

The humanistic burden of atopic dermatitis in Greece: a cross-sectional study

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Abstract

The purpose of this study was to evaluate the quality of life (QoL) and psychosocial burden in adult Greek patients with atopic dermatitis (AD) using validated tools and to investigate factors that influence AD's humanistic burden. This observational, cross-sectional study was conducted in Greece (January-September 2023) with 150 adult members of the patient association "Epidermia", all diagnosed with AD. Data was collected through a structured questionnaire, including socio-demographic details, clinical history, AD severity (using the Patient-Oriented Eczema Measure [POEM]), QoL, sleep disorders, and psychological health. Based on POEM scores, 11% of participants had clear/almost clear skin, 27% had mild eczema, 51% had moderate eczema, and 12% had severe/very severe eczema. AD had a moderate or very/extremely large impact on QoL for 29% and 42% of participants, respectively. Insomnia affected 55%, while 31% had mild anxiety, 23% had moderate/severe anxiety, 10% had moderate depression, and 8% had moderately severe/severe depression. AD severity was associated with reduced QoL and higher rates of insomnia, anxiety, and depression. Our study highlights significant associations between AD severity, QoL, and psychosocial factors, emphasizing the need for comprehensive management strategies.

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin condition characterized by flares and remissions. Symptoms of AD include inflammation, itching, rashes, scaling, dryness, and increased susceptibility to infection.¹ AD is associated with both epidermal barrier defects and immunological dysregulation, while recent evidence suggests that it is a systemic disorder. Genetic variations and mutations affecting the epidermal barrier are central aspects of the emergence of AD.^{1,2}

AD is the most common non-fatal skin disorder, affecting an estimated 230 million people worldwide. Moreover, it can occur at any age, and its prevalence ranges from 2% to 30% of the general population.^{1,3} Approximately half of the patients suffering from AD experience a moderate to severe form of the disease.¹ The prevalence differs by gender and age, being lower in men than in women and decreasing with advanced age.³ Only one study has examined the prevalence of AD among Greek adults over a 12-month period. This study reports that prevalence ranges from 1.7% to 6.4%, depending on the definition of AD used.⁴

AD is a global health problem with significant adverse effects on various areas of life.^{1,5} The humanistic burden of AD has been studied in both pediatric and adult populations, highlighting its

impact on patients, their families, and caregivers.^{1,6-8} Additionally, patients with AD often experience intense itching and skin pain, leading to sleep disturbances and difficulties in daily functioning. These issues significantly affect their quality of life (QoL), with the impact being particularly severe for those with more advanced stages of the disease.^{5,9-12} AD patients also face stigma and psychological difficulties in their everyday lives.¹

To the best of our knowledge, published data regarding the humanistic burden of AD in the adult population in Greece are limited. To be more specific, such data have been retrieved from a recently published nationwide survey targeting individuals who self-reported as AD patients through telephone interviews, collecting comprehensive information about the humanistic burden associated with the condition.⁷ However, disease burden seems to be one of the commonly used decision-making criteria from various stakeholders across the healthcare system, such as clinicians, patients, policymakers, funders, program managers, regulators, and scientific communities. For example, disease burden is involved in health technology assessments, development of guideline recommendations, health insurance coverage decisions, selection of essential medicines and diagnostics, *etc.*¹³ Given the developing treatment landscape, it is expected that country data regarding AD burden will be extremely significant in supporting healthcare policy decision makers. Hence, the objective of this study was to estimate the QoL and psychosocial burden in adult Greek patients with AD through validated assessment tools as well as to explore parameters that may influence AD humanistic burden.

Materials and Methods

Study design and participants

A non-interventional cross-sectional observational study was conducted in Greece from January 2023 to September 2023. All adult members of the Panhellenic Society of Patients with Psoriasis and Psoriatic Arthritis “Epidermia”, diagnosed with AD, regardless of current treatment regimen and disease severity, were eligible to participate as long as they were capable of understanding and signing the consent form. They were invited through an e-mail sent by the management board of the association. They were informed about the scope of the study and that data collection would be anonymous and confidential. Moreover, they were informed that their participation in this study was voluntary, and they had the right to withdraw their consent at any time. The protocol of the study was approved by the management board of “Epidermia” and the study was conducted in accordance with the Helsinki Declaration.

Data collection

A structured questionnaire, developed as a Google Form, was used for data collection. To assess the face validity of the questionnaire, a pilot study was initially conducted with 10-20 patients. A questionnaire was distributed *via* e-mail to 170 eligible participants; two e-mails were undeliverable (n=168), and 150 individuals responded, yielding a response rate of 89.28%. This questionnaire consisted of two sections. The first section focused on patients’ socio-demographic characteristics and clinical history, while the second section focused on data regarding the patients’ QoL and psychosocial burdens.

Specifically, socio-economic characteristics included age, gender, self-reported weight and height, marital and occupational status, smoking habits, and occupations related to AD.

Moreover, participants were asked to provide data regarding their medical history, such as the age of AD diagnosis and comor-

bidities. Disease severity was assessed using the self-reported, repeatable Patient-Oriented Eczema Measure (POEM) assessment tool.¹⁵ POEM scores range from 0 to 28 and are categorized into five levels of atopic eczema severity as follows: 0-2 (mild/almost nonexistent); 3-7 (mild); 8-16 (moderate); 17-24 (severe); and 25-28 (very severe). QoL was assessed using the Dermatological Life Quality Index (DLQI), which is a certified translated version of the questionnaire available in Greek.¹⁶ The DLQI assesses the impact of dermatological conditions on symptoms and emotions, daily activities, leisure time, work and school, personal relationships, and the effects of treatment. The scores range from 0 to 30 and are categorized as follows: 0-1 (no effect in QoL); 2-5 (small effect); 6-10 (moderate effect); 11-20 (very large effect); and ≥ 21 (extremely large effect).

Sleep difficulty was assessed using the Greek version of the Athens Insomnia Scale (AIS), with scores ranging from 0 to 24, with a higher score indicating greater insomnia symptom severity.^{17,18} A score ≥ 6 , a widely accepted cutoff score, was used to identify participants with insomnia.

Depression was measured using the Greek-validated translation of the Patient Health Questionnaire (PHQ).^{19,20} Its score ranges from 0 to 27, with higher scores indicating a need for clinical evaluation. The values 0-4, 5-9, 10-14, 15-19, and 20-27 indicate none or minimal, mild, moderate, moderately severe, and severe depression, respectively.

Anxiety was assessed through the Greek-validated translation of the Generalized Anxiety Disorder (GAD) scale, ranging from 0 to 21.^{19,21} The values of 0-4, 5-9, 10-14 and 15-21 indicate minimal, mild, moderate, and severe anxiety, respectively.

Statistical analysis

To detect a small to medium effect size of 0.31 with a statistical power of 0.95, a sample size of 144 participants is required. This calculation is based on a Wilcoxon signed-rank test, assuming a normal distribution and a significance level of 0.05. The effect size of 0.31 was estimated based on data from the literature, using the DLQI score with a mean of 9 (standard deviation [SD]=6.5) from previous studies and an expected mean of 11 (SD=6.5) for the current study.^{22,23} Normally distributed continuous variables were summarized with the mean and SD, while skewed variables were summarized using the median and 1st-3rd quartiles (Q1-Q3). Categorical variables were presented with absolute (n) and relative (%) frequencies. The association between two categorical variables was assessed with Fisher’s exact test, while the association between continuous variables and AD severity groups was assessed through one-way analysis of variance (ANOVA) and Kruskal-Wallis’s test for normally distributed and skewed continuous variables, respectively. Appropriate univariate and multiple generalized linear models (GLM) were applied to determine factors that might be independently associated with QoL and psychosocial burden. Baseline demographic, lifestyle, anthropometric, and clinical characteristics of patients were used as potential independent factors. In the case of QoL, sleep, anxiety and depression, logistic regression models were fitted with a binary categorization of the dependent variables as follows: DLQI score (0: DLQI score <11; 1: DLQI score ≥ 11), AIS-8 score (0: AIS-8 score <6; 1: AIS-8 score ≥ 6), GAD-7 score (0: GAD-7 score <5; 1: GAD-7 score ≥ 5), and PHQ-9 score (0: PHQ-9 score <5; 1: PHQ-9 score ≥ 5), respectively. All tests were 2-sided, and the significance level was set at 5% for all analyses. This was a complete case analysis, as the proportion of missing data was low. The data management, cleaning, and analysis were performed using STATA software (version 17.0, 2017, STATA Corp).

Results

Participants baseline characteristics

The mean age (SD) of participants was 37.6 (12.7) years, with 44.7% being males. According to body mass index (BMI), no participants were classified as underweight, 41% were overweight, and 12% were obese.

Regarding occupational status, most participants (77%) did not work in dermatitis-related occupations. Among those who worked in dermatitis-related occupations, most were laboratory or technical workers (21%). The 47% of participants were current smokers (Table 1).

The median (Q1-Q3) age of study participants at diagnosis of AD was 10 (2-20) years. In total, 58% of the participants reported at least one comorbidity. The most common comorbidities were asthma (29%), rhinitis (28%), and food allergies (25%). Just over half of the sample (51%) had a family history of AD, rhinitis, or asthma. The median (Q1-Q3) POEM score was 9 (6-13) points. Overall, 51% had moderate eczema, and 12% had severe to very severe eczema (Table 2).

Impact of AD on QoL, sleep difficulties, and mental health

The median (Q1-Q3) DLQI score was 9 (4-15). Overall, 29% and 42% of the participants had a moderate and a very large/extremely large effect on their QoL due to AD, respectively.

The impact of AD on QoL increased with the severity of the condition. Among individuals with clear or almost clear/mild eczema, 11% reported that AD had a very large or extremely large effect on their QoL. This percentage rose significantly to 54% among those with moderate eczema and further increased to 89% for individuals with severe or very severe eczema ($p < 0.001$).

Moreover, 55% of the study participants experienced insomnia. The proportion of subjects with insomnia increased concomitantly with AD severity, recording rates of 16%, 75%, and 94%, respectively, for participants with clear or almost clear/mild, moderate, and severe/very severe eczema.

The median GAD-7 score (Q1-Q3) was 5.0 (3.0-9.0). Regarding the impact of AD on anxiety, 31% had mild anxiety, 23% had moderate/severe anxiety. Anxiety severity increased with AD severity. Specifically, the proportion with moderate/severe anxiety increased from 13% in those with clear or almost clear/mild eczema to 56% in those with severe/very severe eczema.

Finally, the mean (Q1-Q3) PHQ-9 score was 4.0 (2.0-8.0). Overall, 28% of participants had mild depression, and 18% had moderate to severe depression. Moreover, 54%, 12%, and 1% of the participants found it somewhat, very, and extremely difficult, respectively, to perform their tasks and manage their home or social relationships. The proportion of patients with mild to moderate depression increased from 20% in those with clear or almost clear/mild eczema to 78% in those with severe/very severe eczema (*Supplementary Table 1*).

Factors associated with QoL, sleep disorders, anxiety and depression

Univariate logistic regression models revealed that an earlier age at AD diagnosis is associated with better QoL outcomes. In contrast, the presence of comorbidities, family history of AD, food allergies, gastrointestinal (GI) problems, asthma, rhinitis, and AD severity is linked to a diminished QoL. The multivariate analysis further confirmed the association of QoL with the presence of GI

problems, rhinitis, and AD severity.

Regarding sleep disorders, obese participants showed higher odds of experiencing insomnia compared to those with a healthy weight at the univariate level. Additionally, an earlier age of AD diagnosis, comorbidities, especially food allergies and rhinitis, and AD severity were associated with increased odds of suffering from insomnia. The multivariate analysis further confirmed the association of insomnia with food allergies and with AD severity (*Supplementary Table 2*).

In terms of anxiety, several factors were associated with its severity at the univariate level. Female gender, diagnosis at an earlier age, family history of AD, presence of food allergies, GI problems, asthma, or rhinitis, and AD severity were significantly associated with a higher probability of suffering from mild to severe

Table 1. Socioeconomic factors.

Demographics - general profile	Participants N=150
Gender, n (%)	
Female	83 (55.3)
Male	67 (44.7)
Age, years	
Mean (SD)	37.6 (12.7)
Weight, kg	
Mean (SD)	76.1 (16.4)
Height, m	N=147
Mean (SD)	1.7 (0.1)
BMI, n (%)	
Underweight	0 (0.0)
Normal weight	70 (46.7)
Overweight	62 (41.3)
Obese	18 (12.0)
Marital status, n (%)	
Unmarried	74 (49.3)
Married/cohabitation	59 (39.3)
Divorced/separated	14 (9.3)
Widow/er	3 (2.0)
Occupational status, n (%)	N=149
Freelancer/self-employed	46 (30.9)
Employee	59 (39.6)
Unemployed	8 (5.4)
Retired	7 (4.7)
Student	25 (16.8)
Household	4 (2.7)
Other	0 (0.0)
Occupation related to AD*, n (%)	N=34
Hairdresser/barber, beautician	6 (17.6)
Food industry worker	4 (11.8)
Healthcare professional, dentist, veterinarian	5 (14.7)
Laboratory worker, laboratory technician	7 (20.6)
Farmer, gardener, florist	3 (8.8)
Janitor, cleaner	5 (14.7)
Painter, artist, decorator	0 (0.0)
Automotive mechanic	2 (5.9)
Construction worker	2 (5.9)
Smoking habits, n (%)	
Smoker	70 (46.7)
Former smoker	24 (16.0)
No smoker	56 (37.3)

SD, standard deviation; BMI, body mass index; AD, atopic dermatitis; *if occupational status was "freelancer/self-employed" or "employee".

anxiety. Multivariate analysis confirmed the association of anxiety with AD severity, with a family history of AD, and the presence of GI problems, rhinitis, or asthma.

Considering depression, at the univariate level, factors including gender, working in dermatitis-related occupations, an earlier diagnosis of AD, food allergies, GI problems, rhinitis, and AD severity were significant predictors of increased odds of experiencing mild to severe depression. However, only AD severity was confirmed in a multivariate analysis (*Supplementary Table 3*).

Discussion

The lives of people with AD are significantly impacted in health, QoL, psychological well-being, and social interactions. To date, only one cross-sectional study has evaluated the burden of moderate to severe AD in Greece.⁷ Therefore, our study aims to contribute to existing knowledge by investigating the effects of AD on QoL, sleep patterns, and psychological problems. Also, we assessed how disease severity and other factors might affect these domains, providing evidence to inform healthcare decisions and optimize patient care strategies.

In our study, according to the POEM score, 11% of the participants had clear or almost clear skin, 27% had mild eczema, and 62% had moderate to very severe eczema. These findings were partially comparable to those reported in the previously conducted Greek study by Gregoriou *et al.*, in which 53.0% of the AD population as defined by the United Kingdom Working Party (UKWP) criteria and 25.8% of the AD population as defined by patient-reported AD diagnosis from a physician (Expert Diagnosis cohort) were classified as suffering from moderate to very severe eczema, respectively.⁷

In the cross-sectional study conducted by Fuxench *et al.* in 2019 in the USA, 60.1% of participants were classified as having mild, 28.9% moderate, and 11% severe disease, based on the POEM score.²⁴ Therefore, the severity of eczema, as assessed by the POEM score, varies among different populations. This might be attributed to the fact that the study used different inclusion criteria, including stricter diagnostic criteria and only individuals aged 18-65.²⁴ However, it is evident that a considerable proportion of participants experience moderate to severe eczema.

Our results revealed significant impacts of AD on participants' QoL, sleep quality, and mental health. Specifically, 89.5% of participants with moderate eczema reported a moderate to extremely large effect on their QoL, while 100% of participants with severe/very severe eczema experienced a similar impact. Consequently, in our study, 91.4% of participants with moderate to very severe eczema reported a moderate to extremely large effect on their QoL. This is higher than the findings of the previously conducted study, which reported that 84.3% (UKWP criteria cohort) and 72.2% (Expert Diagnosis cohort) of participants with moderate/very severe eczema experienced a moderate to extremely large effect on their QoL.

In our study, the mean (SD) DLQI score for overall participants was 9.9 (6.8), resembling the UKWP criteria cohort in the prior Greek study (mean DLQI score: 10.92, 95% confidence interval [CI]: 9.24-12.59). However, our mean DLQI score was notably higher than the Expert Diagnosis cohort in the same study (mean DLQI score: 5.29, 95% CI: 4.66-5.93). This difference may be due to the different definitions of AD population in these studies. The similarity in DLQI scores between our study and the UKWP cohort in the previous Greek, may be attributed to the stricter definition of AD patients used. In our study, participants

were members of a patient association and, therefore, had AD diagnosis by a physician, whereas the UKWP cohort used the self-diagnosed assessment tool with one-year recall. On the other hand, the Expert Diagnosis cohort included participants who had been diagnosed with AD by a doctor at least once in their lifetime, which might explain the notably lower DLQI score observed in that group due to the wider recall period. More related results in the DLQI scores were presented in a study conducted in the USA.²⁴ Moreover, another US study involving 186 individuals showed a mean (SD) DLQI score of 9.9 (7.4), aligning closely with our study's score; these scores increased as disease severity worsened.²⁵ In addition, the findings of systematic review and meta-analysis confirm the substantial impact of worsening disease on QoL.⁵

In our multivariate analysis, we discovered that beyond the disease severity affecting QoL, rhinitis and GI issues also significantly impacted QoL, consistent with the previous study by Gregoriou *et al.* This underscores the necessity of providing dermatological treatment and integrating QoL screening tools in dermatology. Nonetheless, AD's complexity suggests that QoL cannot solely be explained by disease severity, as our study reports correlations between other variables.

Our findings aligned with existing literature, revealing a robust connection between the severity of AD and symptoms of insomnia, alongside allergic comorbidities.^{1,8-10,22,26,27} While variations exist among the validated assessment tools for insomnia and sleep disorders across studies, most agree on the correlation

Table 2. Medical profile and severity of atopic dermatitis.

Medical profile	N=150
Age at AD diagnosis, years	N=149
Median (Q1-Q3)	10.0 (2.0-20.0)
Comorbidities, n (%)	
None	63 (42.0)
One	37 (24.7)
Two	25 (16.7)
Three or more	25 (16.7)
Comorbidities, n (%)	N=150
Asthma	44 (29.3)
Chronic obstruction pneumonopathy	0 (0.0)
Food allergies	38 (25.3)
Conjunctivitis	22 (14.7)
Gastrointestinal problems	16 (10.7)
Rhinitis	42 (28.0)
Diabetes	6 (4.0)
Hypertension	7 (4.7)
Heart failure	0 (0.0)
Other	0 (0.0)
Family history of atopic dermatitis, rhinitis, or asthma	N=149
Yes	77 (51.7)
No	72 (48.3)
AD severity (POEM), n (%)	
Clear or almost clear	16 (10.7)
Mild eczema	40 (26.7)
Moderate eczema	76 (50.7)
Severe eczema	15 (10.0)
Very severe eczema	3 (2.0)
POEM score	
Median (Q1-Q3)	9.0 (6.0-13.0)

SD, standard deviation; Q, quartiles; POEM, Patient Oriented Eczema Measure; AD, atopic dermatitis.

between the severity and frequency of AD symptoms and sleep disturbances.^{8-10,22,26,27} Studies have noted nocturnal escalation in itching behavior, suggesting the circadian rhythm's role in modulating symptom severity.²⁸ Consequently, individuals affected by AD experience disrupted sleep characterized by increased restlessness due to associated itchiness, frequent awakenings, reduced sleep duration, and daytime fatigue, thereby elucidating these associations.

Furthermore, our study reaffirmed the positive correlation between the severity of AD and symptoms of anxiety and depression. Despite variations in the assessment tools utilized across studies, a consistent trend emerged.^{5,8,12,22,23,27,29} Anxiety levels were further influenced by the presence of GI comorbidities and a family history of AD, rhinitis, or asthma among patients. One plausible explanation for the correlation between AD and psychological comorbidities is the social stigma attached to visible skin lesions. This stigma can significantly impact individuals with AD, leading to increased rates of depression and anxiety.

This study has several limitations that should be taken into account. First, the sample size was relatively small. Additionally, the exclusion of any tools for diagnosing AD, even self-reported ones, due to the nature of web-based surveys, may have restricted the range of outcomes evaluated. Furthermore, participants' responses may have been affected by recall bias or reporting bias, leading them to respond based on perceived expectations rather than true experiences. Lastly, because the study employed a cross-sectional design, we can only hypothesize about the direction of effects, which limits our ability to draw definitive conclusions. These limitations must be considered when interpreting the study results and designing future research in this field.

Conclusions

These findings underscore the complex impact of AD, emphasizing the necessity for comprehensive management approaches. The study reveals a significant burden on AD patients in Greece, who experience impairments in QoL, sleep, and social activities. Recognizing this burden is crucial for guiding healthcare decisions to benefit AD patients and alleviate societal burdens. The results suggest that prioritizing the management of patients' psychosocial well-being can benefit both healthcare systems and society.

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Online Supplementary Material:

Supplementary Table 1. QoL, sleep problems, anxiety, and depression in AD patients based on DLQI.

Supplementary Table 2. Factors associated with QoL and insomnia (univariate and multivariate models) (n=150).

Supplementary Table 3. Factors associated with anxiety and depression (univariate and multivariate models) (n=150).