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

response to biologics were reported. TNF inhibitors were used without concomitant medications in 50.0% (6 of 12) of cases, which achieved CR with a mean resolution period of 12.0 days (range, 4-18 days). When used concomitantly with corticosteroid (8.3%, 1 of 12), the patient died because of disease severity. Concomitant intravenous immunoglobulin therapy (IVIG) was reported in 1 case (8.3%, 1 of 12), which achieved CR. When used concomitantly with corticosteroids and IVIG combination (16.7%, 2 of 12), both patients achieved CR. Lastly, 2 cases (16.7%) achieved CR and PR, respectively, with a combination of corticosteroids and cyclosporine.

TNF inhibitors were the only biologic treatments reported for pediatric SJS/TEN. Although children have a better prognosis than adults with SJS/TEN, mortality has been reported in up to 16% according to a nationwide database.[2] In the cases reported, only 1 patient had a fatal outcome associated with TNF inhibitor treatment.[2]

The pathogenesis of SJS/TEN is driven by TNF expression by drug-specific T cells in response to drug or drug-peptide complexes.[3] TNF inhibitors can halt disease progression by interfering with pathways that induce epithelial cell death.[3] An RCT comparing the effectiveness of etanercept with that of corticosteroids in an adult population found significant decreases in skin healing time, gastrointestinal hemorrhage incidence, and TNF/granulysin secretions along with increases in T-regulatory cell populations.[4] There has been evidence of elevated interleukin-15 levels being significantly correlated with disease severity and mortality in SJS/TEN, suggesting another potential target for biologic treatment.[5]

This systematic review was limited by small sample size, reporting bias, exclusion of non–English-language studies, and low evidence of included studies, affecting the generalizability of findings. Further trials specific to pediatric SJS/TEN treatments are needed.

Muskaan Sachdeva, BHSc,[a] Asfandyar Mufti, MD,[b] Patrick Kim, BHSc,[c] Khalad Maliyar, BA,[a] and Cathryn Sibbald, MD, MSc, FRCPC, FAAD[b,d,e]

From the Faculty of Medicine[a]; Division of Dermatology, Department of Medicine[b]; Section of Dermatology, Division of Pediatric Medicine, The Hospital for Sick Children[d]; and Division of Dermatology, Department of Medicine, Women's College Hospital,[e] University of Toronto, Canada and Michael G. DeGroote School of Medicine, McMaster University.[c]

Funding sources: None.

IRB approval status: Not applicable.

Reprints not available from the authors.

Correspondence to: Cathryn Sibbald, MD, MSc, FRCPC, FAAD, Staff Physician, Section of Dermatology, Division of Paediatric Medicine, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario, Canada M5G 1X8

E-mail: cathryn.sibbald@sickkids.ca

Conflicts of interest

None disclosed.

REFERENCES

1. Lerch M, Mainetti C, Beretta-Piccoli BT, Harr T. Current perspectives on Stevens-Johnson syndrome and toxic epidermal necrolysis. *Clin Rev Allergy Immunol*. 2018;54(1):147-176.
2. Hsu DY, Brieva J, Silverberg NB, Paller AS, Silverberg JI. Pediatric Stevens-Johnson syndrome and toxic epidermal necrolysis in the United States. *J Am Acad Dermatol*. 2017;76(5):811-817.e4.
3. Hunger RE, Hunziker T, Buettiker U, et al. Rapid resolution of toxic epidermal necrolysis with anti-TNF-alpha treatment. *J Allergy Clin Immunol*. 2005;116:923-924.
4. Wang C-W, Yang L-Y, Chen C-B, et al. Randomized, controlled trial of TNF-α antagonist in CTL-mediated severe cutaneous adverse reactions. *J Clin Invest*. 2018;128(3):985-996.
5. Su S-C, Mockenhaupt M, Wolkenstein P, et al. Interleukin-15 Is associated with severity and mortality in Stevens-Johnson Syndrome/toxic epidermal necrolysis. *J Invest Dermatol*. 2017;137(5):1065-1073.

https://doi.org/10.1016/j.jaad.2020.12.080

Risk of respiratory infection in patients with plaque psoriasis

To the Editor: Understanding the risk of respiratory infection in psoriasis and the impact of immunosuppressive treatment is important to inform preventive measures for COVID-19. Therefore, we report data on respiratory infection in patients with psoriasis from a study linking an inception cohort[1] to population-based health care registers on outpatient care, inpatient care (The National Patient Register[2]), and prescriptions (The Prescribed Drug Register[3]).

The Stockholm Psoriasis Cohort enrolled patients with new-onset psoriasis and population controls, predominately in Stockholm, Sweden, between 2001 and 2005.[1] The study had ethics approval, and participants provided informed consent (Appendix

Table I. Patient characteristics* of patients and controls

	Controls	Mild psoriasis	Moderate-to-severe psoriasis
Subjects (n)	835	339	187
Male sex n (%)	482 (42)	189 (44)	99 (47)
Age at index, mean (SD)	45 (15)	43 (16)†	45 (18)
BMI, median (IQR)	24 (22, 27)	25 (22, 27)	25 (22, 29)†‡
Current smoking n (%)	155/827 (19)	108/336 (32)†‡	83/185 (45)‡§
Frequency of alcohol intake n (%)			
Never	65/819 (8)	39/331 (12)	38/176 (22)
Once per month	198/819 (24)	73/331 (22)	26/176 (15)
Two to four times per month	317/819 (39)	131/331 (40)	59/176 (34)
Two to three times per week	196/819 (24)	77/331 (23)	38/176 (22)
Four time per week or more	43/819 (5)	11/331 (3)	15/176 (9)
Comorbidity n (%)			
Diabetes	18/812 (2)	13/339 (4)	5/187 (3)
Neoplasm	35/810 (4)	17/295 (6)	10/147 (7)
Stroke	6/810 (1)	2/298 (1)	1/147 (1)
Myocardial infarction	17/809 (2)	5/297 (2)	6/147 (4)
Asthma	80/809 (10)	25/295 (8)	17/148 (11)
Hay fever	76/805 (9)	30/293 (10)	10/148 (7)
Thyroid disease	32/807 (4)	22/295 (7)†‡	7/145 (5)
Hepatitis	13/806 (2)	5/297 (2)	2/147 (1)
Inflammatory bowel disease	12/809 (1)	3/298 (1)	3/147 (2)

IQR, Interquartile range; *SD*, standard deviation.

*With the exception of age at indexation, all characteristics were measured at enrolment.

†$P < .05$ versus controls.

‡Standardized mean difference greater than 0.15 versus controls. Mild psoriasis was defined as PASI below five in the absence of phototherapy and systemics, and moderate-to-severe psoriasis was defined as PASI above five or treatment with phototherapy and systemics.

§$P < .001$ versus controls.

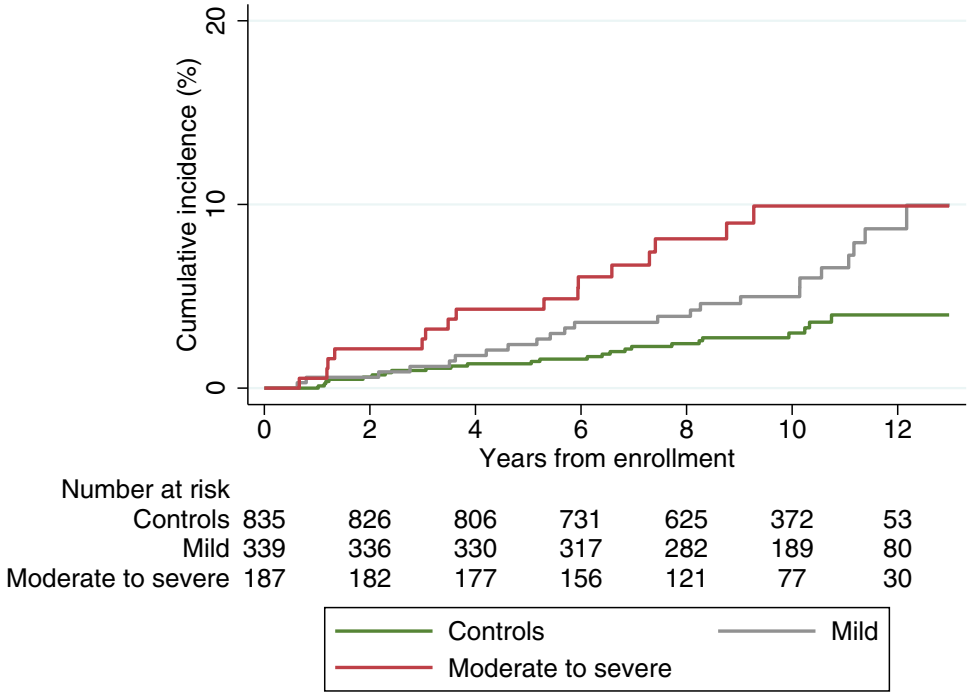

Fig 1. Cumulative incidence of respiratory infection defined as a diagnosis in specialist outpatient care for controls, patients with mild disease at onset, and patients with moderate- to-severe disease at onset.

1 for information on the study; available at https://data.mendeley.com/datasets/vh2k3nvsn9/1).

For the analyses at hand, the exposures were mild and moderate-to-severe plaque psoriasis. In a separate analysis, immunosuppressive treatment for psoriasis as observed in the Prescribed Drug Register was a time-dependent exposure. The outcomes in the study were the first respiratory infection after onset from the National Patient Register; and prescriptions of antibiotics and antivirals used to treat respiratory infection from the Prescribed Drug Register (see Supplementary Table I (Table S2.1). Supplementary Table II (Table S2.2), and Supplementary Table III (Table S2.3); available at https://data.mendeley.com/datasets/vh2k3nvsn9/1). Covariates comprised sex, age, and characteristics associated with both respiratory infections and psoriasis for which the standardized mean difference between groups exceeded 0.15.

Patients with mild and moderate-to-severe psoriasis were compared with controls. Cox Proportional Hazard models[4] were used to compare time to first diagnosis, and negative binomial regression models[5] were used to compare the incidence of prescriptions between groups. We also compared the incidence of prescriptions of antibiotics and antivirals for respiratory infections when patients were treated with immunosuppressive treatment compared with when they were not.

In total, 339 patients with mild plaque psoriasis, 187 patients with moderate-to-severe plaque psoriasis, and 835 controls were included. Among the 526 patients, 121 were treated with immunosuppressants. Baseline characteristics are presented in Table I.

The cumulative incidence of respiratory infection is presented in Fig 1. Follow-up and incidence are presented Supplementary Table 4 (Table S3.1; available at https://data.mendeley.com/datasets/vh2k3nvsn9/1). In multivariable analyses psoriasis was associated with increased risk of inpatient or specialist outpatient diagnosed respiratory infection: hazard ratios of 2.0 (95%confidence interval [CI], 1.1-3.6) for patients with mild disease; and 2.5 (95% CI, 1.3-4.9) for patients with moderate-to-severe disease. In multivariable analysis of prescriptions, mild disease was associated with an incidence rate ratio of 1.3 (95% CI, 1.1-1.5) and moderate-to-severe disease with an incidence rate ratio of 1.5 (95% CI, 1.2-1.9).

The 121 patients treated with immunosuppressants were on average exposed to immunosuppressants for 3.1 years and unexposed to immunosuppressants for 5.4 years. The incidence of infection per person-year on and off immunosuppressive treatment was estimated at 0.31 and 0.29, respectively ($P = .31$).

Psoriasis is associated with increased risk of respiratory infection independently of known risk factors for infection, with moderate-to-severe psoriasis conferring higher risk than mild psoriasis. Immunosuppressive treatment did not further increase the risk for respiratory infection. These findings can inform risk mitigation strategies and preventive efforts for patients with psoriasis during the COVID-19 pandemic. Limitations include data on infections not coming to clinical attention and generalizability.

Axel Svedbom, MSC,[a] Lotus Mallbris, MD, PhD,[a] and Mona Ståhle, MD, PhD[a,b]

From the Division of Dermatology and Venereology, Department of Medicine,[a] and the Dermatology and Venereology Clinic,[b] Karolinska University Hospital, Stockholm, Sweden.

Funding sources: This study was funded by Stockholm County Council, the Swedish Medical Research Council, Hudfonden and the Swedish Psoriasis Association.

IRB approval status: Approved. DNR: 00-448.

Reprints not available from the authors.

Correspondence to: Axel Svedbom, MSC, B2:01, Karolinska Universitetssjukhuset, Solna 171 76 Stockholm, Sweden

E-mail: axel.svedbom@ki.se

Conflicts of interest

Axel Svedbom is an employee of ICON plc, a contract research organization. Lotus Mallbris is an employee of Eli Lilly and Company. Mona Ståhle has received honoraria for serving as an advisor and for participating in symposia arranged by Abbvie, Novartis, Pfizer, Eli Lilly, Janssen-Cilag, and Leo Pharma.

REFERENCES

1. Mallbris L, Larsson P, Bergqvist S, Vingard E, Granath F, Stahle M. Psoriasis phenotype at disease onset: clinical characterization of 400 adult cases. *J Invest Dermatol*. 2005;124:499-504.
2. Ludvigsson JF, Andersson E, Ekbom A, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health*. 2011;11:450.
3. Wettermark B, Hammar N, Fored CM, et al. The new Swedish Prescribed Drug Register—opportunities for pharmacoepidemiological research and experience from the first six months. *Pharmacoepidemiol Drug Saf*. 2007;16:726-735.
4. Cox. Regression models and life tables. *J R Stat Soc*. 1972;34:187-220.
5. Lawless JF. Negative binomial and mixed Poisson regression. *Can J Stat*. 1987;15:209-225.

https://doi.org/10.1016/j.jaad.2020.12.083