A Nationwide Increase in the Incidence of Atopic Dermatitis and the Possible Influence of the COVID-19 Pandemic

Johnatan Nissan MD[1,3,6], Michal Baum MD[2,6], Abdulla Watad MD[1,3,6], Yoav Elizur MD[1,3,6], Gilad Halpert PhD[1,3], Arnon Dov Cohen MD[4,5], and Howard Amital MD MHA[1,3,6]

[1]Internal Medicine B, Sheba Medical Center, Tel Hashomer, Israel
[2]Internal Medicine C, Sheba Medical Center, Tel Hashomer, Israel
[3]Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel Hashomer, Israel
[4]Clalit Health Services, Tel Aviv, Israel
[5]Siaal Research Center for Family Medicine and Primary Care, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva, Israel
[6]Gray Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel

ABSTRACT **Background:** The association between new-onset atopic dermatitis (AD) and the coronavirus disease 2019 (COVID-19) pandemic was scarcely documented in the literature.

Objectives: To evaluate the incidence of AD in a large nation-wide cohort over 6 years, focusing on changes in incidence following the onset of the COVID-19 pandemic.

Methods: This retrospective cohort study included all members of the largest HMO in Israel (n=4.8 million) from 2017 to 2022. Patients with newly diagnosed AD were identified using the ICD-10 code for AD (L20). Incidence rates were calculated as the number of new diagnoses per 1000 person-years. The pre-COVID period was 1/2017 to 1/2020, and post-COVID 2/2020 to 12/2022. Age-adjusted incidence rates were calculated based on the World Health Organization's standard population.

Results: The overall crude incidence of AD across the study period was 3.38/1000 person-years (PYs). From 2017 to 2022, there was a 36.97% increase in the crude incidence and a 40.44% increase in the age-adjusted incidence, with a mean annual incidence change of +6.5% and +7.1%, respectively. Both crude and adjusted annual incidence increases were significant ($P < 0.001$, $R^2 = 0.98$; $P < 0.001$, $R^2 = 0.99$, respectively). The incidence of AD at the follow-up before the COVID-19 pandemic was 3.07/1000 PYs, and after was 3.71/1000 PYs.

Conclusions: We observed a significant and nearly consistent annual increase in AD incidence from 2017 to 2022, across various sex and age groups. Further research is needed to explore the impact of the COVID-19 pandemic on rising trends in AD incidence.

IMAJ 2025; 27: 615–620

KEY WORDS: atopic dermatitis, autoimmunity, coronavirus disease 2019 (COVID-19), inflammation, vaccination

The initial outbreak of the coronavirus disease 2019 (COVID-19) was in late 2019. The World Health Organization (WHO) declared COVID-19 a global pandemic in March 2020. In addition to the burden that COVID-19 disease generated, it also had an impact on the prevalence of various immune-mediated disorders [1].

Atopic dermatitis (AD) is a common chronic inflammatory skin disease with complex and multifactorial pathophysiology and multiple risk factors, including genetic and environmental risk factors such as a Western lifestyle, air pollution, and stress [2,3]. It has also been postulated that a previous severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection may also trigger AD [4].

The literature regarding the possible association between new-onset AD and COVID-19. As COVID-19 was a major public health crisis, it is important to investigate its influence on new-onset AD to better understand its complexity and pathophysiology.

We assessed the incidence of AD in a large population-based nation-wide cohort and evaluated the incidence change following the COVID-19 pandemic.

PATIENTS AND METHODS

DATA SOURCE

The data were extracted from the Clalit Health Services (CHS) extensive computerized database. CHS serves about 4.8 million members, more than half of Israel's population, and is Israel's largest health maintenance

organization. CHS's population is ethnically, geographically, and socioeconomically diverse and has continuous real-time input operating systems. The database is undergoing constant data validation, including logistic tests, such as matching diagnoses from several sources. Its validity was confirmed to be high in a previous study [5].

POPULATION AND STUDY DESIGN

This retrospective cohort study included all members of CHS. The data were collected from 1 January 2017 until 31 December 2022. Data mining methods were performed to collect relevant diagnoses and demographic information. The diagnosis was extracted using the ICD-9 code for AD (L20).

VARIABLES

Incidence was demonstrated as the number of new diagnoses per 1000 person-years (PYs). To compute the incidence of AD, the main outcome, the monthly number of new AD diagnoses in each sex/age group, was divided by the monthly sum of person-years in the equivalent sex/age group members in the CHS. The pre-COVID period was defined as the follow-up time from 01/2017 until 01/2020. The post-COVID time was defined as 02/2020 (the month with the first known case of infection in Israel) until 12/2022. Age-adjusted incidence was calculated based on the WHO world standard population [6].

STATISTICAL ANALYSIS

Annual incidence trend significance was calculated using simple linear regression, with the year as the independent variable and the incidence as the dependent variable. The coefficient of determination was used to assess the proportion of the variation of the incidence variable. We calculated 95% confidence intervals (95%CIs) to estimate parameter precision and uncertainty. All *P*-values were two-tailed, and the alternative hypothesis was considered significant if $P \leq 0.05$. Statistical analysis and data visualization were performed using Python v3.10 (Python Software Foundation) and Microsoft Excel™ 2019, Version 2401 (Microsoft® Corporation, Redmond, WA, USA)

ETHICS

This study was approved by the CHS Ethics Committee (Approval number 0212-17-COM).

RESULTS

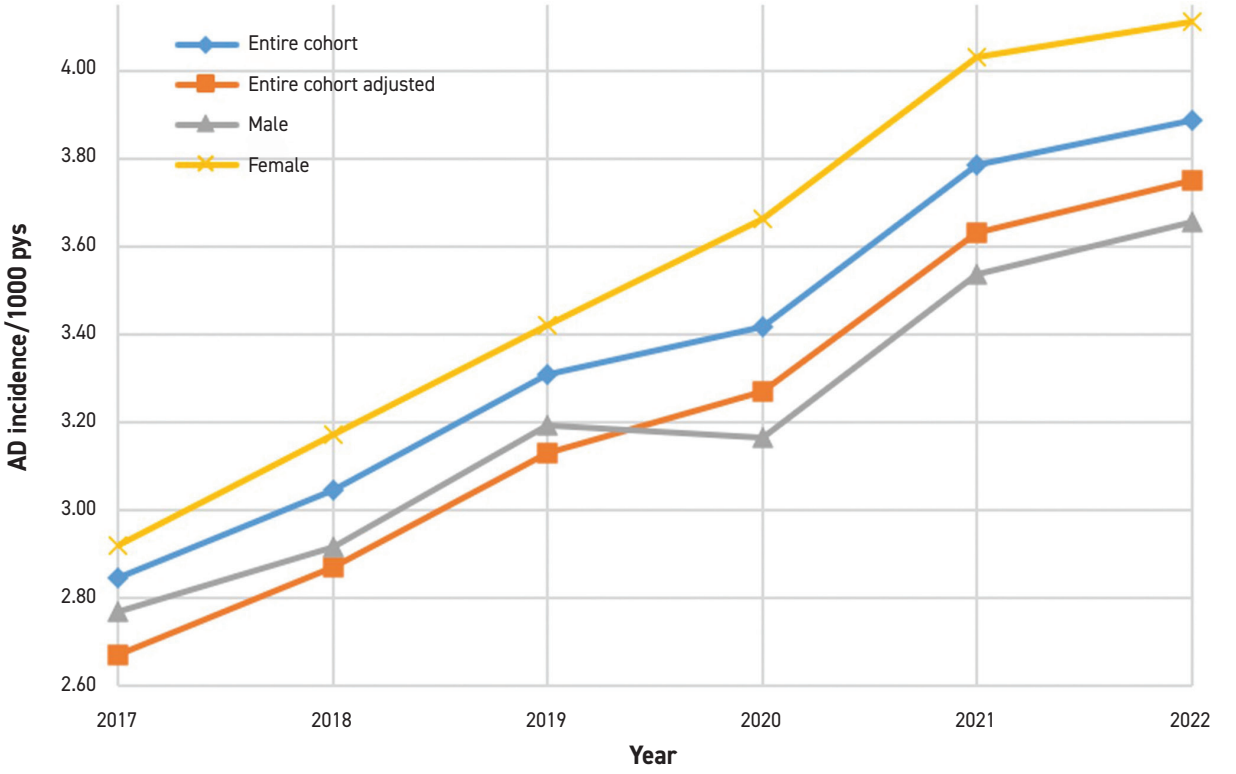
At the beginning of the follow-up time, 01/2017, there were a total of 4.425 million individuals (50.98% females) in the cohort. At the end of the follow-up period, 12/2022, the cohort included a total of 4.817 million individuals (50.72% females). Cohort age group distribution at the beginning and end of the follow-up time is presented in Table 1. The crude incidence of AD during the entire follow-up time was 3.38/1000 PYs. The incidence among females and males was 3.55/1000 PYs and 3.20/1000 PYs, respectively. The annual number of new cases, crude and age-adjusted incidence, sex-specific incidence, and incidence change of AD are presented in Table 1 and Figure 1.

There was a 36.97% and 40.44% increase in the crude and age-adjusted incidence, respectively, from 2017 to 2022, and a mean annual incidence change of +6.5% and +7.1%, respectively. Both crude and adjusted annual incidence increases were significant ($P < 0.001$, $R^2 = 0.98$; $P < 0.001$, $R^2 = 0.99$, respectively). Among males and females, the change during the follow-up time was 32.12% and 40.75%, respectively, and the mean annual change was +5.46% and 7.12%, respectively. The age group's incidence through the study period is presented in Figure 2, and the age group incidence by sex is presented in Table 2. The median age of diagnosis of AD of the entire cohort was 8.0 (mean ± SD: 18.63 ± 22.04) years old,

Table 1. Annual incidence of atopic dermatitis per 1000 person-years 2017–2022

Year	New cases	Crude		Age-adjusted		Female crude		Male crude	
		Incidence	Change	Incidence	Change	Incidence	Change	Incidence	Change
2017	12,677	2.84	–	2.67	–	2.92	–	2.77	–
2018	13,774	3.04	7%	2.87	7.5%	3.17	8.6%	2.91	5.1%
2019	15,176	3.31	8.8%	3.13	9.1%	3.42	7.9%	3.19	9.6%
2020	15,923	3.42	3.3%	3.27	4.5%	3.66	7%	3.16	-0.9%
2021	17,868	3.79	10.8%	3.63	11%	4.03	10.1%	3.54	10.1%
2022	18,592	3.89	2.6%	3.75	3.3%	4.11	2%	3.66	3.4%

Figure 1. Annual incidence of atopic dermatitis per 1000 person-years 2017–2022
AD = atopic dermatitis, PY = person-years



and 5 (16.88 ± 22.37) and 10 (20.15 ± 21.63) years old among males and females, respectively. The median age of diagnosis by sex and year is demonstrated in Figure 1.

The incidence of AD at the follow-up time before the COVID-19 pandemic was 3.07/1000 PYs, and the incidence after was 3.71/1000 PYs. The AD incidence among females and males increased from 3.17 and 2.97/1000 PYs before the pandemic to 3.96 and 3.46/1000 PYs after the COVID-19 pandemic. The incidence of AD before and after the COVID-19 pandemic among different age groups is shown in Table 2.

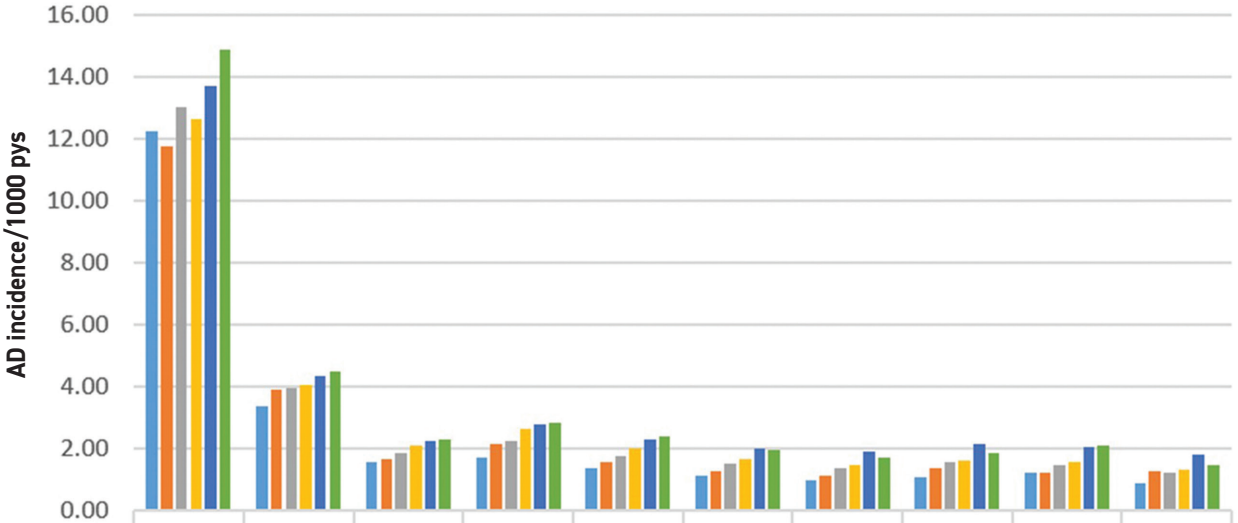
DISCUSSION

To the best of our knowledge, this is the first study to provide nation-wide real-world data about the incidence of AD multiple years after the beginning of the COVID-19 pandemic. Our study's main finding is a major and almost consistent annual increase in AD incidence from 2017 to 2022 over a broad range of sex/age groups. Our findings indicate a possible influence of the COVID-19 pandemic on the occurrence of AD.

The COVID-19 pandemic was a major public health event that included important exclusive features that might have influenced the epidemiology of AD, including widespread viral infection and largely administered new mRNA vaccinations, in addition to viral spread prevention strategies such as social distancing, lockdowns, and hand hygiene.

Reviewing our findings from a high-level view, the influence of the COVID-19 pandemic on the crude annual incidence of AD change might seem less impressive, as there was already a major increase before the pandemic and after its peak in 2022. Alternatively, some evidence might weaken this point of view. For example, Weil and colleagues [7] presented real-world retrospective large nation-wide Israeli data, which evaluated the incidence of AD between 2008 and 2017. The data presented in this previous study indicated variable trends of AD incidence in different age groups through the examined 10-year study follow-up time. As this study's follow-up time was adjacent to ours (it ended in 2017, the first year of our follow-up), and it is also a nation-wide study from a different large Israeli healthcare provider

Figure 2. Annual incidence of atopic dermatitis per 1000 person-years 2017–2022 by age group
AD = atopic dermatitis, PY = person-years



	Under 4	5–14	15–24	25–34	35–44	45–54	55–64	65–74	75–84	Above 85
2017	12.22	3.37	1.53	1.69	1.37	1.09	0.97	1.07	1.20	0.85
2018	11.78	3.89	1.65	2.11	1.56	1.24	1.13	1.33	1.22	1.23
2019	13.03	3.93	1.85	2.24	1.72	1.48	1.34	1.54	1.46	1.23
2020	12.61	4.05	2.06	2.60	1.97	1.66	1.43	1.59	1.53	1.31
2021	13.68	4.35	2.22	2.78	2.28	1.98	1.87	2.11	2.05	1.79
2022	14.88	4.48	2.28	2.80	2.37	1.93	1.67	1.86	2.08	1.43

Age group (in years)

(the second largest HMO after the CHS). This key comparable study might represent similar previous trends in our HMO population.

Our study showed a declining overall AD incidence trend consistent among different age groups. In addition, there were only a few years with an apparent incidence increase of specific age groups, and most were not consecutive (except for the < 6 months age group in 2011–2013). These study findings might strengthen the hypothesis that our 6-year increasing trend of AD incidence is unlikely to be incidental nor a continuation of a previous trend. Moreover, our study's 2020–2021 major annual incidence increase was more prominent than any other yearly incidence increase in this previous Israeli study.

During our follow-up time, the greatest annual increase in AD incidence was demonstrated between the years 2020 and 2021, which was also persistent in almost every sex/age group. Although the first confirmed SARS-CoV-2 cases were at the beginning of 2020, the year 2021 was a key year in the COVID-19 pandemic timeline, when several noticeable events happened, including the spread of the Alpha, Delta, and part of the Omicron variants. In addition, some possible association between SARS-CoV-2 infection and AD is related to a more long-term impact.

Interestingly, a recent systematic review [8] suggested that most studies found no statistically significant changes in the incidence or prevalence of AD due to the pandemic in different populations. However, the studies reported in this review have an end follow-up time at the end of 2020 or the beginning of 2021, are smaller, some of them reported an increased but insignificant incidence, and most evaluated only specific age groups. These are crucial limitations, including their limited timeframe, as there was a significantly wide SARS-CoV-2 infection spread during 2021 and 2022, which might weaken the suggestion that the COVID-19 pandemic had no impact on AD incidence.

Table 2. Annual incidence of atopic dermatitis per 1000 person-years 2017–2022 by sex and age group

	Age group (years)	2017	2018	2019	2020	2021	2022	2017–2022 change	*P*-value
Males	Under 4	12.82	12.48	13.81	12.99	14.12	15.49	20.80%	0.035
	5–14	3.25	3.58	3.71	3.67	4.04	4.13	27.17%	0.003
	15–24	1.10	1.00	1.20	1.31	1.49	1.57	42.30%	0.004
	25–34	1.11	1.52	1.57	1.76	1.99	1.88	69.01%	0.007
	35–44	1.05	1.23	1.29	1.50	1.73	1.79	69.97%	< 0.001
	45–54	0.86	0.98	1.23	1.25	1.54	1.59	84.50%	< 0.001
	55–64	0.85	0.97	1.20	1.28	1.59	1.46	70.91%	0.005
	65–74	1.10	1.42	1.60	1.66	2.14	1.90	72.14%	0.01
	75–84	1.36	1.51	1.96	1.96	2.52	2.69	98.72%	< 0.001
	Above 85	1.25	1.55	1.83	2.00	2.46	2.00	59.94%	0.03
Females	Under 4	11.59	11.03	12.20	12.22	13.23	14.24	22.83%	0.01
	5–14	3.50	4.22	4.16	4.46	4.68	4.85	38.54%	0.004
	15–24	1.95	2.28	2.48	2.79	2.95	3.00	53.99%	< 0.001
	25–34	2.26	2.69	2.91	3.43	3.56	3.70	63.81%	< 0.001
	35–44	1.69	1.89	2.15	2.45	2.82	2.94	74.04%	< 0.001
	45–54	1.31	1.49	1.72	2.07	2.41	2.26	72.88%	0.003
	55–64	1.07	1.26	1.46	1.56	2.11	1.86	74.49%	0.009
	65–74	1.04	1.26	1.49	1.54	2.09	1.82	74.42%	0.012
	75–84	1.09	1.01	1.08	1.20	1.70	1.62	48.39%	0.026
	Above 85	0.62	1.05	0.88	0.90	1.40	1.09	76.45%	0.117

A different trend was displayed by Hurley and colleagues [9]. They demonstrated a higher rate of AD among Irish infants born during the first COVID-19 lockdown (March to May 2020) compared to a birth cohort of pre-pandemic-born children. Our findings regarding infants of a broader age group (under the age of 4 years) demonstrated a decreased incidence from 2019 to 2020 but an increased incidence from 2020 to 2021 and from 2021 to 2022. This trend may align with our study's findings, as children born during the 2020 lockdowns were one year old in 2021 and two years old in 2022. Accordingly, our cohort showed an increased incidence among the under-4 age group during these years. Moreover, a recent study [10] demonstrated a higher risk of developing AD in offspring with maternal SARS-CoV-2 infection during pregnancy, which might partly explain the increased incidence in our study from 2020 to 2022 in the under-4 age group.

Another recent nation-wide retrospective cohort study [11] from South Korea involving almost 7 million individuals found an increased long-term risk of various autoimmune and auto-inflammatory dermatological disorders. Although AD incidence was not evaluated in this study, the overall findings support the hypothesis that COVID-19 may act as a catalyst for autoimmune responses, aligning with the rise in AD incidence observed during these years in our study.

Another factor that might elevate the incidence of AD is the influence of SARS-CoV-2 infection on the new onset of AD, as its possible influence was evaluated in a large cohort study [4]. As some studies have shown, the pandemic caused AD disease exacerbation [12,13], but it might have led to a higher physician attendance rate among milder cases, which could have led to higher documentation of the disease. Vaccinations, which were widely administered in Israel, were also suggested as a cause of disease exacerbation [14] and of new-onset AD in very few reports [15].

The 2020–2021 lockdowns represent another possible factor that could have affected the disease's onset. Lockdowns might have influenced clinic attendance; however, the literature regarding it is heterogeneous [8]. This unclear influence might be inflected in the increase between 2019 and 2020 among almost every age group, even among older adults who are at higher risk for severe COVID-19. Lockdowns are also possibly associated with less exposure to sunlight alongside low humidity, which may apply an

immunosuppressive effect on skin inflammation [3]. In addition, quarantines could have caused lifestyle changes that could increase Th2 phenotype pathogenicity [2].

Another notable perspective is the overall decreased air pollution during the pandemic [16], as it was vastly associated in the literature with increased risk for AD [2]. However, the obligation to stay home might have led to more prominent exposure to indoor pollutants, possibly associated with a higher risk of AD onset [2]. The well-established psychological impact of the pandemic [17,18] might also contribute to the incidence trend, as psychosocial stress is commonly considered a risk factor for AD [19].

Another speculative explanation for this trend is the possible increase in awareness of the disease than in the past several years. This increased awareness could have been derived from the noteworthy approval of several biological treatments for AD by the U.S. Federal Drug Administration since 2017 and the inclusion of some of them in the Israeli national treatments funding program. Moreover, to be entitled to the treatment's funding, a documented AD history must be present, which might encourage formal documentation of this diagnosis. In addition, physicians might tend to determine a precise diagnosis when having specific treatment options. However, the increases among patients under the age of 4 years, which until the middle of 2022 were not approved for any of the new drugs, might weaken these hypotheses, although having the lowest increase.

To put our research in context, we have shown that there was a significant increase in AD incidence in the past 6 years, while the recent literature suggests that AD prevalence has reached a plateau in countries with high AD prevalence [20].

Our study has several limitations. We did not have any information regarding the cohort's COVID-19 history and we only evaluated a few years following the pandemic; therefore, we could see a long-term trend of this incidence. The study's main strength is its large and diverse cohort that can represent the entire county's population.

CONCLUSIONS

We found a major and almost consistent annual increase in AD incidence from 2017 to 2022 over a broad range of sex and age groups. Further studies should assess the impact of COVID-19 on this increase in incidence.

Correspondence

Dr. H. Amital
Dept. of Medicine B, Sheba Medical Center, Tel Hashomer 52621, Israel
Phone: (972-3) 530-2652
Fax: (972-3) 535-4796
Email: howard.amital@sheba.health.gov.il

References

1. Zebardast A, Hasanzadeh A, Ebrahimian Shiadeh SA, Tourani M, Yahyapour Y. COVID-19: A trigger of autoimmune diseases. *Cell Biol Int* 2023; 47 (5): 848-58.
2. Stefanovic N, Flohr C, Irvine AD. The exposome in atopic dermatitis. *Allergy* 2020; 75 (1): 63-74.
3. Balato N, Megna M, Ayala F, Balato A, Napolitano M, Patruno C. Effects of climate changes on skin diseases. *Expert Rev Anti Infect Ther* 2014; 12 (2): 171-81.
4. Schmitt J, Ehm F, Vivirito A, et al. Large cohort study shows increased risk of developing atopic dermatitis after COVID-19 disease. *Allergy* 2024; 79 (1): 232-4.
5. Cohen AD, Dreiher J, Regev-Rosenberg S, et al. [The quality indigators program in Clalit Health Services: the first decade]. *Harefuah* 2010; 149 (4): 204-9, 265. [Hebrew].
6. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. World (WHO 2000-2025) Standard - Standard Populations - SEER Datasets. [Available from https://seer.cancer.gov/stdpopulations/world.who.html].
7. Weil C, Sugerman PB, Chodick G, et al. Epidemiology and economic burden of atopic dermatitis: real-world retrospective data from a large nationwide Israeli healthcare provider database. *Adv Ther* 2022; 39 (6): 2502-14.
8. Ne CKH, Suaini NHA, Aung WT, Ong KGS, Samuel M, Tham EH. Impact of COVID-19 pandemic on adults and children with atopic dermatitis and food allergy: systematic review. *J Allergy Clin Immunol Glob* 2023; 3 (1): 100181.
9. Hurley S, Franklin R, McCallion N, et al. Allergy-related outcomes at 12 months in the CORAL birth cohort of Irish children born during the first COVID 19 lockdown. *Pediatr Allergy Immunol* 2022; 33 (3): e13766.
10. Kim M, Choi Y, Lee M, et al. Maternal SARS-CoV-2 infection during pregnancy and subsequent risk of atopic dermatitis in offspring: a nationwide birth cohort study in South Korea. *Br J Dermatol* 2024; 190 (4): 576-7.
11. Heo Y-W, Jeon JJ, Ha MC, Kim YH, Lee S. Long-term risk of autoimmune and autoinflammatory connective tissue disorders following COVID-19. *JAMA Dermatol* 2024.
12. Hernández N, Sanclemente G, Tamayo L, López Á, Seidel A. Atopic dermatitis in the COVID-19 era: Results from a web-based survey. *World Allergy Organ J* 2021; 14 (8): 100571.
13. Pourani MR, Ganji R, Dashti T, et al. Impact of COVID-19 pandemic on patients with atopic dermatitis. *Actas Dermo-Sifiliográficas* 2022; 113 (3): 286-93.
14. Han TY, Shim DH, Lee YJ, et al. Effect of COVID-19 (SARS-CoV-2) vaccination on patients with atopic dermatitis treated with dupilumab: a multicenter, observational study. *Ann Dermatol* 2023; 35 (1): 38-45.
15. Martora F, Battista T, Ruggiero A, et al. The impact of COVID-19 vaccination on inflammatory skin disorders and other cutaneous diseases: a review of the published literature. *Viruses* 2023; 15 (7): 1423.
16. Yang M, Chen L, Msigwa G, Tang KHD, Yap P-S. Implications of COVID-19 on global environmental pollution and carbon emissions with strategies for sustainability in the COVID-19 era. *Sci Total Environ* 2022; 809: 151657.
17. Weich S. Mental health after COVID-19. *BMJ* 2022; 376: o326.
18. Chen PJ, Pusica Y, Sohaei D, Prassas I, Diamandis EP. An overview of mental health during the COVID-19 pandemic. *Diagnosis* 2021; 8 (4): 403-12.
19. Arndt J, Smith N, Tausk F. Stress and atopic dermatitis. *Curr Allergy Asthma Rep* 2008; 8 (4): 312-7.
20. Kohring C, Akmatov MK, Dammertz L, Heuer J, Bätzing J, Holstiege J. Trends in incidence of atopic disorders in children and adolescents - Analysis of German claims data. *World Allergy Organ J* 2023; 16 (7): 100797.