not receive a second dose. One patient with a history of hyperemesis gravidarum had a recurrence of repetitive vomiting the day of the first dose, but no recurrence with the second.

All 51 patients (77.3%) tolerated the second dose and none had what would be considered dose-limiting symptoms that would preclude future vaccine administration. No severe reactions or new cases of anaphylaxis were observed. Patients with nonanaphylactic reactions after dose 1, but with symptoms concerning immunoglobulin E (IgE)–mediated reactions including hives and angioedema, successfully received their second dose without preceding skin testing for risk stratification. The 2 patients with anaphylaxis tolerated their second dose with a graded-dose protocol. Neurologic and gastrointestinal symptoms were also mild and temporary. Our experience does not support extensive skin testing to aid in the decision to give a second dose to patients with mild to moderate symptoms, similar to what others have found.[8–10] The mechanisms of these reactions are unknown, although immediate reactions may be related to non-IgE–mediated mechanisms, whereas delayed symptoms may be owing to vaccine-induced immune response. This presents an opportunity for shared decision-making when discussing the second dose of mRNA vaccine in a patient who had a reaction to the first dose.

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# Atopic comorbidity has no impact on severity and course of Coronavirus disease 2019 (COVID-19) in adult patients



In the beginning of the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, chronic airway diseases were discussed to be risk factors for a severe outcome of COVID-19, as epithelial barrier dysfunction in allergic rhinitis or asthma was suspected to increase susceptibility for SARS-CoV-2 infection, potentially leading to increased symptoms or prolonged recovery.[1,2]

This was based on previous investigations revealing pollen exposure can decrease immune defense against respiratory viruses.[3,4] Moreover, high airborne pollen concentrations were correlated with increased SARS-CoV-2 infection rates, whereas pollen or particulate matter was not found to serve as transmitters for viral particles.[4,5] Studies have revealed that $T_H2$-dominated diseases are associated with lower viral defense mechanisms owing to a reduced antiviral interferon response, altogether increasing the susceptibility for respiratory viral infections or even systemic infections in patients with atopy.[1,3,4] Several international studies, however none from Germany, have investigated possible effects of atopic disorders on COVID-19 disease and recently even a protective effective was supposed.[6,7]

In a retrospective, questionnaire-based study, we aimed at analyzing the impact of atopic diseases on the course and severity of COVID-19 in adult patients with confirmed SARS-CoV-2 infection in our

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**Table 1**
Demographic data, reported symptoms and regeneration time in atopic (group 1) and non-atopic (group 2) patients

| | Group 1 (atopy) | Group 2 (controls) | Significance[a] |
|---|---|---|---|
| n | 53 | 54 | |
| Female | 24 (45.3%) | 28 (51.9%) | 0.50 |
| Age (y), median (range) | 42 (31-52) | 43 (33-58) | 0.92 |
| Symptomatic | 52 (98.1%) | 52 (96.3%) | 0.57 |
| Asymptomatic | 1 (1.9%) | 2 (3.7%) | |
| Quarantine only | 50 (94.3%) | 51 (94.4%) | 0.98 |
| Outpatient care | 4 (7.5%) | 3 (5.6%) | 0.68 |
| Hospitalization | 3 (5.7%) | 3 (5.6%) | 0.30 |
| Oxygen supply | None | 2 (3.7%) | 0.16 |
| Experienced symptoms | | | |
| Fever | 29 (54.7%) | 22 (40.7%) | 0.15 |
| Smell or taste | 33 (62.3%) | 35 (64.8%) | 0.78 |
| Gastrointestinal | 15 (28.3%) | 8 (14.8%) | 0.09 |
| Skin changes | 4 (7.5%) | 6 (11.1%) | 0.53 |
| General symptoms | 47 (88.7%) | 42 (77.8%) | 0.13 |
| Myalgia | 33 (62.3%) | 29 (53.7%) | 0.37 |
| Headache | 35 (66%) | 32 (59.3%) | 0.47 |
| Rhinorrhea | 20 (37.7%) | 25 (46.3%) | 0.37 |
| Pulmonary symptoms | 31 (58.5%) | 31 (57.4%) | 0.91 |
| Dry cough | 26 (49.1%) | 27 (50%) | 0.92 |
| Productive cough | 3 (5.7%) | 7 (13%) | 0.20 |
| Shortness of breath without oxygen supply | 11 (20.8%) | 8 (14.8%) | 0.42 |
| Shortness of breath with oxygen supply | 0 | 1 (1.9%) | 0.32 |
| Self-reported regeneration time | | | |
| <2 wk | 39 (73.6%) | 37 (68.5%) | 0.565 |
| >2 wk | 14 (26.4%) | 17 (31.5%) | |

[a]Mann-Whitney *U* test.

region. Patients were recruited after identification by the local health authorities or when presenting at the Department of Allergology of our university hospital. All subjects had SARS-CoV-2 infection before the local rise of mutant B1.1.7.

A total of 107 patients were included, of whom 53 (49.5%; mean age, 44.4 years) presented a history of symptomatic atopic diseases in the past 12 months whereas 54 subjects without atopic history served as controls (50.5%; mean age, 44.5 years). Characteristics of 107 patients are given in Table 1. Baseline data revealed no significant differences between atopic (group 1) and nonatopic subjects (group 2) with regard to sex or age. In group 1, 8 of 53 patients (15.1%) had atopic dermatitis, 47 of 53 patients (88.7%) had allergic rhinoconjunctivitis, and 14 of 53 patients (26.4%) had allergic asthma. All patients had a known sensitization to inhalative allergens. In regard to plant-derived allergens, grass (64.2%) and birch (50.9%) pollens were reported most frequently, and sensitization to nonherbal allergens were most often to mites (34%), cat (30.2%), or dog (18.9%) allergen. In group 1, 5 patients (9.4%) received allergen-specific immunotherapy when COVID-19 infection occurred. In addition, 9 of 53 patients (17%) were treated with local or systemic immunosuppressive medications (n = 3 topical nasal steroids, n = 4 steroid ointment, n = 6 inhalative steroids, n = 1 cyclosporine, n = 1 methotrexate and etanercept). In group 2, only 1 patient had omalizumab owing to chronic urticaria, although no other immunoactive drugs were reported to be taken.

Statistical analysis did not reveal a significant difference in experienced symptoms, treatment regimen, or recovery time between both groups. Furthermore, patients with atopy receiving immunotherapy or immunosuppressive medication did not have any significant differences for any of the parameters investigated. Hospitalization rates were comparable in both groups with n = 3, respectively (5.7% and 5.6%).

In conclusion, our data support the evidence that atopic comorbidities have no unfavorable impact on severity and course of COVID-19. Several studies have analyzed the effect of atopic diseases on the expression of Angiotensin-converting enzyme 2 (ACE2) or transmembrane protease 2, which induces the receptor binding of SARS-CoV-2.[6,7] It was found that linterleukin 13 (IL), most often overexpressed in the context of $T_H2$ inflammation, can significantly downregulate ACE2 expression.[2,6,7] Respiratory allergies, elevated limmunoglobulin E (IgE) levels, and topical and inhalative corticosteroids were also associated with a decreased ACE2 expression.[2,6] Altogether, this implicates that a decreased ACE2 expression in atopic manifestations may potentially reduce viral entrance of SARS-CoV-2 and thus lowers susceptibility for COVID-19 infection or disease severity in individuals with atopic background.[2,6,7]

As severe COVID-19 cases have been associated with eosinopenia, previous studies have discussed a potential antiviral role of eosinophils in the immune system.[6,8] In terms of their function in innate immunity, eosinophils are capable of antigen presentation and recognition of viral particles and release of proinflammatory mediators through degranulation and promotion of type 2 cytokines.[8] Atopic diseases are often associated with elevated eosinophil levels, which can be induced by the $T_H2$-derived cytokine interleukinIL 5. An increased antiviral immune response in SARS-CoV-2–infected patients with atopy with eosinophilia may be speculated, but further analysis is needed. With regard to most often prescribed medication, inhalative, intranasal, or systemic corticosteroids and allergen-specific immunotherapy have beneficial effects for local viral defense.[9] Furthermore, large-cohort analyses of patients with severe asthma have revealed that risk of infection, course of COVID-19 disease, or mortality is not increased when patients require treatment with biologicals.[10] Clinicians should be aware that patients who have atopic diseases might stop taking their effective medication as they fear severe COVID-19 illness, but owing to the potential benefit of these therapies, an unnecessary discontinuation should be avoided, requiring good clinical care and patient education.[9]

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# Positive associations of pollutants and aeroallergens with allergic rhinitis in adults with asthma



Allergic rhinitis (AR) is a widely prevalent condition (~20%), but there is a knowledge gap in our understanding of the risk factors for AR at a real-world and population level—in particular, exposure to potentially modifiable environmental triggers (eg, pollutants, aeroallergens).[1,2] The existing literature that evaluates the association of pollutants has especially focused on children and the results have been inconsistent.[3,4] We used the national Asthma Specialist Tool to Help Manage Asthma and Improve Quality (Asthma IQ) database[4] to evaluate individual and joint associations of self-reported environmental triggers, specifically pollutants and aeroallergens, with AR in adults in this large-scale, real-world sample.

The Asthma IQ (www.asthmaiq.org), a web-based tool developed by the American Academy of Allergy, Asthma, and Immunology (AAAAI), is intended to help asthma specialists better understand and apply the asthma guidelines of the National Asthma Education and Prevention Program in their practice to improve the quality of asthma care.[5] All data accessed (2008-2016) and analyzed were deidentified and researchers were granted access to the Asthma IQ database through a written request to the AAAAI.

This cross-sectional study was conducted in adults with asthma. The dependent variable evaluated was having AR, treated as a binary variable and defined by the AAAAI Joint Task Force rhinitis practice parameters as 1 or more of the following symptoms: sneezing, nasal congestion, rhinorrhea or postnasal drip, and itchy nose or throat.[6] The exposure variables of interest were self-reported nonallergic and allergic asthma triggers including pollutants (occupational exposures, air pollution, smells, and smoke) and aeroallergens (animals, cockroaches, dust, indoor mold, and outdoor pollens or molds), respectively.

Binary logistic regression models were used to evaluate the associations of triggers (pollutants and aeroallergens) with AR while adjusting for age, race, and body mass index (BMI) (data missing 32%, treated as separate BMI category). However, an important covariate, data on sex, was missing for most of the sample (87.7%). Associations of the number of triggers (as an ordinal variable) with AR were also evaluated. We assessed the interaction between pollutants and aeroallergens by including them and their product in the regression models. A 4-level categorical variable was developed to indicate the combined and unique effects of pollutants and aeroallergens. *P* values less than .05 were used to indicate statistical significance. Analyses were performed using Stata Version 15.0 (StataCorp LLC, College Station, Texas).

A total of 9676 patients were included in the analysis, with a mean age of 46 (± 17) years. The age distribution was as follows: 18 to 29 years (21%), 30 to 49 years (37%), 50 to 69 years (34%), and 70 years and older (9%). Most patients were White (72%), 11% were Black, and 10% were Hispanic. Patients with BMI less than 30 represented 27% of the sample, whereas 21% had BMI 25 to 29, 20% had a BMI less than 25, and 32% had a missing BMI.

A total of 3247 (34%) patients had AR. The prevalence of AR did not vary significantly by age group ($P = 0.26$). There were small but significant differences in the prevalence of AR by race and ethnicity (White: 34%; Black: 30%; Hispanic: 31%; Other: 35%; $P = .01$).

Self-reported triggers were associated with an increased odds of having AR after controlling for covariates (age, race, BMI) (Table 1). In adjusted analyses, there was a direct dose-response relationship between the number of triggers and the odds of having AR (Table 1).

When triggers were grouped as pollutants or aeroallergens, patients who reported exposure to pollutants were more likely (odds ratio [OR], 1.54; 95% confidence interval [CI], 1.25-1.88) to have AR, whereas patients who reported aeroallergens were twice as likely (OR, 2.19; 95% CI, 1.97-2.44) to have AR, after adjusting for covariates.

A statistically significant interaction between pollutants and aeroallergens was found in the adjusted analysis. Compared with participants who reported neither pollutants nor aeroallergens, those who reported both were more than twice as likely to have AR (OR, 2.59; 95% CI, 2.26-2.98).

Allergic rhinitis is a common but complex disease, with an interaction between multiple environmental and genetic factors that contribute to the clinical phenotype.[7] Our findings reveal that self-reported nonallergic and allergic asthma triggers, including both pollutants and aeroallergens, were individually associated with an increased odds of having AR. In addition, we found that the cumulative number of triggers also increased the odds of having AR. Previously, researchers have investigated the associations of environmental triggers individually with AR prevalence; however, exposure to these triggers is rarely isolated in the real world.[7,8] Furthermore, data on modifiable pollutant triggers (occupational exposures, air pollution, smells, and smoke) triggers is limited, and our findings emphasize the importance of identifying these so that clinicians can

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