

Report

Psychosomatic factors of atopic dermatitis exacerbation

Natasa Maksimovic¹, MD, PhD, Milica Zaric¹, MD, Suncica Bjelica², MD,
Jelena Eric Marinkovic³, MD, PhD, and Slavenka Jankovic¹, MD, PhD

¹Faculty of Medicine, Institute of
Epidemiology, University of Belgrade,
Belgrade, Serbia,

²Institute for Medical Research Belgrade,
University of Belgrade, Belgrade, Serbia,
and

³Faculty of Medicine, Institute of Medical
Statistics and Informatics, University of
Belgrade, Belgrade, Serbia

Correspondence

Natasa Maksimovic, MD, PhD
Faculty of Medicine, Institute of
Epidemiology
University of Belgrade
Visegradska 26A
Belgrade 11000
Serbia
E-mail: natamax07@yahoo.com

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Abstract

Background The aim of this study was to estimate whether the stress, lack of social support, and poor emotional relationships influence the recurrence of AD in adults.

Methods Case-control study comprised 66 outpatients with AD and 132 controls with different skin diseases believed to be slightly influenced by psychosomatic factors.

Participants were treated at the Department of Dermatology – Military Medical Academy and City Department for Skin and Venereal Diseases from January to June 2014. Stressful life events were assessed using the Paykel's Interview for Recent Life Events. The attachment relationship and perceived social support were assessed with the Experiences in Close Relationships Scale and with the Multidimensional Scale of Perceived Social Support, respectively. Univariate and multivariate logistic regression analyses were applied.

Results AD patients had significantly higher anxiety scores when initiating a close emotional relationship and when avoiding an affective attachment (OR = 1.49; CI = 1.13–1.97; $P = 0.005$ and OR = 1.63; CI = 1.16–2.30; $P = 0.005$, respectively). Perceived social support from family and friends was significantly lower among cases compared to controls (OR = 0.93; CI = 0.88–0.98; $P = 0.009$ and UO = 0.94; CI = 0.89–0.99; $P = 0.027$, respectively).

Conclusions AD patients had higher anxiety scores, and those with low social support tended to have more frequent disease recurrence. The number of stressful life events did not differ between studied groups.

Introduction

Atopic dermatitis (AD), along with other atopic diseases, is one of the most prevalent chronic diseases worldwide. In the past few decades, the prevalence of AD has increased.^{1,2} Possible explanation for substantial and rapid increase in AD prevalence could be the changes in environmental factors rather than changes in genetic factors.³

Psychological distress plays an important role in exacerbating and perpetuating the itch-scratch cycle in AD. Stress increases secretion of inflammatory mediators, which further influence the damages of skin barrier^{4,5} and may have an impact on skin inflammation.⁶ Also, Alexopoulos and Chrousos⁷ suggested that AD patients might be experiencing chronic stress, and the severity of their disease could be linked to the intensity of their stress. Hashizume and Takigawa⁸ reported that psychological stress exacerbates AD. Correspondingly, a few studies have shown that, compared to healthy controls, the patients with AD react differently to laboratory stress and experience disease worsening after exposure to stress.⁹ Using Trier Social Stress Test, Buske-Kirschbaum *et al*¹⁰ showed higher eosinophils and IgE levels in AD patients compared to the healthy individuals after exposure to audience stress. These results emphasize that

the patients with AD show different immunological reactions to psychological stressors compared to nonatopic persons.¹¹ AD may also be associated with psychological problems, such as anxiety, depression, sleep disorders, and personality disorders.^{12,13} There is an increased risk for emotional problems in patients with AD, beside the fact that many of these patients cope well with their disease.¹⁴

Although the association between AD and psychological problems in children and adolescents has already been recognized,¹⁵ there are only a few studies investigating the association between stress and AD in adults, in spite of the fact that AD is highly prevalent in adults as well as in children.¹⁶ So, the aim of this paper was to estimate whether the stress, lack of social support, and poor emotional relationships as psychological stressors influence the recurrence of AD in adults.

Materials and methods**Patients**

The research was designed as a case-control study in the period of January 2014 to June 2014 and comprised 66 outpatients with AD treated at the Department of Dermatology – Military Medical Academy, and at City Department for Skin and Venereal

Diseases. Inclusion criteria were being 17 years of age and older with four years of elementary school as minimum.

AD was diagnosed according to patient's medical history, typical clinical presentation (pruritus, erythema, dry skin), and based on Hanifin and Rajka diagnostic criteria.¹⁷ Control group consisted of 132 patients with different skin diseases, diagnosed according to the most recent criteria and believed to be slightly influenced by psychosomatic factors (e.g. contact dermatitis, insect bites, bacterial infection, skin tumors, ichthyosis). Any patients with a diagnosis of alopecia, acne vulgaris, psoriasis, vitiligo, urticaria, lichen planus, seborrheic dermatitis, and pruritus were excluded from the study.

The study protocol was approved by the Ethics Committee of the Faculty of Medicine. A written informed consent was obtained from each participant.

Instruments

Data on gender, age, marital status, education, personal and family history of AD, other atopic diseases, anxiety, and depression were obtained using a standardized questionnaire.

For evaluation of severity and extent of disease in patients with AD, the Eczema Area and Severity Index (EASI)¹⁸ was used. The patients with AD were classified into three groups according to their EASI score: mild ($EASI < 7.07$), moderate ($EASI 7.071$ to 15.60), and severe ($EASI > 15.61$) disease.

Data on impact of stressful life events on disease exacerbation were obtained using the Paykel's Interview for Recent Life Events¹⁹ that comprised 61 stressful events and had the possibility of adding any important event. The events are arranged by the level of their unpredictability and unpleasantness, so at the top of the list are the most important and most unpleasant events. The first 25 events on the scale represented major and very significant events, with the first five being the most significant for the individual, so-called "life catastrophes".²⁰ The participants were asked if any of these events had occurred in the last 12 months, and if so, they were asked to report the date of the event. For each patient, the total number of events was computed.

The attachment relationship was measured with the Experiences in Close Relationships Scale (ECRS).²¹ The ECRS consisted of 36 items referred to the feelings in emotional relationships. Each statement is estimated at seven-point scale, ranging from one ("strongly disagree") to seven ("strongly agree"). The first 18 statements made the scale which evaluated anxiety associated with affective bonding. Statements 19–36 constituted a scale for the assessment of avoidance associated with affective bonding. Higher scores indicated higher attachment anxiety and attachment avoidance. A linguistically and cross-culturally adapted Serbian version of the questionnaire, developed with the author's permission, was used. Cronbach's alpha coefficient was 0.91 for both the study and control groups, which indicated the reliability and validity of the questionnaire.

To assess perceptions of social support adequacy from three specific sources: family, friends, and significant others, the Multidimensional Scale of Perceived Social Support²² was used. The questionnaire consisted of 12 statements, which could be divided according to three sources of support and were scored on a seven-point scale. Higher scores indicated greater perceived support. We used a validated and cross-culturally adapted Serbian version of the questionnaire developed with the authors' permission. Evaluation of measuring characteristics of the questionnaire indicated the reliability and validity with Cronbach's alpha coefficient value of 0.86 for study group and 0.91 for control group.

Statistical analysis

To describe the examined population, central tendency (mean and median) and variability measures (standard deviation – SD) as well as relative numbers (percentages) were used. Continuous variables were presented as mean $\pm$ SD and categorical variables as frequencies and percentages.

The differences between groups were evaluated using t-test and χ^2 test. After that, univariate and multivariate logistic regression analyses were applied. The dependent variable was patient's status (patients with AD/patients with other skin diseases). Each regression model (for attachment style, social support, and stressful life events) included the following independent variables: age, sex, marital status, place of residence, and occupation. Odds ratios (OR) were estimated from regression coefficients.

P value < 0.05 was considered as significant. Statistical analysis was performed using the Statistical Package for the Social Sciences-SPSS, version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

Case-control study comprised 198 adult participants, 17 years of age and older: 66 AD patients (cases) and 132 persons with some other dermatological disease that was not associated with psychosomatic factors (the control group or controls).

Study participants were different in terms of age and body mass index (BMI), with cases generally being younger and having lower BMIs. There were no differences between groups regarding gender, place of residence, marital status, level of education, or profession. The results are shown in Table 1.

Table 2 shows characteristics of AD patients related to the disease. The average age of AD participants at the onset was almost 14 years, and the duration of disease was about 21 years. The severity of disease was assessed using the EASI score that was 12, on average. Most of the patients (almost 70%) had mild to moderate form of disease.

Table 3 represents psychosomatic factors in AD patients and controls.

The average number of stressful life events was higher in controls (2.00 ± 2.21) compared to cases (1.76 ± 1.87), in the

Table 1 Demographic characteristics of study population

Characteristic	Patients with atopic dermatitis (n = 66)	Control group (n = 132)	P
Age (years; mean $\pm$ SD)	34.18 $\pm$ 13.43	44.97 $\pm$ 14.07	0.000 ^a
Gender (N, %)			
Men	29 (43.9)	49 (37.1)	0.355 ^b
Women	37 (56.1)	83 (62.9)	
Body mass index (mean $\pm$ SD)	20.40 (3.41)	21.55 (3.82)	0.043 ^a
Place of residence (N, %)			
Rural	6 (9.1)	24 (18.2)	0.093 ^b
Urban	60 (90.9)	108 (81.8)	
Marital status (N, %)			
Married ^c	36 (54.5)	53 (40.2)	0.055 ^b
Other ^d	30 (45.5)	79 (59.8)	
Education level (N, %)			
Elementary school	8 (12.1)	8 (6.1)	0.068 ^b
Secondary school	36 (54.5)	63 (47.7)	
Higher school	3 (4.5)	21 (15.9)	
University degree	19 (28.8)	40 (30.3)	
Employment status (N, %)			
Unemployed ^e	22 (33.3)	52 (39.4)	0.696 ^b
Employed ^f	44 (66.7)	80 (60.6)	

^at-test.^b χ^2 test.^cMarried, extramarital alliance.^dUnmarried, divorced, widow/widower.^eStudent, housewife, retired.^fAgricultural laborer, laboratory technician, laborer, officer, technician, expert, free occupation.**Table 2** Characteristics of atopic dermatitis patients

Characteristic	
Age at the disease onset (mean $\pm$ SD)	13.95 $\pm$ 11.91
Duration of the disease in years (mean $\pm$ SD)	21.29 $\pm$ 14.81
EASI (mean $\pm$ SD)	11.77 $\pm$ 8.71
Severity of disease ^a /Number (%)	
Mild	22 (33.3)
Moderate	24 (36.4)
Severe	30 (30.3)

EASI, Eczema Area and Severity Index.

^aAccording to EASI tertile.

year before survey, but the observed difference was not statistically significant ($P = 0.455$).

Patients with AD reported one of the three significant stressful life events, more often than controls: big financial problems, loss of a valuable object, or being under an investigation (data not shown).

Compared to the control group, AD patients had significantly higher anxiety scores when initiating a close emotional relationship, as well as when avoiding an affective attachment, which was confirmed by the multivariate logistic regression analysis

(OR = 1.49; CI = 1.13–1.97; $P = 0.005$ and OR = 1.63; CI = 1.16–2.30; $P = 0.005$, respectively). After control of any possible confounding, it was shown that social support observing was independently associated with exacerbation of AD. In addition, cases were afraid of losing their partner's love significantly more often than controls. They were more often worried that the partner did not want to stay with them, worried too much about their relationship, and that the partner was interested in someone else when he/she was not around. Also, AD patients considered much more often that their need for extreme closeness sometimes scared and pushed people away, and the fact that they did not have necessary care and attention drove them crazy more often compared to controls (data not shown).

The perceived social support from family and friends was significantly lower in cases compared to controls (OR = 0.93; CI = 0.88–0.98; $P = 0.009$ and OR = 0.94; CI = 0.89–0.99; $P = 0.027$, respectively), while there was no statistically significant difference in the observed social support from the significant others.

Discussion

To our knowledge, there is a lack of studies that investigate association between psychological distress and AD exacerbation, besides the fact that AD is a common chronic or recurrent skin disorder especially among children, though it also affects the adult population.

There are many environmental factors proven to be linked to AD, such as house dust mite, animal dander, molds, cockroach infestation, occupational exposure, environmental tobacco smoke, air pollution, aeroallergens, and climate,^{23–25} but psychological stress is considered to be the most important.^{12,26,27} In the past decade, the consciousness about psychosocial effects of skin diseases, like psoriasis, has been increasing.^{28–30} Our results showed that AD patients had significantly higher anxiety levels concerning the emotional relationships and avoided emotional relations significantly more often compared to controls. In the study of Park and Kim,³¹ a significant positive trend between stress level and AD prevalence was observed, with 1.26% of adults who felt low stress levels reporting AD, compared to 3.47% of those with high stress level. Another study by Kim *et al.*³² also showed a significant difference in distress prevalence among AD patients and controls. Namely, the patients with AD reported at least one type of psychological distress significantly more common compared to healthy individuals (18.7% and 8.9%, respectively). Univariate analysis showed significant relationship between AD and depression, anxiety, and somatisation.³² According to the results of Emi *et al.*,³³ AD subjects showed a significantly higher level of anxiety, depression, and anger, compared to healthy controls, especially those with remarkable skin itching and consequent scratching. Also, the degree of itching affected the skin symptoms severity and the psychological response of patients.

Table 3 Psychosomatic risk factors of studied population

Risk factors	Atopic dermatitis patients (n = 66) mean ± SD	Controls (n = 132) mean ± SD	Univariate logistic regression analysis			Multivariate logistic regression analysis ^a		
			OR ^b	95% CI ^c	P	OR ^b	95% CI ^c	P
Stressful life events	1.76 ± 1.87	2.00 ± 2.21	0.94	0.82–1.09	0.444			
Attachment								
Anxiety attachment score	2.72 ± 1.09	2.05 ± 1.13	1.64	1.26–2.14	<0.001	1.49	1.13–1.97	0.005
Avoidance attachment score	2.76 ± 0.95	2.25 ± 0.91	1.77	1.28–2.45	0.001	1.63	1.16–2.30	0.005
Social support								
Family	22.52 ± 5.56	24.86 ± 5.40	0.93	0.88–0.98	0.007	0.93	0.88–0.98	0.009
Friends	22.00 ± 5.26	23.28 ± 5.98	0.96	0.92–1.01	0.143	0.94	0.89–0.99	0.027
Significant others	23.86 ± 5.94	23.92 ± 5.90	1.00	0.95–1.05	0.952			
Total score	68.38 ± 12.05	72.06 ± 13.82	0.98	0.96–1.00	0.071	0.97	0.95–1.00	0.034

^aWith control for age, gender, marital status, residence, and profession.^bOdds ratio.^cConfidence interval.

Our study did not show any difference in average number of stressful life events between cases and controls. The patients with AD had a higher degree of attached anxiety and depression, compared to controls, but observed differences were not statistically significant.

In the majority of AD patients, direct association between disease exacerbation and stressful life events was emphasized.¹³ Psychological diagnostic tests indicate that depression and anxiety level is directly associated with AD recurrence.^{34,35} Also, AD patients often have problems with anger control,³⁶ and conditions manifested with anger often relate to AD exacerbation.³⁷ Inside conflicts lead to AD exacerbation, whereas on the other hand, AD increases the psychological pressure itself, which makes a so-called vicious cycle.³⁸ Also, some studies revealed that AD affected overall health-related quality of life, whereby greater severity of disease was associated with greater impairment in the quality of life.³⁹

The evaluation of the observed social support from family, friends, and significant others showed that AD patients observed lower social support from all three mentioned sources compared to controls. The observed differences were statistically significant for social support from friends and family. It is also determined that, after controlling of confounding, social support observing was independently associated with exacerbation of AD. According to Dunkel-Schetter and Bennett,⁴⁰ the observing or belief in possibility of support has more beneficial effect on a person's health than support itself. The importance of support is proven in other studies which have shown that the understanding of AD and accounting for attitudes by family members is obvious for successful control of the disease.⁴¹

One of the reasons that most probably led to our findings related to stressful life events and attached anxiety and depression was the selection of controls. As our control group comprised skin patients considered to have none or a negligible psychosomatic component, there was a possibility that the role

of stressful life events, anxiety, and depression in AD patients was underestimated.

This case-control study was undertaken to investigate the influence of different psychosomatic factors on the exacerbation of AD. However, like the other case-control studies, our study has several limitations. Firstly, the selection of the adequate controls was difficult. Besides the fact that the control group consisted of patients with different skin diseases where psychosocial factors did not have any significance, there is a possibility of a negligible influence, still sufficient to underestimate the significance of these factors in the recurrence of AD. The more appropriate control group would certainly be a healthy population. One of the limitations was a small number of participants, and that could be the reason why some common risk factors (e.g. stress) had not been shown to be independent predictors of AD recurrence.

In conclusion, we may say that the risk of AD recurrence is increased in persons with a lower level of social support. Also, the anxiety is higher, especially when initiating close relationships, so these persons tend to avoid affective bonding. However, the number of stressful life events did not differ between those two groups, which is one interesting fact, considering that higher frequency of stressful events is expected in the group of patients. Further investigations on this topic are required.

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