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The risk of COVID-19 infection in patients with atopic dermatitis: A retrospective cohort study

To the Editor: The dermatology community remains concerned about the risk of COVID-19 in individuals with atopic dermatitis (AD). Using Symphony Health-derived data from the COVID-19 Research Database,[1] we aimed to assess the risk of contracting COVID-19 in adults with AD while controlling for demographic factors and comorbidities known or speculated to be COVID-19 risk factors and assess the risk of contracting COVID-19 in adults with AD treated with dupilumab.

Subjects aged ≥20 years were eligible for inclusion. All subjects with at least 2 diagnoses of AD prior to January 1, 2020, were included in the AD cohort. Subjects with no record of AD diagnosis prior to January 1, 2020, were randomly placed in the control group in a 10:1 size ratio compared with the AD group. Individuals without known ethnicity or race, type of payment, and/or sex were then excluded. Laboratory-confirmed cases of COVID-19 between January 1, 2020, and April 17, 2021, were identified (Supplemental Fig I available via Mendeley at https://data.mendeley.com/datasets/j95wfcyy3j/1). A description of the methodology for this retrospective study is provided in Supplemental Methods (available via Mendeley at https://data.mendeley.com/datasets/t26gnt3pss/1), Supplemental Table I (available via Mendely at https://data.mendeley.com/datasets/ww6b5n327m/1), and Supplemental Table II (available via Mendeley at https://data.mendeley.com/datasets/tbh86d3z8r/1).

The AD and non-AD cohorts included 39,417 and 397,293 subjects, respectively (Table I). Poisson regression revealed a crude COVID-19 incidence rate ratio (IRR) of 1.41 (95% CI 1.34-1.48) for adults

Table I. Patient characteristics stratified by atopic dermatitis status

Characteristics	Atopic Dermatitis (n = 39,417)	No Atopic Dermatitis (n = 397,293)	*P* Value
Age, mean (SD)	54.9 (17.0)	57.3 (16.0)	<.0001
Sex, n (%)			<.0001
Female	23,555 (59.8)	223,412 (56.2)	
Male	15,862 (40.2)	173,881 (43.8)	
Race/ethnicity, n (%)			
Caucasian	25,187 (63.9)	295,823 (74.5)	<.0001
Hispanic	4468 (11.3)	36,035 (9.1)	
African American	6969 (17.7)	52,415 (13.2)	
Asian	1822 (4.6)	6670 (1.7)	
Other	971 (2.5)	6350 (1.6)	
Payment type, n (%)			
Assistance program*	24,065 (61.1)	209,202 (52.7)	<.0001
Medicare, private, cash	15,352 (39.0)	188,091 (47.3)	
Confirmed COVID-19, n (%)	1807 (4.6)	12,910 (3.3)	<.0001
Comorbidities, n (%)			
Asthma	3428 (8.7)	5024 (1.3)	<.0001
Rhinitis†	5317 (13.5)	3927 (1.0)	<.0001
COPD	1519 (3.9)	9667 (2.4)	<.0001
CHF	896 (2.3)	6598 (1.7)	<.0001
Chronic ischemic heart disease	1464 (3.7)	12,097 (3.0)	<.0001
DM2	4185 (10.6)	29,258 (7.4)	<.0001
DM1	192 (0.5)	1631 (0.4)	.025
Overweight or obese	2580 (6.6)	10,906 (2.8)	<.0001
CKD	1442 (3.7)	10,831 (2.7)	<.0001
Hypertension	8880 (22.5)	56,510 (14.2)	<.0001
HIV	155 (0.4)	623 (0.2)	<.0001

COPD, Chronic obstructive pulmonary disease; *CHF*, congestive heart failure; *CKD*, chronic kidney disease; *DM2*, type 2 diabetes mellitus; *DM1*, type 1 diabetes mellitus.
*Includes Medicaid.
†Allergic and/or vasomotor.

Table II. Poisson regression for risk of contracting COVID-19 in patients with atopic dermatitis

Factor	Crude IRR (95% CI)	*P* Value	Adjusted IRR (95% CI)*	*P* Value
AD vs no AD—main analysis	1.41 (1.34-1.48)	<.0001	1.18 (1.12-1.24)	<.0001
AD vs no AD—sensitivity analysis 1†	1.51 (1.45-1.56)	<.0001	1.18 (1.12-1.24)	<.0001
AD vs no AD—sensitivity analysis 2‡	1.33 (1.14-1.56)	<.0001	1.31 (1.11-1.53)§	.001
AD vs no AD—age subgroup analysis				
Age 20-40 y	1.32 (1.18-1.47)	<.0001	1.18 (1.05-1.33)	.007
Age ≥41 y	1.44 (1.37-1.53)	<.0001	1.18 (1.12-1.25)	<.0001
AD vs no AD—sex subgroup analysis				
Men	1.36 (1.26-1.47)	<.0001	1.16 (1.07-1.25)	<.0001
Women	1.45 (1.36-1.54)	<.0001	1.20 (1.12-1.28)	<.0001
Dupilumab vs no systemic medication	0.62 (0.49-0.78)	<.0001	0.66 (0.52-0.83)	<.0001
Methotrexate vs no systemic medication	0.80 (0.54-1.17)	.25	0.82 (0.56-1.21)	.32
Prednisone vs no systemic medication	1.16 (1.04-1.30)	.007	1.13 (1.01-1.26)	.03
Cyclosporine vs no systemic medication	1.37 (0.96-1.94)	.08	1.20 (0.84-1.71)	.32
Azathioprine vs no systemic medication	1.68 (0.87-3.24)	.12	1.61 (0.83-3.10)	.16
Dupilumab vs methotrexate	0.78 (0.50-1.21)	.26	0.80 (0.51-1.27)	.35
Dupilumab vs prednisone	0.53 (0.42-0.68)	<.0001	0.58 (0.45-0.74)	<.0001
Dupilumab vs cyclosporine	0.45 (0.30-0.68)	<.0001	0.57 (0.36-0.90)	.02
Dupilumab vs azathioprine	0.37 (0.18-0.73)	.004	0.40 (0.20-0.82)	.01

AD, Atopic dermatitis; *IRR*, incidence rate ratio.

*Adjusted for sex, age, race/ethnicity, payment type, and comorbidities (eg, asthma, rhinitis, overweight/obese, congestive heart failure, chronic ischemic heart disease, chronic kidney disease, chronic obstructive pulmonary disease, essential hypertension, human immunodeficiency virus, type 2 diabetes mellitus, and type 1 diabetes mellitus).

†Sensitivity analysis 1 includes subjects with missing race or ethnicity, type of payment, and/or sex.

‡Sensitivity analysis 2 includes subjects aged 20-59 years with zip code in California or New York and excludes subjects with a history of asthma, rhinitis, overweight or obese, congestive heart failure, chronic ischemic heart disease, chronic kidney disease, chronic obstructive pulmonary disease, essential hypertension, human immunodeficiency virus, type 2 diabetes mellitus, and/or type 1 diabetes mellitus.

§Adjusted for sex, age, race/ethnicity, payment type.

with AD compared with adults without AD (Table II). After adjusting for demographic factors and baseline comorbidities, the IRR remained statistically significant but was reduced to 1.18 (95% CI 1.12-1.24).

In a sensitivity analysis including subjects with missing race or ethnicity, sex, and/or type of payment (to account for selection bias), the risk of COVID-19 associated with AD remained unchanged (adjusted IRR 1.18). In another sensitivity analysis (to address potential type I error) including subjects aged 20-65 years with zip codes in California or New York and excluding subjects with comorbidities associated with COVID-19 (n = 32,857), the adjusted IRR point estimate was higher (1.31, 95% CI 1.11-1.53) than that in the main analysis.

Dupilumab was associated with lower risk of contracting COVID-19 (adjusted IRR 0.66, 95% CI 0.52-0.83) compared with no systemic medication. Additionally, AD subjects on dupilumab showed significantly lower associated risk of contracting COVID-19 infection compared with AD subjects exposed to prednisone, cyclosporine, and/or azathioprine (Table II).

The limitations include the inability to account for treatment duration and establish a strong causal relationship. Moreover, assessment of disease burden according to diagnostic codes might have missed individuals who never underwent COVID-19 laboratory testing. A prospective study with scheduled COVID-19 testing would address this limitation.

In this large population-based study, we found small increased risk of contracting COVID-19 to be associated with AD in adults. However, adult AD subjects had a higher prevalence of baseline comorbidities, previously identified as COVID-19 risk factors,[2,3] compared with adults without AD. Our results were attenuated after adjusting for baseline comorbidities, suggesting that residual confounding may explain the remaining association. Studies are needed to identify which demographic characteristics or comorbidities are the strongest COVID-19 risk factors for adults with AD.

Dupilumab was associated with lower risk of contracting COVID-19 infection compared with other systemic medications. Interestingly, interleukin 4 activity (blocked by dupilumab)[4] has been known to be associated with severe COVID-19 infections.[5] Based on the current evidence, dupilumab does not appear to increase COVID-19 risk in patients with AD.

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Conflicts of interest

Dr Wu is or has been an investigator, consultant, or speaker for AbbVie, Almirall, Amgen, Arcutis, Aristea Therapeutics, Boehringer Ingelheim, Bristol–Myers Squibb, Dermavant, Dr Reddy's Laboratories, Eli Lilly, Galderma, Janssen, LEO Pharma, Mindera, Novartis, Regeneron, Sanofi Genzyme, Solius, Sun Pharmaceutical, UCB, Valeant Pharmaceuticals North America LLC, and Zerigo Health. Dr Egeberg has received research funding from Pfizer, Eli Lilly, Novartis, Bristol-Myers Squibb, AbbVie, Janssen Pharmaceuticals, the Danish National Psoriasis Foundation, the Simon Spies Foundation, and the Aage Bang's Foundation, and honoraria as consultant and/or speaker from AbbVie, Almirall, Leo Pharma, Galápagos NV, Sun Pharmaceuticals, Samsung Bioepis Co, Ltd, Pfizer, Eli Lilly, Novartis, Galderma, Dermavant, UCB, Mylan, Bristol–Myers Squibb, and Janssen Pharmaceuticals. Dr Thyssen has been an advisor, speaker, or investigator for AbbVie, LEO Pharma, Regeneron, Pfizer, Sanofi Genzyme, Almirall, and Eli Lilly. Dr Ge and Authors Martin, Liu, and Thatiparthi have no conflicts of interest to declare.

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Impact of the COVID-19 pandemic on hospitalizations of patients with moderate-to-severe skin diseases: A retrospective cohort analysis from a Central European Center

To the Editor: The COVID-19 pandemic created a global health emergency, forcing infection prevention measures into the clinical routines of patients with skin disorders. Our location in southwest Germany, near Italy, led to COVID-19 cases starting in February 2020. Evidence shows that the elderly and those with comorbidities are more vulnerable for severe SARS-CoV-2 disease, with higher mortality rates. We evaluated the impact of the pandemic on dermatologic patients, including both inpatients and day hospital outpatients, throughout 2020 compared with 2019. We analyzed a total of 6206 patients from January 1, 2019, to December 31, 2020 (Tables I and II). Diagnoses were recorded with ICD-10 codes for each hospital visit individually, visits referring to both admissions and day hospital visits. Nonmelanoma skin cancer, including Merkel cell carcinoma and malignant melanoma, followed by eczema, leg ulcers, desensitization to allergens, and psoriasis, were the most frequent reasons for admission at our department in 2019, consistent with previous years.[1] Pan-German data showed a 13% decrease in inpatients in 2020 compared with 2019.[2] Similarly, we noticed an 8% ($P < .001$) decline in patient admissions (Table I). Proportionally, admissions below the age of 65 years decreased, whereas those above the age of 65 years increased to 58% of all hospitalizations ($P > .99$, Table I). We had fewer admissions of patients with inflammatory skin diseases (eg, eczema/psoriasis) and patients with lower leg ulcers ($P < .001$). Interestingly, patients admitted with herpes zoster as main diagnosis and receiving intravenous treatment as per German guidelines increased by 52% ($P < .05$) and were recorded throughout the year, possibly induced by stress-associated immunosuppression.[3] We specifically aimed at not postponing admissions for oncologic patients, but reduced outpatient assessments could