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The COVID-19 Pandemic and Recent Earthquake in Zagreb Together Significantly Increased the Disease Severity of Patients with Atopic Dermatitis

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Keywords
Atopic dermatitis · COVID-19 · Disease severity · Earthquake · Mental health

Abstract
Background/Objective: Stress may affect patients with atopic dermatitis (AD). The aim of this study was to examine the impact of the COVID-19 pandemic and the earthquake in Zagreb, Croatia (March 2020), on AD patients and their disease severity, symptoms/itch, and perceived stress. ***Methods:*** Our observational cross-sectional study included three groups of AD patients diagnosed by a physician: group 1 (n = 50), who experienced both the pandemic (quarantine) and the earthquake; group 2 (n = 50), who experienced only the pandemic; and group 3 (n = 50), the comparison group, who experienced neither disaster (patients examined 2018–2019). Groups 1 and 2 were examined May–June 2020, immediately after the national lockdown/quarantine. Disease severity (SCORAD), data from the Perceived Stress Scale (PSS), and information on patients' confirmed allergies were recorded for all groups, while groups 1 and 2 additionally completed a questionnaire concerning their disease, hand hygiene, and experience during the pandemic and/or earthquake. ***Results:*** The patients exposed to both disasters reported more pronounced AD worsening ($p < 0.001$; $r = 0.388$) and more frequent itching ($p < 0.001$; $r = 0.350$) than those exposed to the pandemic only. Notably, we found certain differences by gender: during the pandemic, women significantly more frequently washed their hands (81% of women washed "very frequently," while 52% of men washed "quite often") and had significantly higher PSS levels than men ($p < 0.05$). Concerning allergies, present or absent, during the pandemic, there was no significant difference in SCORAD between groups 1 and 2, neither when analyzed separately for indoor nor for outdoor allergens. The most commonly reported psychological disturbances during the pandemic were concern (46%), anger (18%), anxiety (16%), depression (9%), and increased alcohol, cigarette, and opioid agent use (6%). ***Conclusion:*** The COVID-19 pandemic together with

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the earthquake significantly increased disease severity and influenced AD worsening, itching, and psychological disturbances. This indicates that stressful events meaningfully affect the course of AD.

Introduction

The COVID-19 pandemic has brought forth changes to many elements of daily life, and people with chronic skin diseases such as atopic dermatitis (AD) have had to adapt to new habits and lifestyle changes in specific ways in order to manage their disease [1]. These are mostly related to social distancing or isolation and prevention measures, which can influence the skin, e.g., frequent hand washing and the use of masks and other protective equipment [2, 3]. Pandemic-associated changes also include fewer consultations, with a greater patient tendency to discontinue immunosuppressive therapy for fear of contracting COVID-19 [3]. Thus, the condition of patients' skin may worsen [2–4]. The psychological disturbances/effects induced by social isolation and quarantine may further aggravate the skin condition through neuroendocrine modulation of skin inflammation [3, 5–9].

COVID-19 was first documented in Croatia at the end of February 2020. Measures to limit the spread were rapidly introduced, culminating in a national lockdown with mandatory social isolation in quarantine, lasting from 22 March to 3 May 2020. During this period, the population could only go out for food, medicine, or because of an emergency. Public transportation stopped running, and schools and businesses closed, and those who could work worked from home. Shortly after the onset of the pandemic, a major 5.3-magnitude earthquake hit the capital, Zagreb. Several aftershocks occurred causing a wide range of destruction [10, 11]. The aim of this study, then, was to examine the impact of these different disasters on AD patients.

Materials and Methods

This retrospective study included 150 AD patients diagnosed and treated in the period between January 2018 and June 2020. Group 1 ($n = 50$) experienced both the pandemic (quarantine) and the earthquake. Group 2 ($n = 50$) included patients outside of Zagreb who did not experience the earthquake but experienced the pandemic. Groups 1 and 2 were examined May–June 2020, immediately after the national lockdown/quarantine. Group 3 ($n = 50$) included patients who experienced neither disaster (examined during the period of 2018–2019, the comparison group).

Disease severity (SCORAD), data from the Perceived Stress Scale (PSS), and information on patients' confirmed allergies were recorded for all groups, while groups 1 and 2 additionally completed a questionnaire concerning their disease, hand hygiene, and experience during the pandemic and/or earthquake. The inclusion criteria were age 18 years or older and a diagnosis of AD from a dermatologist according to the Hanifin and Rajka criteria [12]. Additional inclusion criteria concerned the dates of examinations: 4 May – 30 June 2020 for groups 1 and 2 and January 2018 – May 2019 for group 3. Excluded were those younger than age 18, pregnant and lactating women, and patients with prior psychiatric disorders or insufficient medical data. We recorded the following data.

SCORAD Index

AD severity was assessed by the SCORAD index, which includes questions on the affected areas of skin (%), subjective symptoms (itch and sleeplessness/insomnia), and objective skin indicators (redness, swelling, oozing/crusting, scratch marks, skin thickening [lichenification], dryness). For SCORAD, each skin manifestation is numerically rated with a 0 (none), 1 (mild), 2 (moderate), or 3 (severe), while the intensity of itch and sleeplessness are assessed with a 3-day recall period on a rating rang scale from 0 (none) to 10 (maximum). The data are added for a maximum possible score of 103. Severity is scored as follows: <25 (mild), 25–50 (moderate), and 50< (severe).

The PSS

The PSS is a validated instrument (questionnaire) that measures the intensity of psychological stress, i.e., the subjective feeling and experience of psychological stress [13, 14]. It examines 10 domains, i.e., emotional states to which respondents associate frequency. Respondents think back over the previous month and mark their answers according to the following rating scale: 0 = never; 1 = almost never; 2 = sometimes; 3 = quite often; 4 = very often. The result is expressed by the sum of all the numerical answers marked by the respondents (with the exception of questions 4, 5, 7, and 8 where the answer 0 is counted as 4 points, 1 is counted as 3 points, 2 is 2, 3 is 1, and 4 is counted as 0). Results fall into one of three categories of stress levels: 0–13 (low), 14–26 (moderate), and 27–40 (high).

Customized Questionnaire

Basic data on the impact of COVID-19 and the earthquake were elicited and recorded by questionnaire (Table 1). Patients filled out a questionnaire customized for this study that contained information concerning their disease-related features/factors during the COVID-19 pandemic: personal data (patient age, gender, and education), disease condition, hand hygiene, and therapy use. The Ethics Committee of the University Hospital Center Sestre Milosrdnice, Zagreb, Croatia, approved this study (No. EP-20098/16-4), which proceeded in accordance with the 1975 Helsinki Declaration as updated in 2013.

Statistical Analysis

Normality of distribution was tested by Kolmogorov-Smirnov test. The Kruskal-Wallis test and post hoc Mann-Whitney U test with Bonferroni correction for multiple comparisons tested for differences between groups concerning stress and severity of eczema. We looked for correlations between sca-

Table 1. Our customized questionnaire

Question	Answer
QUESTION 1. During the COVID-19 pandemic I washed my hands:	Very frequently Quite often Rarely Very rarely
QUESTION 2 During the COVID-19 pandemic I used disinfectants:	Very frequently Quite often Rarely Very rarely
QUESTION 3. The condition of my skin on the hand during the COVID-19 pandemic and possible changes/deterioration:	None, I did not have lesions Mild deterioration Moderate deterioration Strong deterioration
QUESTION 4. My level of education is:	Primary education Secondary education Academy or university education
QUESTION 5. Skin condition/status and/or lesions during the pandemic:	Improved Stayed the same Slightly deteriorated Moderately deteriorated Severely deteriorated
QUESTION 6. Itching during the pandemic compared to before the pandemic:	None, I did not feel itching Milder in comparison More moderate in comparison More severe in comparison
QUESTION 7. Compared to before the pandemic, my sleep during the pandemic was:	I did not experience sleep disturbances Mildly more disturbed Moderately more disturbed Much more disturbed
QUESTION 8. Personal COVID-19 infection status and that of close contacts:	My close contacts and I did not have the infection/symptoms. Some of my friends were infected Some of my family members were infected I was infected
QUESTION 9. Staying inside for long periods of time:	Improved my skin condition due to less frequent allergen exposure Did not influence my skin condition Exacerbated my skin condition due to stress Other (please write in)_____
QUESTION 10. Among the following psychological disturbances, I currently feel: (multiple responses are possible)	Concern Anger Anxiety Depression More alcohol/cigarette use and/or similar substances Other None of the above
QUESTION 11. During the COVID-19 pandemic, I used my prescribed AD therapy:	I didn't use it at all Rarely Average/medium use Frequently

Table 2. Comparison of disease severity (SCORAD) and perceived stress levels (PSS) between the three groups

Group		Disease severity (SCORAD)	PSS
Earthquake + pandemic group Group 1 (I); *N* = 50	Median (IQR) min–max	36 (24.5–48) 1–79	19 (16–23) 1–29
Pandemic group Group 2 (II); *N* = 50	Median (IQR) min–max	23.5 (14.75–31.25) 0–78	15 (12–20) 9–26
Non-disaster group Group 3 (III); *N* = 50	Median (IQR) min–max	16.5 (2–38) 0–76	18 (15–23.25) 0–29
	p; ε^2	<0.001; 0.143	0.011; 0.061
	p; r^2 I versus II	<0.001; 0.143	0.005; 0.078
	p; r^2 I versus III	<0.001; 0.154	0.717; 0.001
	p; r^2 II versus III	0.094; 0.028	0.018; 0.056

p values and effect size (r^2) for intergroup comparisons according to Mann-Whitney with Bonfferoni correction for the multiple comparison test (with cut-off value for interpretation $p < 0.017$) are presented in the last three rows. IQR, interquartile range; *p*, level of significance for the Kruskal-Wallis test; ε^2, effect size.

lar variables (age, PSS, and SCORAD) by looking at scatter plots and by calculating the Spearman correlation coefficient. We compared scalar variables between two categories (e.g., gender) with the Mann-Whitney U test for normally distributed data and the *t* test for data without a normal distribution. Wilcoxon test was used for comparison of itching due to COVID-19 and earthquake in group 1, while the Mann-Whitney test for comparison of itching between group 1 and 2. The χ^2 test was used for a comparison of proportions. The magnitude of the difference between groups (effect size) was quantified by r where $r = \sqrt{(t^2/(t^2+df))}$ (t = t-statistics; df = degrees of freedom) for the t test or $r = Z/\sqrt{N}$ (Z = Z-statistics; N = number of cases) for the Mann-Whitney U test. Interpretation was based on the Cohen criteria: r = 0.1–0.3 was a small effect size, 0.3–0.5 was medium, 0.5–0.7 was large, and >0.7 was considered very large. The effect size for χ^2 (Cramer's V or Kendall's τ) was similarly interpreted. Effect size for the Kruskall-Wallis test was estimated by ε2 and for interpretation, the squared value of r was used.

Results

See Table 2. Group 1 (both disasters) had significantly higher SCORAD results than group 2 (COVID-19 only) and group 3 (controls). The SCORAD result for group 2 was higher but not significantly higher than for group 3 ($p = 0.094$; $r = 0.028$). According to results from the questionnaire, skin lesion deterioration ($p < 0.001$; $r = 0.388$) and itching ($p < 0.001$; $r = 0.350$) were more commonly reported by group 1 than group 2 (shown in Fig. 1).

COVID-19 infection in persons close to our patients did not correlate with AD patient SCORAD or PSS. Prescribed therapy use increased as disease severity increased ($r = 0.506$; $p < 0.001$) (a linear, positive, moderate correlation), and it was greater for group 1 than group 2 ($p < 0.001$; $r = 0.360$). A higher correlation between SCORAD and therapy use was recorded for group 2 ($r = 0.521$; $p < 0.001$) than for group 1 ($r = 0.330$; $p = 0.019$). In group 3 (those treated before the pandemic), men had significantly higher SCORAD scores than women {median 32 (interquartile range [IQR] 9–57) versus 9.7 (IQR 0–36.3) ($p = 0.011$, $r = 0.356$)}.

Of the 100 patients who experienced the pandemic (groups 1 and 2) (shown in Fig. 2), women washed their hands significantly more often ($p < 0.001$; $r = 0.405$) – men washed their hands quite often (52%), while women did so very frequently (81%). The use of disinfectants did not differ by gender. Self-reported data for the patients who experienced the pandemic ($N = 100$, groups 1 and 2) showed that hand lesion deterioration did not correlate with hand washing frequency or disinfectant use, and no differences by gender were seen (shown in Fig. 1). No significant differences in hand lesion deterioration between group 1 and group 2 were found.

Disease severity (SCORAD) between groups with proven allergies did not change during the pandemic. Thus, among AD patients who are allergic to indoor allergens (18 [36%]) and experienced only the pandemic and stayed in quarantine, their SCORAD was not significantly different from those who tested negative to indoor allergens. Most patients who experienced quarantine

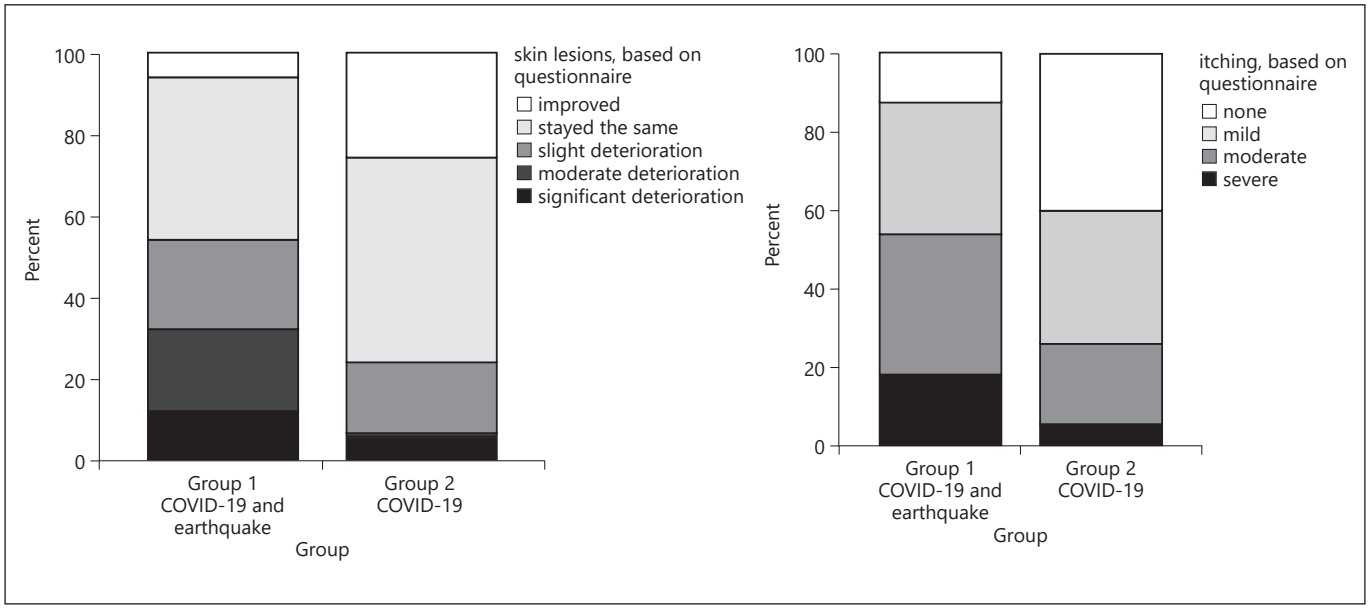

Fig. 1. Comparison of proportion of subjects who experienced lesions and itching during the pandemic and earthquake (group 1; $N = 50$) and during the pandemic alone (group 2; $N = 50$).

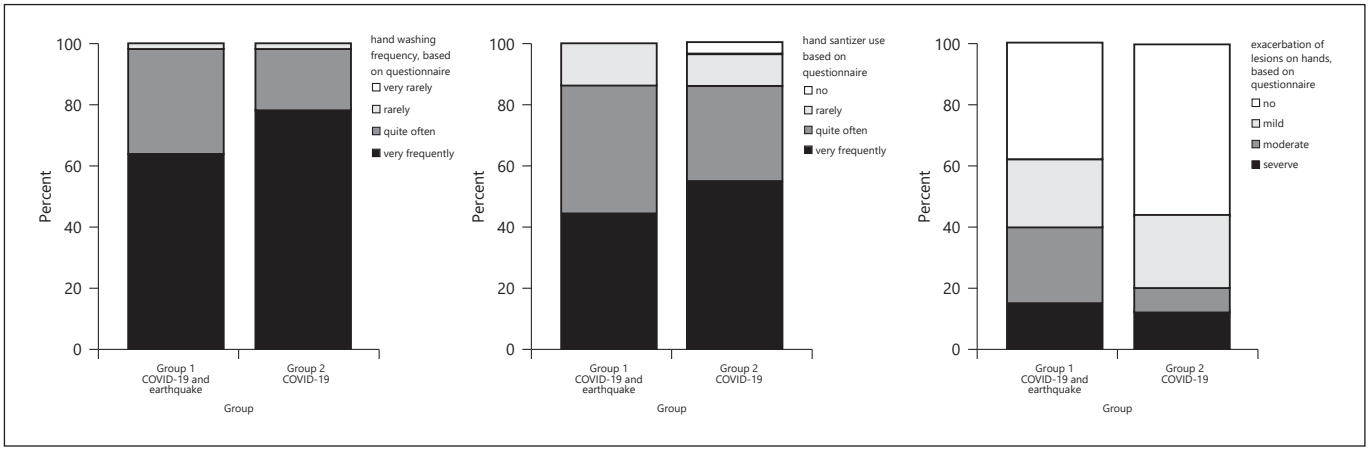

Fig. 2. Comparison of proportion of subjects by category (hand washing, disinfectant use, and exacerbation/occurrence of lesions on the hands) between groups 1 (COVID-19 and earthquake; $N = 50$) and 2 (COVID-19; $N = 50$) (comparison of proportion of subjects according each categories).

(60%) reported that staying indoors did not have an effect on their disease, while 27% thought their condition had worsened, and 21% reported improvement.

The women who experienced one or both disasters (i.e., the women from groups 1 and 2) had significantly higher PSS levels than the men from the same groups, with a low effect size; $p = 0.004$; $r = 0.233$. Women also significantly more commonly reported stress (65.3 vs. 40%; $p = 0.035$, $r = 0.223$); specifically, they reported stress due to fear of infection significantly more than men (40 vs. 4%; $p < 0.001$; $r = 0.337$). The most commonly reported psychological disturbance during the pandemic/quarantine was concern (46%; 54% in group 1: 38% in group 2), followed by anger (18%; 20% in group 1: 16% in group 2), anxiety (16%; 24% in group 1: 8% in group 2), depression (9%; 10% in group 1: 8% in group 2), and increased

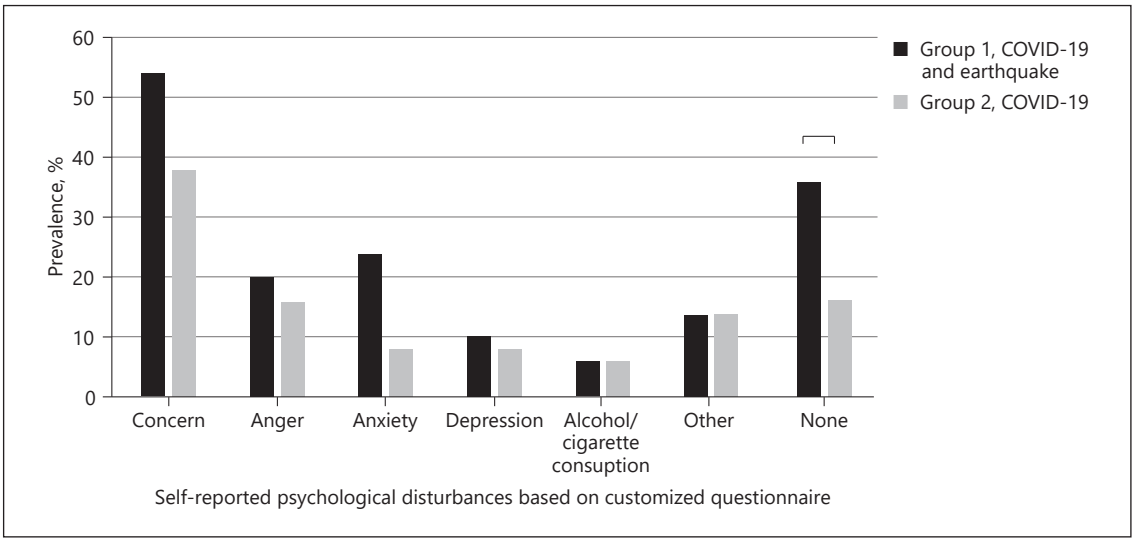

Fig. 3. Self-reported psychological disturbances for the group that experienced both disasters (group 1; $N = 50$) and the group exposed to the pandemic only (group 2; $N = 50$) (multiple responses were possible).

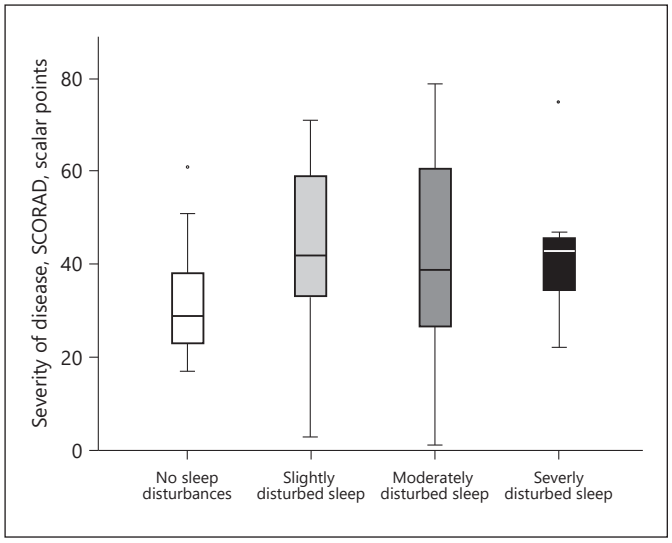

Fig. 4. Connection between patient disease severity (SCORAD) and earthquake-related sleep disturbances for the group that experienced both disasters ($N = 50$; group 1) (comparison of SCORAD between these categories).

consumption of alcohol, cigarettes, and opioid agents (6% in both groups), while 26% reported no disturbances (16% in group 1: 36% in group 2) and 14% answered "other" (same percentage in both groups; shown in Fig. 3). When analyzing patients' sleep disturbances results, no correlation between SCORAD and sleep disturbances was seen (shown in Fig. 4) (Table 3). Also, sleep disturbances did not differ by gender.

Discussion

Our results show that more pronounced AD worsening was recorded by patients exposed to both disasters compared to the pandemic alone. It is likely that worsening was predominantly influenced by the earthquake since a comparison of SCORAD results shows that while scores were higher for group 2 (pandemic only) than for group 3 (neither disaster), these two groups did not differ significantly in AD severity (SCORAD). Similarly, one study by Kodama et al. [15] looked at occurrences of AD after a major earthquake in Hanshin (Japan) and recorded more exacerbations in areas with major damage (38% of patients) than in areas of minor damage (34%) and undamaged areas (7%). Therefore, our results confirm that the combined influence of the two simultaneous disasters (the pandemic and earthquake) was significant – together, they increased AD severity, deterioration, and symptoms. So, when working with patients in the immediate and long term aftermath of a disaster, healthcare providers need to be sensitive to these indications that those from areas of greater damage, and those experiencing multiple disasters/stressors are more likely to see their

Table 3. Earthquake-related sleep disturbances, SCORAD, and PSS results for group 3 ($N = 50$) (Spearman's correlation)

		Earthquake-related sleep disturbances	PSS	SCORAD
Earthquake-related sleep disturbances	*r*	1	0.502	0.262
	p		0	0.066
SCORAD	*r*	0.262	0.309	1
	p	0.066	0.029	
PSS	*r*	0.502	1	0.309
	p	0		0.029

r, Spearman's correlation coefficient; *p*, level of significance.

AD flare up. It must also be noted here that those who experienced both disasters saw their AD/disease severity positively correlate with their perceived stress level. Thus, we can assume that disease severity may increase with each increase in the number of experienced events, wherein the type of disaster can also have an influence. In addition, since women had significantly higher perceived stress levels than men, preventive measures for women should include a focus on coping with stress. Also, we would like to mention that since AD severity was not significantly associated with hand washing/disinfecting, allergies, and sleep disturbances during the pandemic/quarantine in our study, more research/studies on these factors are necessary.

To our knowledge, our cross-sectional study, based on the analysis of AD patients' reports and examinations, presents the first complex research regarding AD features during the pandemic. However, the limitations of this study are the lack of patient prospective data recorded over a longer period after the onset of the disaster, the non-validated, customized questionnaire, and a control group based on retrospective data, i.e., we want to acknowledge the risk of selection bias due to study design and the retrospective/historical patient control group. Finally, we believe more could be learned to support the early recognition and timely treatment of pandemic-related problems in patients with chronic diseases such as AD.

Conclusion

Greater consideration must be given to AD patients' needs during major stressful events, including the planning and adoption of certain healthcare measures that include psychological support which could minimize AD exacerbation during a disaster.

Key Message

AD patients' disease severity, perceived stress, and symptoms/itch were affected by the pandemic and recent earthquake in Zagreb.

Statement of Ethics

The Ethics Committee of the University Hospital Center Sestre Milosrdnice, Zagreb, Croatia, approved this study (No. EP-20098/16-4), which proceeded in accordance with the 1975 Helsinki Declaration as updated in 2013. Written informed consent from participants was not required in accordance with local/national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Liborija Lugović-Mihić conceived the study, wrote the protocol, oversaw data collection, wrote the manuscript, contributed to the design of the study and edited the manuscript. Jelena Meštrović-Štefekov, Hrvoje Cvitanović, Vedrana Bulat, Tomislav Duvančić, Maja Tolušić-Levak, Elvira Lazić-Mosler, and Gaby Novak-Bilić collected data, contributed to the design of the study and provided technical support. Nives Pondeljak designed and adapted the database system and contributed to the design of the study. All the authors approved the submitted version for publication.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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