Atopic dermatitis is not associated with SARS-CoV-2 outcomes

Uros Rakita[1] · Trisha Kaundinya[2] · Armaan Guraya[3] · Kamaria Nelson[4] · Brittany Maner[5] · Jaya Manjunath[4] · Gabrielle Schwartzman[4] · Brittany Lane[6] · Jonathan I. Silverberg[4,7]

Abstract
Atopic dermatitis is characterized by immune dysregulation, which may predispose toward worse COVID-19 outcomes. We conducted a retrospective cohort study to investigate the relationship of atopic dermatitis with COVID-19 symptom severity, hospitalization, length of hospital stay, requirement for oxygen therapy, long-term morbidity and mortality. Multivariable logistic regression models were constructed to examine the impact of atopic dermatitis (independent variable) on COVID-19 symptom severity, hospitalization, length of hospital stay, requirement for oxygen therapy, long-term morbidity and mortality (dependent variables). SARS-CoV-2 positive adult patients with diagnosed AD had similar odds of hospitalization (adjusted odds ratio [95% confidence interval]: 0.51 [0.20–1.35]), acute level of care at initial medical care (0.67 [0.35–1.30]), severe-critical SARS-CoV-2 (0.82 [0.29–2.30]), requirement of supplemental non-mechanical 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]) and COVID-19 death (0.002 [< 0.001 – > 999]) compared to patients without AD. Our findings suggest AD is not an independent risk factor for COVID-19 severity or complications.

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease associated with systemic T-helper 2 activation and respiratory comorbidities, e.g. asthma and rhinitis. Concern exists regarding potential for poorer COVID-19 outcomes in AD patients, though previous studies had mixed findings [1–5]. We investigated the relationship between AD and COVID-19 outcomes in adults.

Methods

The study was approved by the George Washington University (GWU) institutional review board. We retrospectively analyzed data from GWU medical records for patients treated for SARS-CoV-2. Sociodemographic traits were compared between those with vs. without AD and severe-critical vs. mild-moderate COVID-19 using chi-squared and student's t test for categorical and continuous variables, respectively (Table 1). Binary logistic regression models were constructed with COVID-19 outcomes as dependent variables (acuity level of initial medical contact, hospitalization, hospitalization duration, COVID-19 symptom severity, requirement of supplemental oxygen therapy, mortality and

✉ Jonathan I. Silverberg
Jonathanisilverberg@gmail.com

1 Chicago Medical School, Rosalind Franklin University, North Chicago, IL 60064, USA

2 Northwestern Feinberg School of Medicine, Chicago, IL 60611, USA

3 Midwestern University Chicago College of Osteopathic Medicine, Chicago, IL 60515, USA

4 Department of Dermatology, George Washington School of Medicine, Washington, DC 20052, USA

5 Ross University School of Medicine, St. Michael, Barbados, BB 11093, USA

6 Michigan State University College of Human Medicine, East Lansing, MI 48824, USA

7 George Washington University School of Medicine and Health Sciences, Suite 2B-425, 2150 Pennsylvania Avenue NW, Washington, DC 20037, USA

Table 1 Sociodemographic and other health-related associations related to diagnosis of atopic dermatitis

Variable	Atopic dermatitis					COVID-19 severity				
	Yes		No		P value*	Asymptomatic-mild		Severe-critical		P value*
	n	%	n	%		n	%	n	%	
Sex					0.4361					0.1972
Male	14	29.17	135	35.53		128	36.16	20	28.17	
Female	33	70.21	245	64.14		226	63.84	51	71.83	
Race					0.6988					**0.0175**
White	9	18.75	63	16.54		66	18.54	5	7.04	
Non-White	39	81.25	318	83.46		290	81.46	66	92.96	
Smoking					0.1853					0.1907
Current/former	9	20.00	106	29.44		91	26.92	23	34.85	
Never	36	80.00	254	70.56		247	73.08	43	65.15	
Insurance coverage					0.1780					0.1322
Private	17	35.42	174	45.67		165	46.35	26	36.62	
Public	31	64.58	207	54.33		191	53.65	45	63.38	
Cancer#					0.7837+					0.6446
Yes	3	6.25	33	8.64		31	8.71	5	7.04	
No	45	93.75	349	91.36		325	91.29	66	92.96	
Immunosuppressant use##					0.9210					**0.0275**
Yes	11	22.92	90	23.56		77	21.63	24	33.80	
No	37	77.08	292	76.44		279	78.37	47	66.20	
AIDS					1.000+					1.0000+
Yes	1	2.08	9	2.36		9	2.53	1	1.41	
No	47	97.92	373	97.64		347	97.47	70	98.59	
Diabetes mellitus					**0.0449**					**< 0.0001**
Yes	6	12.50	98	25.65		71	19.94	32	45.07	
No	42	87.50	284	74.35		285	80.06	39	54.93	
Chronic heart failure					0.4928+					0.0629+
Yes	1	2.08	20	5.24		14	3.93	7	9.86	
No	47	97.92	362	94.76		342	96.07	64	90.14	
Obstructive lung disease					**0.0016**					**0.0350**
Yes	18	37.50	69	18.06		66	18.54	21	29.58	
No	30	62.50	313	81.94		290	81.46	50	70.42	
Hypertension					0.3172					**< 0.0001**
Yes	16	33.33	156	40.84		127	35.67	44	61.97	
No	32	66.67	226	59.16		229	64.33	27	38.03	
Chronic kidney disease					0.5592+					**0.0209**
Yes	2	4.17	30	7.85		22	6.18	10	14.08	
No	46	95.83	352	92.15		334	93.82	61	85.92	
	n	Mean (SD)	n	Mean (SD)	P value**	n	Mean (SD)	n	Mean (SD)	P value**
Age	48	47.88 (17.09)	381	52.29 (16.70)	0.0861	356	50.18 (16.26)	71	60.38 (16.83)	**< 0.0001**
BMI	48	30.30 (8.56)	367	31.47 (8.03)	0.3465	344	30.97 (7.95)	69	33.20 (8.58)	**0.0368**

Missing values were encountered in 3 (0.7%) for sex, 1 race (0.2%), 25 (5.8%) smoking, 1 (0.2%) insurance status. There were no missing values for immunosuppressant use, cancer diagnosis, AIDS diagnosis, CHF, OLD, Hypertension, CKD

The other skin diseases included onychomycosis (n=98), acne (n=47), actinic keratosis (n=16), allergic contact dermatitis (n=18), alopecia unspecified (n=52), basal cell carcinoma (n=5), cutaneous lupus (n=2), unspecified dermatitis (n=25), dermatomyositis (n=1), condyloma accuminata (n=8), hand dermatitis (n=7), hemangioma (n=2), herpes simplex infection (n=32), herpes zoster infection (n=8), hidradenitis suppurativa (n=15), hirsutism (n=8), hyperhidrosis (n=10), impetigo (n=2), irritant contact dermatitis (n=8), melanoma (n=1), paronychia (n=1), pityriasis rosea (n=1), plantar wart (n=11), psoriasis (n=11), prurigo nodularis (n=1), rosacea (n=9), scabies (n=1), seborrheic dermatitis (n=39), seborrheic keratosis (n=22), squamous cell carcinoma (n=3), tinea (n=53) and urticaria (n=17)

Boldface indicates significance

Table 1 (continued)

+Fisher exact test used to calculate significance in instances when 25% of cells had frequencies < 5

*Chi-squared test

**t test

#Cancer diagnosis includes solid tumor, leukemia and lymphoma. Specific diagnosis and cancer treatment status not available

##Immunosuppressant drugs (n; % of total dataset) included adalimumab ($n=4$; 0.93%), azathioprine ($n=2$; 0.47%), cyclosporine ($n=1$; 0.23%), dupilumab ($n=1$, 0.23%), etanercept ($n=1$, 0.23%), hydroxychloroquine ($n=20$; 4.65%), infliximab ($n=3$; 0.7%), ixekizumab ($n=1$; 0.23%), methotrexate ($n=12$; 2.79%), methylprednisolone ($n=8$; 1.86%), mycophenolate mofetil ($n=8$; 1.86%), prednisone ($n=49$; 11.4%), rituximab ($n=1$; 0.23%), sirolimus ($n=1$; 0.23%), tacrolimus ($n=8$; 1.86%), tofacitinib ($n=1$; 0.23%), other ($n=7$; 1.63%)

long-term morbidity) and AD as the independent variable. Multivariable models adjusted for socio-demographics and comorbidities. Crude and adjusted odds ratio (OR) and 95% confidence intervals (CI) were estimated.

Results

Overall, 430 adults were identified with confirmed SARS-CoV-2 and a diagnosed skin disease, including 48 (11.2%) with diagnosed AD. Most (81.25%) AD patients were non-White. There were no significant differences of age, BMI, sex, race, insurance coverage, malignancy or AIDS diagnoses or immunosuppressant use between those with vs. without AD. Patients with vs. without AD had lower rates of diabetes mellitus (DM; 12.50 vs. 25.65%, $P=0.0449$) and higher rates of obstructive lung disease (37.50 vs. 18.06%, $P=0.0016$). COVID-19 severity was associated with older age, higher BMI, non-White race, immunosuppressant use, obstructive lung disease, hypertension, chronic kidney disease and DM.

Among SARS-CoV-2 positive adult patients, those with vs. without AD had similar COVID-19 clinical outcomes. In fully adjusted models, diagnosed AD had similar odds of hospitalization (adjusted odds ratio [95% confidence interval]: 0.51 [0.20–1.35]), acute level of care at initial medical care (0.67 [0.35–1.30]), severe-critical SARS-CoV-2 (0.82 [0.29–2.30]), requirement of supplemental non-mechanical 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]) and COVID-19 death (0.002 [<0.001–>999]) compared to those without AD. Similar results were observed in unadjusted models (Table 2).

Discussion

These findings are consistent with studies that found no association of AD with COVID-19 morbidity. AD patients may be more susceptible to acquiring SARS-CoV-2 infection [3], though findings are inconclusive [5]. Current evidence indicates that AD patients are not at increased risk of mechanical ventilation [3, 4], hospitalization [2], longer hospital stay [4], intensive care unit admission [4] or death [2, 4]. In one retrospective study, AD was inversely associated with COVID-19 hospitalization [1]. We further demonstrate that AD is not associated with various other COVID-19 outcomes, including supplemental oxygen therapy, lingering symptoms and acuity level of initial care.

Study strengths include examination of multiple COVID-19 outcomes and controlling for confounders in multivariable analyses. Limitations include small sample size of AD patients, recruitment from a single metropolitan academic center, racial homogeneity and lack of stratified analysis by SARS-CoV-2 variants or AD features. Future studies with larger samples can further elucidate potential associations between AD and COVID-19.

Table 2 Association of atopic dermatitis with COVID-19 severity and hospitalization

Outcome	Atopic dermatitis n (%)		Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
	Yes	No				
Hospitalization#						
No	38 (84.44)	259 (71.75)	1.00 (ref)	–	1.00 (ref)	–
Yes	7 (15.56)	102 (28.25)	0.47 (0.20–1.08)	0.0756	0.51 (0.20–1.35)	0.1772
Visit type#						–
Outpatient	22 (45.83)	141 (37.11)	1.00 (ref)	–	1.00 (ref)	–
Inpatient	26 (54.17)	239 (62.89)	0.70 (0.38–1.28)	0.2424	0.67 (0.35–1.30)	0.2304
Oxygen therapy#						
No	41 (85.42)	313 (83.47)	1.00 (ref)	–	1.00 (ref)	–
Yes	7 (14.58)	62 (16.53)	1.07 (0.45–2.51)	0.8788	1.33 (0.50–3.58)	0.5686
COVID-19 severity#						
Asymptomatic-mild	42 (87.50)	314 (82.85)	1.00 (ref)	–	1.00 (ref)	–
Severe-critical	6 (12.50)	65 (17.15)	0.69 (0.28–1.70)	0.4178	0.82 (0.29–2.30)	0.7062
Hospital duration#						
1–6 days	3 (42.86)	59 (59.60)	1.00 (ref)	–	1.00 (ref)	–
≥ 7 days	4 (57.14)	40 (40.40)	1.97 (0.42–9.26)	0.3924	2.24 (0.36–13.85)	0.3857
Course##						
Recovered	46 (97.87)	338 (94.15)	1.00 (ref)	–	1.00 (ref)	–
Chronic complications	1 (2.13)	12 (3.34)	0.61 (0.08–4.82)	0.6412	0.58 (0.06–5.31)	0.6328
Death	0 (0)	9 (2.51)	<0.001 (<0.001–>999)	0.9631	0.002 (<0.001–>999)	0.7781

#Binary logistic regression models were constructed with atopic dermatitis diagnosis as the independent variable and COVID-19 outcomes as the dependent variables. Dependent variables included hospitalization (yes vs. no), visit type (inpatient vs. outpatient), oxygen therapy (yes vs. no), COVID-19 severity (severe-critical vs. asymptomatic-mild) and hospital duration (1–6 days vs ≥ 7 days)

##Multinomial logistic regression models were constructed with atopic dermatitis diagnosis as the independent variable (yes/no) and COVID-19 course as the dependent outcome variable (chronic complications or death vs recovered). Crude odds ratios (OR) and 95% confidence intervals (CI) were generated for unadjusted models

Adjusted OR and 95% CI were generated for age [continuous], sex [male/female], race [White/non-White], immunosuppressant use [yes/no], smoking [current-former/never], BMI [continuous], insurance status [public/private], diagnosis of cancer [yes/no], and AIDS [yes/no]

Declarations

References

1. Keswani A, Dhana K, Rosenthal JA et al (2020) Atopy is predictive of a decreased need for hospitalization for coronavirus disease 2019. Ann Allergy Asthma Immunol 125:479–481. https://doi.org/10.1016/j.anai.2020.07.012
2. Nguyen C, Yale K, Casale F et al (2021) SARS-CoV-2 infection in patients with atopic dermatitis: a cross-sectional study. Br J Dermatol. https://doi.org/10.1111/bjd.20435
3. Patrick MT, Zhang H, Wasikowski R et al (2021) Associations between COVID-19 and skin conditions identified through epidemiology and genomic studies. J Allergy Clin Immunol 147:857-869. e7. https://doi.org/10.1016/j.jaci.2021.01.006
4. Yang JM, Koh HY, Moon SY et al (2020) Allergic disorders and susceptibility to and severity of COVID-19: a nationwide cohort study. J Allergy Clin Immunol 146:790–798. https://doi.org/10.1016/j.jaci.2020.08.008
5. Yiu ZZN, Harding-Oredugba G, Griffiths CEM et al (2021) Risk of COVID-19 infection in adult patients with atopic eczema and psoriasis: a single centre, cross-sectional study. Br J Dermatol. https://doi.org/10.1111/bjd.20062