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Impact of COVID-19 pandemic on adults and children with atopic dermatitis and food allergy: Systematic review

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Background: The coronavirus disease 2019 (COVID-19) pandemic caused significant disruptions to health care services and health impacts on patients with atopic dermatitis (AD) and/ or food allergy (FA).

Objective: We evaluated the impact of the COVID-19 pandemic and disease on AD/FA patients.

Methods: A comprehensive systematic literature search was conducted from December 2019 to 2022. Screening and data extraction were done following the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines, and the Mixed Methods Appraisal Tool, or MMAT, was used to assess risk of bias.

Results: In total, 159 studies were included. Five of 7 studies reported no significant changes in overall incidence or prevalence of AD during the pandemic, although some studies noted an increase in the elderly and infants. Telehealth served as an effective alternative to face-to-face consultations, with mixed levels of patient and provider satisfaction. Dissatisfaction was most marked in patients with more severe disease, who thought that their disease was inadequately managed through telemedicine. Higher levels of general anxiety were recorded in both AD/FA patients and caregivers, and it was more pronounced in patients with severe disease. Most studies reported no significant differences in postvaccination adverse effects in AD patients; however, results were more varied in FA patients. Conclusion: Our review identified the impact of COVID-19 pandemic- and disease-driven changes on AD/FA patients. Telemedicine is uniquely suited to manage atopic diseases, and

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hybrid care may be a suitable approach even in the postpandemic era. COVID-19 vaccines and biologics can be safely administered to patients with atopic diseases, with appropriate patient education to ensure continued care for highrisk patients. (J Allergy Clin Immunol Global 2024;3:100181.)

Key words: Atopic dermatitis, food hypersensitivity, telemedicine, mental health, hospitalizations, morbidity, severity, coronavirus

At the height of the coronavirus disease 2019 (COVID-19) pandemic, health care services saw significant disruptions resulting from the extensive movement restrictions that were implemented to contain the spread of the virus. This included curtailment of many essential services, cancellation of elective procedures with ensuing longer waiting times and delayed access to diagnostic and therapeutic services, and adoption of telemedicine as a mitigation strategy.^{1,2}

The impact of COVID-19 on asthma emergency and hospital admissions as well as asthma control in adults and children has been well documented.³⁻⁵ However, there have been comparatively few studies evaluating its impact on other atopic conditions such as atopic dermatitis (AD) and food allergy (FA).

Pandemic-related disruptions to health care provision and telemedicine may translate to delays in diagnosis and/or treatment of AD and FA. On the one hand, in both adults and children, these may also lead to reduction in access to medications or emergency medical services as well as delays in access to timely oral food challenge (OFC) and oral immunotherapy (OIT) for FA management, which collectively could affect disease control and morbidity.⁶ On the other hand, more time spent indoors and/or movement restrictions brought about by the pandemic may have positive effects on AD's severity—for example, through reduced exposure to outdoor triggers, by permitting greater flexibility in work or school schedules that allows better compliance with treatment regimens, and by varying impacts on mental health, which can also affect AD control.

Furthermore, antigenic stimuli such as COVID-19 infection and vaccination have been postulated to cause poorer health outcomes in certain preexisting illnesses by causing disease exacerbations. Treatments for AD and FA, such as biological therapy and immunotherapy, may also affect the effectiveness of COVID-19 vaccines in people with AD and/or FA. The above observations have been published in small case series across different countries, but the full impact of the pandemic on patients with these atopic diseases has not been systematically evaluated.

Given the widespread health care service disruptions brought about by the pandemic, changes to health-seeking behavior, the increasing role of telemedicine, and emerging evidence of impact

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Atopic dermatitis
Coronavirus disease 2019
Dermatology Life Quality Index
Emergency department
Food allergy
Health-related QoL
Mixed Methods Appraisal Tool, version 2018
Oral food challenge
Oral immunotherapy
Preferred Reporting Items for Systematic Reviews
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Quality of life

of COVID-19 disease on AD/FA patients, this could potentially affect health outcomes for AD/FA patients. This review thus aims to systematically evaluate the impact of COVID-19 pandemicdriven changes on AD and FA care, focusing on (1) the impact on AD/FA incidence and prevalence, (2) the impact on AD/FA disease control, morbidity, and treatment disruptions, (3) emergency department (ED) visits, hospitalizations, and clinic presentations, and (4) the role of telehealth and alternative initiatives. Moreover, the review also aims to establish the impact of COVID-19 disease and vaccinations in patients with AD/FA, in particular the (5) impact of AD/FA disease and AD/FA treatments on COVID-19 morbidity, (6) COVID-19 vaccination outcomes in AD/FA patients, and (7) mental health, psychological impact, and quality of life (QoL) concerns in AD/FA patients.

METHODS

The protocol for this systematic review was created according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) 2020 guidelines⁷ and was registered in the International Prospective Register of Systematic Reviews (329173).

Search strategy for identification of studies

A systematic literature search of Medline (Ovid), Embase (Ovid), Scopus, Cochrane Library, and CINAHL was performed on June 16, 2022, and updated in December 2022 with the help of librarians (A.C., M.S.). Searches were limited to studies published between December 2019 and December 2022 to capture studies evaluating the impacts of the current COVID-19 pandemic, which began in December 2019. The reference lists of relevant studies, systematic reviews, and meta-analyses were searched to identify eligible articles that might have been missed in the original database searches. The complete search terms and strategies can be found in Tables E1-E5 in this article's Online Repository at www.jaci-global.org.

Inclusion and exclusion criteria

Detailed eligibility criteria for inclusion are provided in the Methods section in the Online Repository at www.jaci-global.org. In brief, all COVID-19–related studies in AD and/or FA patients from all age groups were considered. All study designs were eligible except case reports, systematic reviews, narrative reviews, meta-analyses, and animal studies, which we excluded.

Conference abstracts and letters to editors were included if sufficient data were available for analysis. Only articles written in English or with an English translation were included.

Study selection

Three reviewers (C.N., N.H., W.T.A.) independently screened all records identified from database searches by title and abstracts. Any disagreement was resolved by discussion with a senior researcher (E.T.). The full texts of potentially relevant studies identified from the initial title and abstract screening stage were reviewed by 3 researchers (C.N., N.H., W.T.A.), independently and in parallel, to determine eligibility according to the predetermined inclusion and exclusion criteria described. Any discrepancies were resolved by consensus, and if necessary, arbitration by the senior researcher (E.T.).

Data collection and synthesis

Data were extracted by the first reviewer (C.N., W.T.A.) and then verified by a second reviewer (N.H., K.O.). The extraction process was carried out in Covidence.⁸

Risk of bias assessment

The Mixed Methods Appraisal Tool (MMAT) v2018 was used to assess risk of bias across different study designs, namely qualitative, quantitative randomized controlled, quantitative nonrandomized, quantitative descriptive, and mixed methods.⁹ Detailed MMAT v2018 criteria can be found in the Methods section in the Online Repository. Each study design was scored against 5 criteria; higher scores equate to a lower risk of bias. Studies were assessed for risk of bias by the first reviewer (C.N., W.T.A.) and then verified by the second reviewer (N.H., K.O.). Any discrepancies were resolved by discussion with a senior researcher (E.T.).

RESULTS

Of the 3723 studies identified, 159 met our eligibility criteria and were included for analysis (Fig 1). Of these studies, 100 reported data on AD, 51 on FA, and 8 on both. Table I provides an overview of the characteristics of the included studies. Detailed demographics of each study can be found in Table E6 in the Online Repository available at www.jaci-global.org. Eleven studies adopted a qualitative or mixed methods study design. The remaining 148 studies were quantitative in nature: 65 nonrandomized observational studies, 1 randomized controlled trial, and 82 descriptive (eg, surveys, chart reviews, case series). Quality assessments of these studies using MMAT v2018 are summarized in Table E7 in the Online Repository. Because all the studies were highly heterogenous, no meta-analyses were performed, and the findings are reported qualitatively in this systematic review.

Impact of COVID-19 pandemic–driven changes on AD and FA care

Impact on AD and FA diagnosis: Incidence and prevalence. Incidence or prevalence data were reported in 6 studies for AD¹⁰⁻¹⁵ and 1 study on both AD and FA.¹⁶ Because studies were mostly heterogeneous, no meta-analyses were



FIG 1. PRISMA flow diagram of included studies. Original reference count was 3741; however, 18 studies were merged with another related study (eg, conference abstracts of a published article), giving a total of 3723 studies. After removing duplicates, 2123 unique abstracts/studies were eligible for screening. An additional 33 records were also obtained by citation searching. In total, 159 studies were eventually included.

performed. In the general population, 5 studies in Cameroon,¹⁰ 3 in Korea,¹¹⁻¹³ and 1 in the United States¹⁴ reported no statistically significant changes in the incidence or prevalence of AD during the pandemic. However, Mandeng Ma Linwa et al¹⁰ in Cameroon noted a significantly increased prevalence of eczema in the elderly population (odds ratio, 1.373; 95% confidence interval, 1.022-1.844) compared to the pre–COVID-19 era (March 1, 2019, to February 29, 2020). In Thailand, Hanthavichai and Laopakorn¹⁵ reported the highest prevalence of eczematous dermatitis in senile outpatients (prepandemic eczema 24.6%, AD 0.6%; pandemic eczema 39.9%, AD 0.4%), although the distribution of the most prevalent dermatologic disorders did not change during the pandemic.

Hurley et al¹⁶ demonstrated higher rates of AD and egg sensitization in a cohort of Irish infants born during the COVID-19 pandemic period (March to May 2020) compared to infants in a birth cohort born before the pandemic. The increased rate of AD was hypothesized to be due to an altered infant microbiome resulting from reduced infective encounters through family members, day nursery, and school attendance. Other reasons such as antibiotic receipt and breast-feeding were also postulated. However, the higher rate of egg sensitization did not translate to a higher incidence of egg allergy at 12 months compared to a national prepandemic birth cohort group. This was attributed to the continuation of early introduction of baked egg soon after diagnosis,¹⁷ a practice that enhances the rate of tolerance in most infants.

Impact on AD and FA disease control and treatment disruptions. Fourteen studies reported outcomes on disease

control and severity of AD during the pandemic. Some showed an overall improvement (n = 4), ¹⁸⁻²¹ while others showed no change $(n = 7)^{22-28}$ or deterioration $(n = 3)^{29-31}$ of, respectively, AD control and severity.

In those who experienced improvement in disease control, one reason was continuation of essential therapy such as dupilumab. A cross-sectional study by Chiricozzi et al¹⁹ involving 1831 adolescent AD patients with moderate to severe AD found a statistically significant disease improvement in patients who continued dupilumab compared to those who ceased therapy. Improved AD control was also separately attributed to reduced trigger exposure (heat, sweating, physical activity) and more time and flexibility for skin care treatment, thus resulting in better treatment compliance during COVID-19 lockdown periods in other studies.^{18,32}

Three studies reported an increased frequency of disease flares and severity during the pandemic.²⁹⁻³¹ These findings were typically correlated with treatment discontinuation, particularly dupilumab,¹⁹ as well as longer AD history and self-isolation.²⁹ Worsening AD facial flares were also associated with increased use of face masks and other personal protective equipment.³³⁻³⁶ A daily personal protective equipment wearing time of more than 6 hours in those with preexisting skin conditions like acne and AD was strongly associated with adverse skin manifestations at various locations.³⁷ Interestingly, analyses of transepidermal water loss in AD health care workers showed higher transepidermal water loss area under the curve after use of hand sanitizer and soap compared to those without AD, suggesting that chronic use

TABLE I. Characteristics in 159 included studies

Characteristic	No. (%)
Atopic condition reported	
AD	100 (62.9)
FA	51 (32.1)
Both	8 (5.0)
Population group*	
Children/adolescents	29
Adults	62
Mixed ages	40
Caregivers/parents	19
Health care professionals, allergists, teachers	12
Age group not stated	6
Quality assessment scoring [†]	
2 points	10 (6.3)
3 points	25 (15.7)
4 points	67 (42.1)
5 points	57 (35.8)
Country or region of study	
Asia	20 (12.6)
Europe	52 (32.7)
Australia	1 (0.6)
North America	53 (33.3)
South America	3 (1.9)
Middle East	18 (11.3)
Africa	1 (0.6)
Global/multiple countries	11 (6.9)

*There is some overlap (some studies have both caregivers and children), so this will not total to 159 studies.

†MMAT v2018 was used for risk of bias analysis. Each study design was scored against 5 criteria, with higher scores indicating a lower risk of bias.

of hand sanitizers may further worsen impaired skin barrier function.³⁸ The Eczema Area and Severity Index scores in adult AD patients also showed an increase from 2.42 ± 1.10 to 5.10 ± 1.57 over a 1-month period during the first lockdown in Italy.³⁹ However, there was no significant change in skin lesion severity or symptom scores (Eczema Area and Severity Index and Severity Scoring of Atopic Dermatits) in AD patients who had acquired COVID-19 infection.^{19,27,28,40}

However, in patients with severe dyspnea—a surrogate measure of increased COVID-19 infection severity—a substantial proportion of patients reported development of mild or severe skin lesions and itching (respectively, mild/severe skin lesions in 25%/11%; mild/severe itching in 36%/12%). This could be attributed to higher IL-13 levels in patients with severe COVID-19.⁴¹ IL-13 is a critical T_H2 cytokine linked to AD exacerbations, which could explain the link between severe COVID-19 infection and worsening of AD control/severity.⁴² Hence, COVID-19 infection does not appear to result in worsening AD control/severity in most patients, except those with severe infection.

Nordhorn et al⁴³ reported that at least 18% of physicians closed their practices for at least a week during the pandemic for reasons such as patient absence and lack of ability to comply with hygiene regulations. As a result, 8.6% of dermatologists reported impaired treatment of moderate to severe AD. Isoletta et al⁴⁴ observed an increased complexity of cases, as evidenced by the increased need for biopsies and systemic therapy in AD patients presenting to the ED after a lockdown period compared to the prepandemic era, suggesting that delayed access for noncritical conditions like AD may have resulted in more advanced disease by the time of presentation.

Self-imposed or involuntary treatment disruption was another major indirect factor influencing disease severity. Twelve studies^{19,45-55} reported treatment disruptions in AD patients, the majority of which evaluated disruptions in dupilumab therapy. Across several studies, ^{19,45,47,51,54,55} the proportion of AD patients experiencing self-imposed or unanticipated treatment disruptions (of immunosuppressive and biologic treatments) was between approximately 7.4% to 14.5%. A common reason among those who chose to discontinue drug therapy was a perceived heightened risk of acquiring COVID-19 infection while receiving dupilumab. ^{19,48,52,54} Regardless, most AD patients receiving dupilumab were comfortable continuing treatment during the pandemic. ^{45,46}

Two studies^{56,57} evaluating the impact of the COVID-19 pandemic on FA disease control and severity outcomes were identified. Musallam et al⁵⁶ found that children with multiple FAs had significantly more FA reactions than children with a single FA during the pandemic. A separate study found a nonsignificant increase in the proportion of FA patients administering epinephrine autoinjectors during the pandemic.⁵⁷ This study had a small sample size, which might explain the nonsignificant findings. We postulate that a disruption of supply chains during the pandemic may have led to reduced availability of specialized foods, in turn leading to increased allergen exposure and FA reactions.

From the perspective of health care professionals, Alvaro-Lozano et al⁵⁸ found that around a quarter of OFCs were canceled and that a large majority experienced disruptions in their clinical practice. Nonetheless, around 27% of providers still initiated food OIT, and 20% continued updosing without modifications. Anagnostou et al⁵⁹ described that infection control measures, space availability, and patient and staff scheduling were the main barriers to peanut OIT during the pandemic. However, as a result of pandemic-related school closures and work-from-home initiatives, patients experienced more flexibility in scheduling appointments. Nachshon et al⁶⁰ also found that OIT updosing tended to be performed in older patients and began with a lower single highest tolerated dose than conventional protocols.

ED visits, hospitalizations, and clinic presentations. Three studies described AD associated ED visits/hospitalizations: there were reduced hospitalizations in Poland⁶¹ and Turkey,⁶² but no changes in Italy.⁴⁴ The data in Italy also showed an increase in the proportion of patients initiating medications before seeking care at the ED, potentially in a bid to delay noncritical care. While there was also an increased proportion of admissions for dermatitis and eczema in Turkey during the pandemic, the total overall number of admissions decreased. Likewise, there was a nonstatistically significant decrease in the number of patients admitted for AD specifically in Turkey. We postulate that the observations in Poland, Turkey, and Italy may be attributed to a general fear of being infected in the hospital environment and of violating lockdown restrictions, leading to overall fewer AD admissions. A causal relationship is well established between emotional stress, stressful life events, and the course of many skin diseases, including dermatitis and eczema.⁶³ Alongside lifestyle changes, these factors may have also contributed to the increased proportion of dermatitis and eczema admissions in Turkey.

Eight other studies reported changes in AD clinic attendance rates during the COVID-19 pandemic: 1 demonstrated a decrease,⁶⁴ 3 reported no change,^{62,65,66} and the remaining 4 studies^{10,67-69} found increased rates of clinic presentations in

specific age groups. Among the pediatric and adolescent populations, the number of medical visits for AD did not change significantly during the pandemic.⁶⁹ These studies had small sample sizes and were conducted at single institutions, so local regulations may have influenced observations. For instance, 4 studies were carried out in Turkey,^{62,64-66} 1 of which observed reduced clinic attendances,⁶⁴ yet no changes were observed in the other 3 studies.^{62,65,66} In this country, following the report of the first COVID-19 case in the country, all schools were closed, stay-athome directives were issued for entire weekends, public holidays were canceled, and intercity travel was restricted. A curfew was applied for people under age 20 and above age 65, and sometimes for everyone during certain periods. The curfew presented a barrier for patients' attending their medical follow-up appointments, particularly for non-life-threatening diseases. Furthermore, only city hospitals were dedicated to COVID-19 cases, while university hospitals and outpatient clinics were considered nonpandemic facilities.⁶⁴ The latter were not required to close services to prioritize COVID-19 patients and hence did not see a significant drop in AD/FA clinic services. Additionally, in Korea, the increase in AD clinic presentations in a military hospital coincided with a ban on medical leave put in place as a result of a COVID-19 outbreak within the military.⁶⁰

Two studies^{70,71} reported that FA-related ED visits and hospitalizations declined during the pandemic. This finding is in line with an overall reduction in all causes of ED pediatric hospitalizations in the same period.⁷¹ Attanasi et al,⁷² however, reported an increase in the number of children presenting with food anaphylaxis, which was attributed to the difficulties in finding specialist allergy products like adrenaline autoinjectors or hydrolyzed formulas as a result of increased time spent at home, income disruptions related to the pandemic, high product demand, and supply chain disruptions.

Eight studies^{56,58,60,73-77} reported the impact of the pandemic on FA-related clinic presentations from the patient perspective. Most reported difficulties accessing FA-related health services, and significantly fewer children utilized any medical service at all.⁷⁴ Only a single center in the United States reported an increase in both telehealth and in-clinic visits during the pandemic; however, no information about the facilities was offered, or reasons for the increased uptake.⁷⁷ There was also a reduced adherence to scheduled appointments and diagnostic OFCs. Substantially fewer caregivers sought medical attention after a food-induced allergic reaction.⁵⁶ Health care adaptations, such as a nurse-led home food allergen introduction service in patients with a history of allergic symptoms, were generally safe and effective, but many patients preferred to wait for a formal hospital OFC⁷⁸⁻⁸⁰ to guide allergen introduction, citing their preference for direct health care access and more inperson support.

Telehealth and alternative health care initiatives. AD was cited as one of the most common suitable dermatologic conditions eligible for telemedicine⁸¹⁻⁸³ in view of its noncritical nature, feasibility of diagnosis by using classic features visible over video streaming without an in-person physical examination, and ability to prescribe therapy remotely. Better attendance rates were recorded for telemedicine encounters compared to in-person visits, which enabled continued access to AD services.^{84,85} Two studies^{86,87} reported good effectiveness of telemedicine in AD follow-up care, preventing delay in treatment of disease flares or worsening of symptoms due to therapeutic interruption.

Teledermatology was also not associated with inappropriate dispensing of antibiotic prescriptions.⁸⁸

From certain AD patients' perspective, however, telemedicine was viewed as less satisfactory than face-to-face consultations.^{26,32,47,89} The dissatisfaction was more marked in patients with moderate to severe AD, where close to 50% were discontented with a telemedicine approach⁴⁷ as a result of the lack of a physical examination, and thus a perceived inadequate assessment of their skin condition and the inability of doctors to fully advise them on appropriate and timely therapeutic options, which could have influenced their preference for face-to-face appointments over telemedicine.⁹⁰ Reported benefits of telemedicine among other satisfied patients were cost savings as well as time efficiency resulting from reduced traveling requirements.^{32,81}

Telehealth was also a safe and efficacious medium for FA management, with generally high patient satisfaction.⁹¹⁻⁹⁵ Mac Mahon et al⁸⁶ and Schoonover et al⁹⁶ reported successful baked egg introduction and modified OIT updosing regimens, respectively, in FA patients during the pandemic, which helped mitigate disruptions in timely FA treatment. However, 1 study⁹⁷ reported a lack of satisfaction among health care practitioners, who stipulated that telemedicine was only useful for patients with known severe conditions who required urgent review and was not useful for diagnostic consultations. In particular, allergists' satisfaction was lowest for virtual OFCs and OITs, if performed.⁹¹ Only 13.7% of health care practitioners in Turkey reported continuation of oral challenge and skin or blood testing for FA diagnosis, with allergists preferring telemedicine for asthma and rhinitis instead.98 The main disadvantages were limited allergy testing opportunities, lack of physical examinaand unsuitability of the modality tion. to severe conditions.^{84,91,92,97,99,100}

Apart from telemedicine, 2 studies described their experience in delivering OFCs to FA patients in adapted settings such as in a nonhospital facility¹⁰¹ and a COVID-19 field hospital,¹⁰² while 2 studies described a pediatric home-based food introduction service¹⁰³ and a group visit model for OFCs.¹⁰⁴ These alternative approaches were safe and effective, with no severe complications (ie, cases requiring advanced airway management or intensive care) and reported high patient satisfaction, although the studies had small sample sizes and each evaluated only a single facility. Wait times were also reduced considerably, with mean wait time for all OFCs down by 1.04 months.¹⁰⁴

Impact of COVID-19 disease and vaccinations on patients with AD/FA

Impact of AD/FA disease and AD/FA treatments on COVID-19 morbidity. Table II summarizes 28 studies^{27,97,105-131} with data on COVID-19 infection morbidity in patients with AD and FA. The majority did not find any significant differences compared to healthy individuals. A few studies reported slight decreases or increases in COVID-19–related outcomes. On closer examination of each of these studies, this was likely due to small sample sizes or due to studies that were conducted in a single hospital, which suggests that the results were subjected to region- or location-specific factors that could have influenced COVID-19–related outcomes. Baseline characteristics of each study population were also different, with some

TABLE II. Impact of AD and FA on COVID-19-related outcomes

Study	Country	Disease type	COVID-19 outcome measured	Association	Outcome, OR (95% confidence interval)
Attauabi ¹⁰⁵	Denmark	AD	COVID-19 PCR positivity	Decrease	
Beken ¹⁰⁶	Turkey	AD, food allergen sensitization	COVID-19 hospitalization, COVID-19 severity	No association	AD and COVID-19 severity 0.477 (0.034-6.586)
Bowe ¹⁰⁷	United States	AD	COVID-19 reinfection	No association	Risk of AD in those with reinfection vs no reinfection HR, 1.06 (0.91-1.24)
Carmona-Pirez ¹⁰⁸	Spain	AD with anxiety disorders	COVID-19 infection	Increase	aOR 1.36 (1.06-1.74)
Carugno ¹⁰⁹	Italy	AD with dupilumab	COVID-19 infection	No association	_
Criado ²⁷	Brazil	AD and antihistamines, oral corticosteroids, dupilumab	COVID-19 severity/ duration	No association	AD and antihistamines: 0.7 (0.3-1.6) AD and oral corticosteroids: 0.3 (0.1-2.3) AD and antihistamines: 3.6 (0.8-17.6)
Fan ¹¹⁰	United States	AD	COVID-19 infection	Increase	aOR: 1.29 (1.15-1.44)
Fritsche ¹¹¹	United States	FA	Postacute sequelae of COVID-19	Increase	1.94 (1.42-2.60)
Keswani ¹¹²	United States	AD, FA	COVID-19 hospitalization, ICU admission, intubation	No association	AD Hospitalization: 0.51 (0.25-0.90) ICU admission: 0.65 (0.22-1.55) Intubation: 0.18 (0.01-0.87) FA Hospitalization: 0.97 (0.57-1.62) ICU admission: 0.97 (0.41-2.01) Intubation: 0.1 (0.21-1.83)
Kridin ¹¹³	Israel	AD and dupilumab	COVID-19 infection, hospitalization	No association	 HR COVID-19 infection Dupilumab vs systemic corticosteroids: 1.13 (0.61-2.09) Dupilumab vs phototherapy: 0.80 (0.42-1.53) Dupilumab vs azathioprine: 1.10 (0.45-2.65) Hospitalization Dupilumab vs systemic corticosteroids: 0.35 (0.05-2.71) Dupilumab vs phototherapy: 0.43 (0.05-3.98) Dupilumab vs azathioprine: 0.25 (0.02-2.74)
Kridin ¹¹⁴	Israel	AD	COVID-19 hospitalization	No association	Extended courses of systemic corticosteroids required in COVID-19–related hospitalization: 1.96 (1.23-3.14)
Kutlu ¹¹⁵	Turkey	AD	COVID-19 severity	No association	_
Marsteller ¹¹⁶	United States	Food allergen sensitization	COVID-19 positivity	No association	_
Miodonska ¹¹⁷	Poland	AD severity	Severe COVID-19	No association	HR 0.45 (0.32-0.65)

(Continued)

TABLE II. (Continued)

Study	Country	Disease type	COVID-19 outcome measured	Association	Outcome, OR (95% confidence interval)
Musters ⁹⁷	Global	AD and dupilumab, corticosteroids, topical treatments	COVID-19 hospitalization	AD and dupilumab: Decrease AD and systemic corticosteroids: Increase	 Hospitalization (aOR) Topical treatments vs dupilumab: 4.99 (1.4-20.84) Systemic corticosteroids vs dupilumab: 2.85 (0.08-38.11) Cyclosporin vs dupilumab: 3.02 (0.14-25.72) Combination therapy including systemic corticosteroids vs nonsteroidal immunosuppressive monotherapy: 45.74 (4.54-616.22) Combination therapy not including systemic corticosteroids vs nonsteroidal immunosuppressive monotherapy: 37.57 (1.05-871.11) Systemic corticosteroid monotherapy vs nonsteroidal immunosuppressive monotherapy: 1.87 (0.03-55.4)
Nguyen ¹¹⁸	United States	AD, including patients receiving immunomodulatory medications (prednisolone, methotrexate, ciclosporin, dupilumab)	COVID-19 infection, hospitalization and mortality rate	No association	_
Pakhchanian ¹¹⁹	Global	AD, including those receiving systemic immunosuppressants	Hospitalization, mortality, severe COVID-19	No association	Hospitalization: 0.89 (0.75-1.04) Mortality: 1.02 (0.62-1.62) Severe COVID-19: 0.8 (0.54-1.19)
Patrick ¹²⁰	United States	AD	COVID-19 infection	Increase	1.48 (1.06-2.06)
Raiker ¹²¹	Global	AD	COVID-19 hospitalization, critical care admission, severe COVID-19	Hospitalization: Decrease Others: No association	Adjusted risk ratio Hospitalization: 0.63 (0.54-0.72)
Rakita ¹²²	United States	AD	COVID-19 severity, complications, hospitalization		Hospitalization: aOR 0.51 (0.20-1.35) Acute level of care at initial medical care: 0.67 (0.35-1.30) Severe to critical SARS-CoV-2: 0.82 (0.29-2.30) Requirement of supplemental nonmechanical oxygen therapy: 1.33 (0.50-3.58) Extended hospital stay: 2.24 (0.36-13.85) Lingering COVID-19 symptoms: 0.58 (0.06-5.31) COVID-19 death (0.002 (<0.001 to >999)
Seibold ¹²³	United States	AD/FA	COVID-19 infection, household transmission	COVID-19 infection AD: No association FA: Decrease Household transmission AD: No association FA: Decrease	HR AD: VID infection: 1.06 (0.75-1.50) FA: COVID-19 infection: 0.50 (0.32-0.81) aOR AD: Household transmission: 1.85 (0.65-5.21) FA: Household transmission: 0.43 (0.19-0.96)
Smith-Norowitz ¹²⁴	United States	AD	COVID-19 positivity (IgM, IgG, Ag)	No association	_

(Continued)

TABLE II. (Continued)

Study	Country	Disease type	COVID-19 outcome measured	Association	Outcome, OR (95% confidence interval)
Ungar ^{125,126}	United States	AD and dupilumab	COVID-19 severity, COVID-19 antibody levels	Dupilumab compared to nonbiologic systemic treatments, other systemic treatments, and limited/ no treatments: Decrease	Systemic treatments vs dupilumab: 3.89 Limited/no treatments vs dupilumab: 1.96 Nonbiologic systemic treatment vs dupilumab: 1.87
Wu ¹²⁷	Denmark	AD and AD treated with dupilumab	COVID-19 infection	AD: Slight increase AD and dupilumab: Decrease	Incidence rate ratio AD: 1.18 (1.12-1.24) AD and dupilumab: 0.66 (0.52-0.83)
Yang ¹²⁸	South Korea	AD	COVID-19 PCR positivity, severe COVID-19 outcomes (ICU admission, invasive ventilation, death)	No association	COVID-19 positivity: 0.93 (0.76-1.13) Severe COVID-19 outcomes: 0.72 (0.18-2.90)
Yiu ¹²⁹	United Kingdom	AD	COVID-19 PCR positivity	No association	<i>aOR</i> 0.60 (0.22-1.64)
Yue ¹³⁰	United States	AD	COVID-19 Severity	Decrease	Adjusted risk ratio Severe COVID-19 in AD vs non-AD: 0.8 (0.7-0.9)
Zhang ¹³¹	Netherlands	AD	COVID-19 infection	No association	Mild AD: 1.11 (0.71-1.73) Moderate to severe AD: 1.00 (0.74-1.36)

aOR, Adjusted OR; HR, hazard ratio; ICU, intensive care unit; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

comprising high-risk populations (eg, ischemic heart disease, vascular disease, pulmonary disease) or more elderly patients, both of which are known risk factors for worse COVID-19 outcomes.¹³²

Dupilumab and tralokinumab are monoclonal biologics commonly used for treatment of severe AD. Studies on the safety of dupilumab on COVID-19 risk have collectively concluded that dupilumab is safe and does not increase the risk of COVID-19– related morbidities.^{22,24,53,132-135} Similarly, Blauvelt et al¹³⁶ demonstrated that COVID-19 infections were predominantly mild or moderate in AD patients who continued receiving tralokinumab therapy during COVID-19 infection. A plausible reason for this might be dupilumab's specific antagonism of the IL-13 and IL-4 pathway (T_H2 targeting) and tralokinumab's targeting of the IL-13 pathway, which does not impede mainly T_H1 pathways involved in immune protection against COVID-19.

Furthermore, dupilumab therapy appeared to be associated with a slightly decreased risk of COVID-19 infection and severity. One study¹³² found a lowered incidence of COVID-19 among patients with AD receiving dupilumab treatment compared to the general Canadian population. At present, the available literature supports the continuation of dupilumab in AD patients during the pandemic.

COVID-19 vaccination outcomes in AD/FA patients. We identified 13 studies reporting adverse effects of COVID-19 vaccination specifically in AD patients (see Table E8 in the Online Repository available at www.jaci-global.org).¹³⁷⁻¹⁴⁹ Most enrolled patients received the Pfizer (BNT162b2) vaccine (71-100%), followed by the 14% to 15% who received the Moderna (Spikevax/mRNA-1273) vaccine,^{138,140,142-144,147} and a minority received the Johnson & Johnson (Janssen) vaccine.^{137,150} Overall, these studies reported no significant differences in postvaccination adverse effects in AD patients compared to healthy patients,^{137,138,141,142} including pediatric AD patients¹⁴⁷ and AD patients treated with tralokinumab.¹³⁹ This was also similar at 30, 60, and 90 days after vaccination,¹⁴³ and there were also no differences in the rates of breakthrough COVID-19 infection. The vaccine was found to be effective in reducing the risk of hospitalization and COVID-19–related mortality in AD patients; it was also found that immunosuppressive drugs (azathioprine, mycophenolate mofetil, methotrexate, cyclosporine, dupilumab) did not impair vaccine effectiveness.¹⁵¹

Several small studies reported increases in AD-related risk after COVID-19 vaccination. In 1 study,¹⁴⁰ AD patients who received the Moderna vaccine did not experience higher risks of typical immunization stress–related responses but appeared to have an increased risk of immediate hypersensitivity reactions. This study, however, had a very small number of AD patients and wide confidence intervals, which reduces the certainty of evidence.

AD patients prescribed corticosteroids or anti-inflammatory therapy within a year of being vaccinated showed minimal risk of adverse outcomes, although they were initially found to be at higher risk of all-cause hospitalization before propensity-matching adjusting for demographic and comorbidities.¹³⁷ Potestio et al¹⁴⁴ similarly found that only a small percentage (2.7%) of AD patients receiving dupilumab developed AD exacerbations after vaccination, all of which were successfully treated with topical corticosteroids or calcineurin inhibitors. This further supports the safety of COVID-19 vaccination in AD patients who are

undergoing treatment with dupilumab. Kridin et al¹⁵¹ reported an increased vaccination uptake in those with adult-onset AD or moderate to severe AD, although this may be attributed to prioritization of vaccination for those receiving immunosuppressive drugs. Among those who tested positive for COVID-19, vaccinated people were more likely than unvaccinated people to self-report an eczema diagnosis.¹⁴⁸ However, no difference in cutaneous symptoms of COVID-19 infection was found between the 2 groups.

Findings were more variable in patients with FA (see Table E9 in the Online Repository available at www.jaci-global. org).^{142,146,150,152-154} Shukla et al¹⁵³ reported no serious adverse effects in FA patients receiving the Oxford-AstraZeneca vaccine/Covishield (85% vaccinated) and the whole inactivated virus-based vaccine Covaxin (BBV152) (12% vaccinated). A single conference abstract¹⁵⁰ reported an association between seafood allergy and anaphylaxis risk for Pfizer, Moderna, and Johnson & Johnson vaccines using data from the Vaccine Adverse Event Reporting System early in the pandemic (January 2020 to December 2021). In FA patients receiving the Oxford-AstraZeneca vaccine, Chiewchalermsri et al¹⁵² found no difference in adverse effects between FA and non-FA groups in the first 6 hours after vaccination. However, there was a statistically significant increased risk of fever, nausea, vomiting, skin rash, and local reaction in the FA group from 24 hours to 7 days after the vaccination. Although reasons for such observations are unclear, a limitation of the study was documentation of adverse reactions via telephone, which may result in inaccuracies when identifying and differentiating adverse skin reactions. There were no data on vaccination efficacy or morbidity in FA patients specifically.

Mental health, psychological impact, and QoL. Eight studies^{23,25,26,29,30,47,131,155} evaluated the psychological impact of the pandemic on AD patients. AD patients typically reported concerns in 2 key areas: generic pandemic-related concerns and ADspecific concerns. Generic pandemic-related concerns included loss of income, fear of COVID-19 infection, and fear of adverse effects after COVID-19 vaccination. Lugovic-Mihic et al¹⁵⁵ found that 59% of AD patients experienced psychological distress during the pandemic caused by generic COVID-19-related concerns. Loss of employment was also found to be associated with worsening mental health in AD patients, while stable or improved mental health outcomes were associated with working from home.²³ Interestingly, while there was a higher level of generic anxiety, depression, and stress^{25,30,47} during the pandemic, this effect was found to be more pronounced in patients with moderate to severe AD compared to those with mild AD.²⁹ Moreover, AD patients tended to be more concerned about the COVID-19 crisis compared to non-AD patients and were more likely to avoid contacting a doctor when experiencing health problems,¹³¹ plausibly because of their reluctance in burdening the health care system for a non-life-threatening condition.

AD-specific concerns included a perception of being more vulnerable to COVID-19 infection and an inability to procure AD medications. Patients with moderate to severe AD were found to be more stressed about medication shortages and perceived an increased vulnerability to COVID-19; they were also more afraid of COVID-19 vaccination's adverse effects.¹³¹ A similar impact was also reported in caregivers of AD patients and children with AD, where 75% and 50% experienced COVID-19–related stressors, respectively. More than 33% of caregivers also believed their child to be more vulnerable to COVID-19 infection.²⁶

Overall, the increased uncertainty, lack of clear information, and disruptions to routine health care were likely reasons for these adverse mental health impacts.

The studies that investigated OoL outcomes in AD patients primarily used health-related QoL (HRQoL) or Dermatology Life Quality Index (DLQI) measures. Overall, all studies reported worsening of HRQoL and DLQI scores in AD patients during the pandemic, 20,31,39,156 commonly because of loss of employment and income as well as COVID-19-related concerns. Adults with higher DLQI experienced a lower burden due to COVID-19 compared to those who were less affected by their disease.⁴⁰ Only weak associations were observed between increasing burden and reduction in QoL. There were also increased HRQoL-reported pain and discomfort in AD patients.^{20,31} Adolescents reported experiencing higher stress levels, which could have also triggered their eczema flares.³² Although preexisting mental health conditions, specifically depression and/or anxiety, were not specifically addressed in the abovementioned study, this lends support to the bidirectional association between mental health and physical health/AD disease control: AD patients with poorer mental health states may be at higher risk of flares and poorer disease control.

There were also similar increases in levels of pandemic-related anxiety and stress levels in caregivers, ¹⁵⁷⁻¹⁶⁰ adults, ¹⁶¹ and children with FA.¹⁶² However, several studies suggested that while overall anxiety increased, FA-specific anxiety remained unchanged or even reduced in most patients and caregivers during the pandemic.^{157,159} This was largely attributed to perceived increased control over exposures and diet resulting from movement restrictions and extended home confinement, resulting in reduced risk of accidental exposure. Santos et al.¹⁶³ also found that elementary school teachers in Canada felt better empowered to manage and supervise FA during mealtimes thanks to new practices such as fixed seating arrangements, restrictions on outside food, and improved cleaning practices.

However, specific subgroups, such as FA patients with a history of FA-related emergency visits, tended to report more FA-related anxiety resulting from concerns around the pandemic's burdens and disruptions to the medical care system.¹⁵⁹ In addition, Warren et al^{161,164} reported an increase in the level of FA-related anxiety/ stress resulting from difficulties obtaining safe, nutritious foods, accidental allergen exposure, and perceived inability to identify and treat FA anaphylaxis, as well as accessing health care for anaphylaxis episodes. This effect was greater in younger and female adults, and from households living below the poverty line. Intolerance of uncertainty and lack of food-related self-efficacy thus also contributed to a lower QoL.¹⁶⁵

There were also negative psychological outcomes related to FA treatment disruptions. Maeta et $a1^{76}$ found that parents who faced disruptions in the progress of their child's home-based food OIT also experienced significant anxiety about ED visits and risk of COVID-19. These children tended to have been prescribed adrenaline before or had severe or multiple food allergies and were at high risk of requiring emergency care, resulting in enhanced anxiety around access to medical care. In contrast, these concerns were not significant for lower-risk FA patients and caregivers undergoing OIT. Leef et $a1^{75}$ reported only a minority of patients (8.5%) cited the pandemic as a major barrier to commencing OIT. ED access during the pandemic was also not a major deterrent to the introduction of baked egg in egg-allergic patients in a home setting.⁸⁶

Similar to AD, FA patients who had increased levels of anxiety and depression were found to have a poorer QoL.¹⁶⁰ However, there was insufficient information as to whether these were related to preexisting mental health issues or as a result of the pandemic. Additionally, a trend toward worse QoL, particularly in the domains of family life, future security, and personal relationships, was observed in children whose caregivers reported negative pandemic-related impacts on their children's behalf.⁷³

Increased food spending, attributed to a lack of availability of specialized foods and disruption of supply chains, also led to increased food insecurity among FA families.¹⁶⁶⁻¹⁷¹ This effect was more pronounced in families with dietary restrictions compared to those without restrictions.¹⁶⁸ Twelve percent of food-allergic families reported buying foods with "may contain" precautionary allergen labeling, although they would have avoided such purchases before the pandemic.¹⁷² However, despite these QoL changes, Ahad et al¹⁶⁹ reported that most families did not think that the risk of an allergic reaction was higher compared to the prepandemic period because of their increased dietary control and confidence with allergy management. Zhang et al¹⁷³ also found that 11.2% indicated that the pandemic was a reason to avoid takeout food, and although there were no changes to takeout practices in FA individuals before and after the pandemic overall, severe allergic reactions occurred mostly in response to Mexican, Chinese, or Asian cuisine.

Conclusion

This systematic review provides a comprehensive overview of the impact of the COVID-19 pandemic on patients with AD and FA. Most studies reported no significant changes in overall incidence or prevalence of AD during the pandemic, but some studies noted an increase in specific subgroups. AD disease morbidity increased mainly in patients who had discontinued essential therapy such as dupilumab; were exposed to triggers that exacerbated the underlying disease, such as personal protective equipment in AD; or experienced severe COVID-19 infection. Delayed health-seeking behavior resulting in more severe AD presentations after lockdown was also notable, and the QoL studies we found suggested key reasons included reluctance to visit health care establishments or to burden hospitals facing overwhelming COVID-19 care needs.

There were clear variations in ED and clinic attendances reported between centers resulting from local or institutionspecific COVID-19 response factors. Disruptions to health care access and treatment regimens were experienced almost universally, but the impact appeared to be worse in high-risk patients with severe or brittle disease, namely severe AD; multiple FA or severe FA with low reactive thresholds; FA requiring supplychain–dependent therapeutics (adrenaline autoinjectors and specialized formulas); and those with preexisting mental health concerns. The negative psychological impact of the pandemic on AD and FA patients was closely tied to these factors.

Vaccines and biologics for COVID-19 can be safely administered to patients with atopic diseases. Nevertheless, it is essential to emphasize efforts to educate patients so that at-risk individuals continue to receive essential therapies during times of crisis.

A central theme across the studies was how telemedicine played a large role in mitigating the impact of health care disruptions on atopic disease management. This technology is particularly suitable for AD and FA, as these are diseases where diagnosis can be made visually (AD) or where physical examination is not required (FA). Many centers globally have since retained telemedicine as a prominent feature of their services even in the postpandemic era—a sure sign that future health care will include a hybrid model with both virtual and in-person care. Innovative practices like the provision of OFCs in non-health care settings and home-based care are also key examples of the importance of embracing agility in medicine to maintain resilience and business continuity.

DISCLOSURE STATEMENT

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