Received: 13 August 2022 | Accepted: 1 September 2022

DOI: 10.1111/jocd.15351

JCD Journal of Cosmetic Dermatology WILEY

ORIGINAL ARTICLE

Nineteen months into the pandemic, what have we learned about COVID-19-related outcomes in patients with psoriasis?

Khalaf Kridin MD, PhD[1,2,3] | Yochai Schonmann MD, MSc[4,5] | Erez Onn MD, MHA[2,6] | Dana Tzur Bitan PhD[7,8] | Orly Weinstein MD, MPH[4,5] | Eran Shavit MD[9,10] | Arnon D. Cohen MD, MPH, PhD[4,5]

[1]Unit of Dermatology and Skin Research Laboratory, Baruch Padeh Poria Medical Center, Tiberias, Israel

[2]Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel

[3]Lübeck Institute of Experimental Dermatology, University of Lübeck, Lübeck, Germany

[4]Clalit Health Services, Tel-Aviv, Israel

[5]Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

[6]Baruch Padeh Medical Center, Poriya, Israel

[7]Department of Behavioral Sciences, Ariel University, Ariel, Israel

[8]Shalvata Mental Health Center, Hod Hasharon, affiliated with the Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Israel

[9]Dermatology Clinic, Wolfson Medical Center, Holon, Israel

[10]The Sackler faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Correspondence
Eran Shavit MD, Dermatology clinic, Wolfson Medical Center, Holon, Israel.
Email: eransh@wmc.gov.il

Abstract

Background: The impact of psoriasis on the outcomes of Coronavirus disease 2019 (COVID-19) is yet to be precisely delineated.

Objectives: To assess the risk of COVID-19, COVID-19-associated hospitalization, and mortality among patients with psoriasis as compared with age-, sex-, and ethnicity-matched control subjects. In addition, we aim to delineate determinants of COVID-19-associated hospitalization and mortality in patients with psoriasis.

Methods: A population-based retrospective cohort study was performed to longitudinally follow patients with psoriasis and their matched controls with regard to COVID-19-related outcomes. The risk of COVID-19 infection, COVID-19-associated hospitalization, and mortality were assessed using uni- and multi-variable Cox regression analyses. Determinants of COVID-19-associated hospitalization and mortality were evaluated using multivariable logistic regression analysis.

Results: The study population included 144 304 patients with psoriasis and 144 304 age- and sex-matched control individuals. Patients with psoriasis displayed a slightly elevated risk of SARS-CoV-2 infection (fully-adjusted HR, 1.05; 95% CI, 1.03–1.08; $p < 0.001$). Relative to controls, patients with psoriasis had comparable multivariate risk of COVID-19-associated hospitalization (fully-adjusted HR, 1.08; 95% CI, 0.99–1.18; $p = 0.065$) and COVID-19-associated mortality (fully-adjusted HR, 0.88; 95% CI, 0.73–1.05; $p = 0.162$). When evaluating individuals hospitalized due to COVID-19, patients with psoriasis were more likely to have type-2 diabetes mellitus (adjusted OR, 1.24; 95% CI, 1.03–1.50; $p = 0.027$) and obesity (adjusted OR, 1.37; 95% CI, 1.13–1.65; $p = 0.001$) relative to controls.

Conclusions: While patients with psoriasis are at a higher risk of contracting SARS-CoV-2 infection, they are not more susceptible to the complications of COVID-19.

KEYWORDS
coronavirus disease 2019, COVID-19, psoriasis, SARS-CoV-2 infection

Abbreviations: CI, confidence interval; COVID-19, Coronavirus disease 2019; HR, hazard ratio; OR, odds ratio; SD, standard deviation.

Khalaf Kridin, Yochai Schonmann, Orly Weinstein, Eran Shavit and Arnon D. Cohen contributed equally to this work.

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), embodies an unprecedented global health crisis with enormous social, mental, and financial ramifications.[1] While most patients with COVID-19 experience a mild upper respiratory tract infection, a sizable portion of patients manifest with acute respiratory distress syndrome, potentially resulting in multiorgan failure and death.[2] Severe COVID-19 is typified by an overshoot of the host immune response with overproduction of proinflammatory cytokines such as tumor necrosis factor (TNF) and interleukin (IL)-6.[3] These cytokines were found to exert an important role in the pathogenesis of psoriasis.[4,5]

COVID-19-related outcomes of patients with psoriasis remain to be accurately established. Our knowledge about the burden of COVID-19 in this group is hindered by the small sample size and short follow-up duration of most studies.[6] In the current study, we aimed to evaluate the risk of SARS-CoV-2 infection, COVID-19-associated hospitalization, and mortality in patients with psoriasis relative to matched control individuals. In addition, we sought to identify determinants of COVID-19 complications in patients with psoriasis.

2 | MATERIALS AND METHODS

2.1 | Study design and dataset

The database of Clalit Health Services, insuring 4.7 million Israeli citizens, was screened for enrollees with a diagnosis of psoriasis, as documented by a board-certified dermatologist. For each eligible patient with psoriasis, a control individual was enrolled after being matched by age, sex, and primary-care clinic. In the current retrospective cohort study, all study participants were longitudinally followed from the onset of the pandemic in Israel (February 27, 2020) until September 2, 2021, death or fulfilling the study outcomes, whichever occurs earlier.

2.2 | Definition of COVID-19-related outcomes

The diagnosis of COVID-19 was based on confirmation of cases by US FDA-approved molecular tests. COVID-19-associated hospitalization was defined in COVID-19-confirmed patients admitted to intensive care units, internal medicine, or COVID-19-specific respiratory inpatient wards. COVID-19-associated mortality was defined in COVID-19-confirmed patients whose cause of death was ascribed to COVID-19 or its complications. Study participants' date of death was ascertained by linking the study cohort with the Ministry of Interior registry.

2.3 | Statistical analysis

Incidence rates of outcomes were calculated and expressed as the number of events per 1000 person-years. Hazard ratios (HR)s for the risk of incident outcomes were obtained by the use of the Cox regression model. The independent associations between demographic and comorbidity variables and COVID-19-associated hospitalization and mortality were assessed by multivariable logistic regression analysis and reported as odds ratio (OR) and 95% confidence intervals (CIs). Two-tailed p-values <0.05 were considered statistically significant. All statistical analyses were performed using SPSS software, version 25 (SPSS: IBM Corp).

3 | RESULTS

The current retrospective cohort study included 144 304 patients with psoriasis and 144 304 age- and sex-matched control individuals. The mean (SD) age of study participants was 50.0 (20.5), 51.3% were females, and 83.0% were of Jewish ethnicity (Table 1).

Patients with psoriasis exhibited a slightly increased risk of SARS-CoV-2 infection (fully-adjusted HR, 1.05; 95% CI, 1.03–1.08; $p < 0.001$). This risk was of significance among males (HR, 1.08; 95% CI, 1.04–1.11; $p < 0.001$) but not females (HR, 1.02; 95% CI, 0.99–1.06; $p = 0.191$; Table 2).

With regard to COVID-19 complications, patients with psoriasis displayed comparable multivariate risk of COVID-19-associated hospitalization (fully-adjusted HR, 1.08; 95% CI, 0.99–1.18; $p = 0.065$) and COVID-19-associated mortality (fully-adjusted HR, 0.88; 95% CI, 0.73–1.05; $p = 0.162$; Table 2). In the psoriasis group, out of 14 449 patients who got infected, 232 (1.61%) deceased due to COVID-19. The corresponding figure in the control group was estimated at 1.68% (234/13931), which is statistically similar ($p = 0.624$).

Determinants of COVID-19-associated hospitalization and mortality in patients with psoriasis as compared with controls were investigated (Tables 3 and 4). Among individuals hospitalized due to COVID-19, psoriasis patients were more likely to have type-2 diabetes mellitus (adjusted OR, 1.24; 95% CI, 1.03–1.50; $p = 0.027$) and obesity (adjusted OR, 1.37; 95% CI, 1.13–1.65; $p = 0.001$) relative to controls (Table 3). Demographic variables and comorbidities were not found to distinguish between psoriasis patients and controls with COVID-19-associated mortality (Table 4).

4 | DISCUSSION

The current population-based study suggests that although psoriasis imposes a slightly increased risk of contracting COVID-19 infection, it is not associated with susceptibility to the infection's complications.

In congruence with our findings, psoriasis was the most frequently encountered immune-mediated disease among a large group of 133 589 patients with COVID-19 and 48 418 patients with COVID-19-associated hospitalization.[7] Psoriasis was associated with an increased probability of contracting COVID-19 infection (OR, 1.48; 95% CI, 1.06–2.07).[8] The mechanism underlying the increased

TABLE 1 Descriptive characteristics of the study population

Characteristic	Psoriasis ($n = 144304$)	Controls ($n = 144304$)	p value
Age at the onset of pandemic, years; mean (SD)	50.0 (20.5)	50.0 (20.5)	0.919[a]
Age at the onset of psoriasis, years; mean (SD)	42.3 (19.9)	NA	
Duration of psoriasis at the onset of pandemic, years; mean (SD)	7.7 (4.9)	NA	
Sex; *n* (%)			
Male	70270 (48.7%)	70270 (48.7%)	1.000
Female	74034 (51.3%)	74034 (51.3%)	
Ethnicity; *n* (%)			
Jews	119838 (83.0%)	119817 (83.0%)	0.917
Arabs	24466 (17.0%)	24487(17.0%)	
Smoking; *n* (%)	45055 (31.2%)	41358 (28.7%)	**<0.001**
COPD; *n* (%)	3042 (2.1%)	2440 (1.7%)	**<0.001**
Diabetes mellitus; *n* (%)	18453 (12.8%)	16129 (11.2%)	**<0.001**
Hypertension; *n* (%)	23237 (16.1%)	21331 (14.8%)	**<0.001**
Hyperlipidemia; *n* (%)	47406 (32.9%)	43485 (30.1%)	**<0.001**
Ischemic heart disease; *n* (%)	9427 (6.5%)	8083 (5.6%)	**<0.001**
Malignancy; *n* (%)	7845 (5.4%)	6839 (4.7%)	**<0.001**
Chronic renal failure; *n* (%)	3400 (2.4%)	2970 (2.1%)	**<0.001**
Obesity; *n* (%)	26086 (18.1%)	21455 (14.9%)	**<0.001**

Abbreviations: BMI, body mass index; *n*, Number; SD, standard deviation.

p-values < 0.05 were considered statistically significant, hence statistically significant values were highlighted in bold.

[a]The mean difference for this variable was 0.09.

TABLE 2 Risk of COVID-19 and its complications among patients with psoriasis as compared with controls

	COVID-19 infection		COVID-19-associated hospitalization		COVID-19-associated mortality	
	Psoriasis ($n = 144304$)	Controls ($n = 144304$)	Psoriasis ($n = 144304$)	Controls ($n = 144304$)	Psoriasis ($n = 144304$)	Controls ($n = 144304$)
Follow-up time, PY	207005.1	207411.1	214573.7	214684.6	215228.4	215263.6
Median follow-up time, years (range)	1.5 (0.0–1.5)	1.5 (0.0–1.5)	1.5 (0.0–1.5)	1.5 (0.0–1.5)	1.5 (0.0–1.5)	1.5 (0.0–1.5)
Number of events	14449	13931	1180	1050	232	234
Incidence rate / 1000 PY (95% CI)	69.8 (68.7–71.0)	67.2 (66.1–68.3)	5.5 (5.2–5.8)	4.9 (4.6–5.2)	1.1 (0.9–1.2)	1.1 (1.0–1.2)
Unadjusted HR (95% CI) [*p* value]	**1.05 (1.02–1.07) [<0.001]**	Reference	**1.12 (1.03–1.22) [0.006]**	Reference	0.98 (0.82–1.17) [0.811]	Reference
Male-specific HR (95% CI) [*p* value][a]	**1.08 (1.04–1.11) [<0.001]**	Reference	**1.15 (1.03–1.29) [0.015]**	Reference	1.04 (0.82–1.31) [0.751]	Reference
Female-specific HR (95% CI) [*p* value][b]	1.02 (0.99–1.06) [0.191]	Reference	1.09 (0.97–1.24) [0.163]	Reference	0.89 (0.66–1.19) [0.424]	Reference
Age- and sex-Adjusted HR (95% CI) [*p* value]	**1.05 (1.02–1.07) [<0.001]**	Reference	**1.12 (1.03–1.22) [0.006]**	Reference	0.94 (0.79–1.13) [0.532]	Reference
Fully adjusted HR (95% CI) [*p* value][c]	**1.05 (1.03–1.07) [<0.001][c]**	Reference	1.08 (0.99–1.18) [0.065][c]	Reference	0.88 (0.73–1.05) [0.162][c]	Reference

Note: Bold: significant value.

Abbreviations: *n*, Number; PY, person-year; HR, hazard ratio; CI, confidence interval; NA, non-applicable.

[a]A total of 70270 male patients with psoriasis and 70270 male controls were included in this stratified analysis.

[b]A total of 74034 female patients with psoriasis and 74034 female controls were included in this stratified analysis.

[c]Multivariate Cox regression model adjusting for age, sex, ethnicity. COPD, chronic renal failure, ischemic heart disease, hypertension, hyperlipidemia, obesity, malignancy, diabetes mellitus, and smoking.

TABLE 3 Determinants of COVID-19-associated hospitalization in patients with psoriasis as compared with controls

	Psoriasis with COVID-19-associated hospitalization (*N* = 1180)	Controls with COVID-19-associated hospitalization (*N* = 1050)	Univariate OR	95% confidence interval	*p* Value	Multivariate OR[a]	95% confidence interval	*p* Value
Age, years; mean (SD)[b]	64.3 (17.5)	63.4 (18.1)	1.03	0.98–1.08	0.206	1.03	0.98–1.08	0.234
Female sex, *n* (%)	530 (44.9%)	486 (46.3%)	0.95	0.80–1.12	0.517	0.96	0.81–1.14	0.234
Jewish ethnicity, *n* (%)	859 (72.8%)	790 (75.2%)	0.88	0.73–1.07	0.190	0.85	0.70–1.04	0.108
Smoking; *n* (%)	385 (32.6%)	305 (29.0%)	1.18	0.99–1.42	0.068	1.17	0.97–1.41	0.107
COPD; *n* (%)	80 (6.8%)	52 (5.0%)	1.40	0.97–2.00	0.068	1.35	0.94–1.95	0.102
Diabetes mellitus; *n* (%)	378 (32.0%)	286 (27.2%)	**1.26**	**1.05–1.51**	**0.013**	**1.24**	**1.03–1.50**	**0.027**
Hypertension; *n* (%)	384 (32.5%)	317 (30.2%)	1.12	0.93–1.62	0.232	1.09	0.90–1.31	0.399
Hyperlipidemia; *n* (%)	605 (51.3%)	517 (49.2%)	1.09	0.92–1.28	0.338	1.05	0.88–1.25	0.604
Ischemic heart disease; *n* (%)	208 (17.6%)	171 (16.3%)	1.10	0.88–1.37	0.400	1.05	0.83–1.33	0.672
Malignancy; *n* (%)	114 (9.7%)	93 (8.9%)	1.10	0.83–1.47	0.514	1.07	0.80–1.43	0.659
Chronic renal failure; *n* (%)	115 (9.7%)	105 (10.0%)	0.97	0.74–1.28	0.841	0.92	0.69–1.23	0.579
Obesity; *n* (%)	355 (30.1%)	251 (23.9%)	**1.37**	**1.13–1.65**	**0.001**	**1.37**	**1.13–1.65**	**0.001**

Note: Bold: significant values.

[a]Adjusted for age and sex.

[b]OR per 10-year increase in age.

TABLE 4 Determinants of COVID-19-associated mortality in patients with psoriasis as compared with controls

	Psoriasis with COVID-19-associated mortality (*N* = 232)	Controls with COVID-19-associated mortality (*N* = 234)	Univariate OR	95% confidence interval	*p* Value	Multivariate OR[a]	95% confidence interval	*p* Value
Age, years; mean (SD)[b]	77.1 (11.3)	76.0 (12.0)	1.09	0.93–1.27	0.308	1.09	0.94–1.28	0.262
Female sex, *n* (%)	83 (35.8%)	94 (40.2%)	0.83	0.57–1.21	0.328	0.81	0.56–1.18	0.279
Jewish ethnicity, *n* (%)	178 (76.7%)	182 (77.8%)	0.94	0.61–1.45	0.786	0.88	0.56–1.37	0.569
Smoking; *n* (%)	88 (37.9%)	80 (34.2%)	1.18	0.81–1.72	0.400	1.13	0.77–1.67	0.538
COPD; *n* (%)	27 (11.6%)	22 (9.4%)	1.27	0.70–2.30	0.431	1.24	0.68–2.26	0.478
Diabetes mellitus; *n* (%)	92 (39.7%)	93 (39.7%)	1.00	0.69–1.44	0.984	1.00	0.69–1.44	0.980
Hypertension; *n* (%)	103 (44.4%)	89 (38.0%)	1.30	0.90–1.88	0.163	1.29	0.88–1.89	0.193
Hyperlipidemia; *n* (%)	155 (66.8%)	141 (60.3%)	1.33	0.91–1.94	0.142	1.32	0.90–1.94	0.153
Ischemic heart disease; *n* (%)	73 (31.5%)	61 (26.1%)	1.30	0.87–1.95	0.198	1.25	0.83–1.88	0.287
Malignancy; *n* (%)	35 (15.1%)	36 (15.4%)	0.98	0.59–1.62	0.929	0.96	0.58–1.60	0.888
Chronic renal failure; *n* (%)	43 (18.5%)	53 (22.6%)	0.78	0.50–1.22	0.272	0.74	0.47–1.17	0.202
Obesity; *n* (%)	77 (33.2%)	67 (28.6%)	1.24	0.84–1.84	0.287	1.25	0.84–1.85	0.277

[a]Adjusted for age and sex.

[b]OR per 10-year increase in age.

incidence of COVID-19 in psoriasis and other inflammatory dermatoses is yet to be delineated.[8] However, it was assumed that SARS-CoV-2 can penetrate the body through defective skin barrier[9] and that the skin can act as a reservoir for the virus spread.[10,11]

Raiker et al. compared COVID-19 related outcomes in patients with psoriasis ($n = 2288$) relative to those without it ($n = 2288$). Psoriasis was not associated with an elevated risk of severe COVID-19, mechanical ventilation, hospitalization, or mortality.[12] Correspondingly, another epidemiological study revealed that inflammatory skin diseases were associated with an apparently milder course of COVID-19, necessitating less frequent mechanical ventilation (OR, 0.19; $p < 0.001$).[8] Utilizing a larger study population, the current study emphasizes that patients with psoriasis are not predisposed to worse outcomes of COVID-19. These findings are of particular importance given that some patients with psoriasis undergo immune-modulating therapy that might render them more susceptible to infections. Still,

psoriasis is not associated with less favorable outcomes of COVID-19. The pathomechanism of this phenomenon is yet to be thoroughly delineated. It has been hypothesized that the response of the already activated immune system in lesional skin of psoriasis might lead to different immunologic rates of viral response. It is well-established that early interferon response results in milder course of COVID-19,[13] thus accounting for the non-inferior outcomes of COVID-19 in psoriasis and other inflammatory dermatosis (despite the putative exposure to immune-modulating and immunosuppressive drugs).

The current study utilizes a large-scale population-based sample to investigate a highly intriguing and clinically relevant question. Relying on molecular tests and the national death registry, study outcomes are highly reliable. Although the study did not adjust for exposure to immune-modulating drugs, this should not have altered the study outcomes. Patients with psoriasis were not more susceptible to COVID-19 complications despite this treatment modality. While the large sample size and sufficient follow-up provide generalizability, further studies assessing patients originating from different ethnicities are necessary.

In conclusion, the current population-based study sheds light on COVID-19-related outcomes among patients with psoriasis followed for a relatively extended period. Patients with psoriasis in Israel are at a slightly increased risk of contracting SARS-CoV-2 infection, but do not go through an elevated hazard of the disease complications. These findings should be further validated in other study populations.

AUTHOR CONTRIBUTIONS

K.K., Y.S., and A.D.C. performed the research. K.K., Y.S., and A.D.C. designed the research study. E.O., D.T.B., O.W., and E.S. contributed essential reagents or tools. K.K., Y.S., and A.D.C. analyzed the data. K.K. and A.D.C. wrote the paper.

ETHICAL APPROVAL

The study was approved by the institutional review board (IRB) of Ben-Gurion University in accordance with the declaration of Helsinki (approval code: 0212-17-COM).

CONFLICT OF INTEREST

ADC served as an advisor, investigator, or speaker for Abbvie, BI, Dexcel Pharma, Janssen, Novartis, Perrigo, Pfizer, and Rafa. None of the other authors have any conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

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

ORCID

Eran Shavit https://orcid.org/0000-0003-2397-6316

REFERENCES

1. Lake MA. What we know so far: COVID-19 current clinical knowledge and research. *Clin Med (Lond)*. 2020;20:124-127.
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506.
3. Najm A, Alunno A, Mariette X, et al. Pathophysiology of acute respiratory syndrome coronavirus 2 infection: a systematic literature review to inform EULAR points to consider. *RMD Open*. 2021;7(1):e001549. doi:10.1136/rmdopen-2020-001549
4. Ogawa E, Sato Y, Minagawa A, Okuyama R. Pathogenesis of psoriasis and development of treatment. *J Dermatol*. 2018;45(3):264-272.
5. Jang DI, Lee AH, Shin HY, et al. The role of tumor necrosis factor alpha (TNF-α) in autoimmune disease and current TNF-α inhibitors in therapeutics. *Int J Mol Sci*. 2021;22(5):1-16.
6. Kridin K, Schonmann Y, Tzur Bitan D, et al. Coronavirus disease 2019 (COVID-19)-associated hospitalization and mortality in patients with psoriasis: a population-based study. *Am J Clin Dermatol*. 2021;22:709-718.
7. Tan EH, Sena AG, Prats-Uribe A, et al. COVID-19 in patients with autoimmune diseases: characteristics and outcomes in a multinational network of cohorts across three countries. *Rheumatology (Oxford)*. 2021;60(SI):SI37-SI50.
8. Patrick MT, Zhang H, Wasikowski R, et al. Associations between COVID-19 and skin conditions identified through epidemiology and genomic studies. *J Allergy Clin Immunol*. 2021;147(3):857-869.e7.
9. Xu Q, Chen L, Zhang L, et al. Pre-existing cutaneous conditions could increase the risk for SARS-COV-2 infection. *bioRxiv*. 2020. 10.1101/2020.06.30.181297
10. Tao J, Song Z, Yang L, Huang C, Feng A, Man X. Emergency management for preventing and controlling nosocomial infection of the 2019 novel coronavirus: implications for the dermatology department. *Br J Dermatol*. 2020;182(6):1477-1478.
11. Elgarhy LH, Salem ML. Could injured skin be a reservoir for SARS-CoV-2 virus spread? *Clin Dermatol*. 2020;38(6):762.
12. Raiker R, Pakhchanian H, Patel VA. 254 COVID-19 related outcomes in psoriasis and psoriasis arthritis patients. *J Invest Dermatol*. 2021;141(5):S45.
13. Park A, Iwasaki A. Type I and type III interferons - induction, signaling, evasion, and application to combat COVID-19. *Cell Host Microbe*. 2020;27(6):870-878.

How to cite this article: Kridin K, Schonmann Y, Onn E, et al. Nineteen months into the pandemic, what have we learned about COVID-19-related outcomes in patients with psoriasis? *J Cosmet Dermatol*. 2022;00:1-5. doi: 10.1111/jocd.15351