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Conflicts of interest

Dr Wu is or has been an investigator, consultant, or speaker for AbbVie, Amgen, Arcutis, Arista 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, Amgen, Leo Pharma, Galapagos 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, Amgen, and Eli Lilly. Dr Ge and Authors Martin, Liu, and Thatiparthi have no conflicts of interest to declare.

REFERENCES

1. COVID-19 Research Database. COVID-19 Research Database Consortium. Accessed May 21, 2021. <https://covid19researchdatabase.org>
2. Sanyaolu A, Okorie C, Marinkovic A, et al. Comorbidity and its impact on patients with COVID-19. *SN Compr Clin Med*. 2020; 2(8):1069-1076. <https://doi.org/10.1007/s42399-020-00363-4>
3. Yang JM, Koh HY, Moon SY, et al. Allergic disorders and susceptibility to and severity of COVID-19: a nationwide cohort study. *J Allergy Clin Immunol*. 2020;146(4):790-798. <https://doi.org/10.1016/J.JACI.2020.08.008>
4. Thibodeaux Q, Smith MP, Ly K, Beck K, Liao W, Bhutani T. A review of dupilumab in the treatment of atopic diseases. *Hum Vaccin Immunother*. 2019;15(9):2129-2139. <https://doi.org/10.1080/21645515.2019.1582403>
5. de Paula CB, de Azevedo ML, Nagashima S, et al. IL-4/IL-13 remodeling pathway of COVID-19 lung injury. *Sci Rep*. 2020; 10(1):1-8. <https://doi.org/10.1038/s41598-020-75659-5>

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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

Table I. Hospital admissions in 2019 compared with those in 2020

Variable	2019	2020	P values
Treatment days per year	17.520	15.608	.140
Total, N	2.411	2.231	<.001*
Male, n (%)	1.302 (54)	1.206 (54)	>.99
Female, n (%)	1.109 (46)	1.025 (45.9)	>.99
Age, mean (SD) in years	64.78 (19.14)	64.76 (19.07)	>.99
Stratified by age (years), n in years (%)			
0-17	30 (1.2)	25 (1.1)	
18-35	208 (8.6)	202 (9.1)	
36-49	251 (10.4)	232 (10.4)	
50-64	552 (22.9)	478 (21.4)	
65-74	422 (17.5)	431 (19.3)	
75-84	625 (27)	617 (28)	
85-94	635 (26.3)	583 (26.1)	
95+	23 (1)	24 (1.1)	
<65 vs ≥65	1370 (56.8)	1294 (58)	>.99
Hospital stay, median in days	6.02	5.88	
Disease classification (ICD-10), n (%)			
NMSC (C44)	684 (28.4)	615 (27.6)	>.99
Malignant Melanoma (C43)	265 (10.9)	253 (11.3)	>.99
Sentinel lymph node extirpation (OPS 05-401)	120 (5)	140 (6)	>.99
Radical lymphadenectomy (OPS 05-404)	17 (<1)	17 (<1)	>.99
Secondary and unspecified malignant neoplasm of lymph nodes (C77)	29 (1.2)	41 (1.8)	>.99
Immunotherapy associated adverse events (K52.1, K71.6, K75.4, E23.1, R50.6)	6 (0.2)	29 (1.3)	.001*
Hidradenitis suppurativa (L73.2)	56 (2.3)	59 (2.6)	>.99
Eczema, dermatitis, prurigo (L20, L28, L30)	185 (7.7)	156 (7.0)	>.99
Psoriasis (L40)	158 (6.6)	115 (5.2)	.798
Herpes zoster (B02)	59 (2.4)	93 (4.2)	<.05*
Erysipelas (A46)	44 (1.8)	43 (1.9)	>.99
Ulceration of the lower leg (I83, I89, L97, I70)	182 (7.5)	93 (4.2)	<.001*
Pyoderma gangraenosum (L88)	23 (1.0)	19 (0.9)	>.99
Pemphigus foliaceus/vulgaris (L10)	8 (0.3)	6 (0.3)	>.99
Bullous pemphigoid (L12)	60 (2.5)	55 (2.5)	>.99
Desensitization to allergens (Z51.6)	176 (7.3)	138 (6.2)	>.99

Statistical analysis was performed with R (version 4.0.4). Categorical variables were tested with the chi-square test, and continuous variables with a *t* test. The Holm method was used for the *P* value adjustment.

NMSC, Nonmelanoma skin cancer.

*Level of significance is $P < .05$.

have led to delays.⁴ Although there were no differences in mean T stages in melanoma patients, we observed a higher proportion of sentinel lymph node extirpations in 2020 (2019: 45.6%, 2020: 47.4%; $P = .462$) (Table D). The increased number of immune-related adverse events ($P = .001$, Table I) likely mirrors the growing patient numbers treated with combined immunotherapy in stage IV melanoma.

Our day hospital allows patient treatment over several hours for skin disorders of moderate intensity. We had a 6% decline in day hospital visits ($P < .05$) and reduced patient numbers ($P < .001$) in almost all diagnosis groups (Table II). We also noticed around 30% ($P > .99$) fewer day hospital visits for patients with epidermolysis bullosa, a rare,

inherited skin fragility disease treated at our Skin Fragility Center, a specialized day hospital (Table II). Our data suggest that the pandemic primarily affected treatment options for patients with inflammatory and rare skin disorders, whereas patients with infectious and oncologic indications were still sufficiently treated. Limitations of this study are its monocentric character and the fact that mildly affected patients were actively short-term postponed in the early phase of the pandemic. Overall, adopting security measures (questionnaires, polymerase chain reaction testing, and visitor restrictions) prevented a significant negative impact for geriatric admissions. Nonetheless, enabling easy access and emphasizing high-quality medical and telemedical care for patients, especially those with inflammatory skin

Table II. Day hospital treatments in 2019 compared with those in 2020

Variable	2019	2020	P values
Treatment days	5.100	4.782	<.05*
Total, N	876	688	<.001*
Male, n (%)	427 (48.7)	324 (47.1)	>.99
Female, n (%)	449 (51.3)	362 (52.6)	>.99
Age, mean (SD), in years	46.85 (22.75)	48.71 (22.68)	.975
Stratified by age (years), n (%)			
0-17	115 (13.1)	73 (10.6)	
18-35	157 (17.9)	140 (20.3)	
36-49	142 (16.2)	104 (15.1)	
50-64	243 (27.7)	172 (25.0)	
65-74	122 (13.9)	108 (15.7)	
75-84	84 (9.6)	76 (11.0)	
85-94	9 (1.0)	13 (1.9)	
95+	4 (0.5)	2 (0.3)	
<65 vs ≥65	219 (25.0)	199 (28.9)	.923
Disease classification (ICD-10), n (%)			
Eczema, dermatitis, prurigo (L20, L28, L30)	194 (22.1)	170 (24.7)	>.99
Psoriasis (L40)	140 (16.0)	104 (15.1)	>.99
Epidermolysis bullosa (Q81)	126 (14.4)	86 (12.5)	>.99
Lichen planus (L43)	5 (0.6)	8 (1.2)	>.99
Cutaneous T-cell lymphoma (C84)	6 (0.7)	8 (1.2)	>.99
Pemphigus foliaceus (L10)	1 (<1)	1 (<1)	>.99
Bullous pemphigoid (L12)	6 (0.7)	9 (1.3)	>.99

Statistical analysis was performed with R (version 4.0.4). Categorical variables were tested with the chi-square test, continuous variables with a *t* test. The Holm method was used for the *P* value adjustment.

*Level of significance *P* < .05

diseases, could reduce long-term complications and prevent irreversible damage.⁵

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Conflicts of interest

None disclosed.

REFERENCES

1. Ansoorge C, Miocic JM, Schauer F. Skin diseases in hospitalized geriatrics: a 9-year analysis from a University Dermatology Center in Germany. *Arch Dermatol Res.* June 2, 2021. <https://doi.org/10.1007/s00403-021-02244-9>
2. Busse R, Nimptsch U. COVID-19 pandemic: historically low bed occupancy rate. *Dtsch Arztebl Int.* Article in German. 2021; 118(10):A-504.

3. Schmidt SAJ, Sørensen HT, Langan SM, Vestergaard M. Perceived psychological stress and risk of herpes zoster: a nationwide population-based cohort study. *Br J Dermatol.* 2021;185(1):130-138.
4. Marson JW, Maner BS, Harding TP, et al. The magnitude of COVID-19's effect on the timely management of melanoma and nonmelanoma skin cancers. *J Am Acad Dermatol.* 2021; 84(4):1100-1103.
5. Miller RC, Stewart CR, Lipner SR. Retrospective study of trends in dermatology telemedicine and in-person visits at an academic center during COVID-19. *J Am Acad Dermatol.* 2021;84(3):777-779.

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Comparison of constitutional and dermatologic side effects between COVID-19 and non-COVID-19 vaccines: Review of a publicly available database of vaccine side effects



To the Editor: In December 2020, the US Food and Drug Administration authorized the emergency use of 2 COVID-19 vaccines. The rapid development and authorization of these vaccines raised safety concerns among the general population.¹ In the Pfizer/BioNTech BNT162b2 messenger RNA (Pfizer/BioNTech) and Moderna messenger RNA-1273 SARS-CoV-2 (Moderna) COVID-19 vaccines phase 3 clinical trials, local and systemic reactions were reported.^{2,3}

We sought to compare constitutional and dermatologic postimmunization side effects of the COVID-19 vaccines versus the hepatitis B virus (HBV) and seasonal influenza (Flu) vaccines on the Vaccine Adverse Event Reporting System (VAERS), a national, self-reported surveillance database.⁴

HBV and Flu (seasonal flu recombinant and inactivated) vaccines were selected because they are 2 established nonlive vaccines that have been administered to the general population for decades. For both COVID-19 vaccines, data were obtained from their rollout in December 2020 until February 26, 2021, whereas for the HBV and Flu vaccines, data were obtained from 1990 until February 26, 2021. Only constitutional and dermatologic side effects with reported rates $\geq 1\%$ for all 4 vaccines were included. Data were analyzed using the χ^2 test in R-4.0.3. At the time the data from VAERS were obtained, Pfizer/BioNTech and Moderna vaccines were approved for adults aged ≥ 16 and 18 years, respectively. The HBV and Flu vaccines are approved for infants since birth and for ages of ≥ 6 months old, respectively.

In our research, reported constitutional side effects were higher for the Moderna and Pfizer/

BioNTech when compared with the HBV and Flu vaccines. The dermatologic side effects reported for Moderna were greater than that of HBV but not Flu. However, Pfizer/BioNTech did not have a statistically significantly higher percentage of dermatologic side effects when compared with HBV or Flu. When comparing Moderna and Pfizer/BioNTech, the majority of constitutional and dermatologic side effects were higher for Moderna in terms of percent of cases reported (Table I).

Of note, Moderna had a significantly higher percentage of injection site reactions (ie, pain, erythema, swelling, and warmth) compared with Pfizer/BioNTech and HBV but not Flu. For the Pfizer/BioNTech vaccine, injection site reactions were lower than for the other vaccines.

In both Pfizer/BioNTech and Moderna trials, younger patients (16-55 and 18 to <65 years old, respectively) experienced more frequent and severe side effects, possibly due to their having a more robust immune system and consequently a higher degree of reactogenicity.^{2,3} Overall, both COVID-19 vaccines have favorable safety profiles and proven efficacy.^{2,3} It is vital for physicians to encourage appropriate vaccination of our patients. Our study may help address patients' concerns regarding the COVID-19 vaccines. Future studies should assess whether similar results are observed in children in whom the vaccine was approved recently. Limitations to our study are the incomplete capture and reporting from the VAERS database, which is self-reported and voluntary, although VAERS has previously successfully detected safety signals for other vaccines such as intussusception for the rotavirus vaccine.⁵ Finally, the population receiving the COVID-19 vaccine may not match those getting the Flu and HBV vaccines.⁴

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