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Assessment of Disease Severity and Quality of Life in Patients with Atopic Dermatitis from South Korea

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Background: Data illustrating the impact of atopic dermatitis (AD) on lives of adults with AD in South Korea are limited.
Objective: To assess the AD disease severity and its impact on quality of life (QoL) in patients with AD from South Korea.
Methods: Patients with AD utilizing the specialist dermatology services of major hospitals in South Korea were assessed for disease severity using Eczema Area and Severity Index (EASI) score, for QoL using Dermatology Life Quality Index (DLQI) (for QoL), and for comorbidities and treatment experience via retrospective review of 12-month medical records. Clinical and sociodemographic characteristics were also measured.
Results: Of the 1,163 patients, 695 (59.8%) were men (mean age [years]±standard deviation: 31.6±12.1). Overall, 52.9% (n=615) patients had moderate-to-severe disease (EASI>7). The QoL of 72.3% (n=840) patients was affected moderately-to-severely (DLQI score: 6~30). Systemic immunosuppressants were used ≥1 over past 12 months in 51.9% (n=603) patients, and the most commonly used were cyclosporines (45.7%, n=531) and systemic corticosteroids (40.5%, n=471). Approximately, 10.8% (n=126) patients consulted or received treatment for AD-related eye problem. Of these, 40% (n=50) patients reported poor, very poor, or completely blind status; approximately, 16.7% patients (n=192) reported having depression or anxiety; and 35.5% (n=410) reported suicidal ideation or suicidal attempt.
Conclusion: A large proportion of patients had moderate-to-severe AD, a compromised QoL, and ocular or mental health comorbidities, indicating a high disease burden despite systemic treatment. These findings highlight the importance of a holistic approach for the evaluation and treatment of patients with AD.

Keywords: Anxiety, Atopic dermatitis, Depression, Quality of life

INTRODUCTION

Atopic dermatitis (AD) is a globally prevalent dermatological disorder with a high disease burden among skin disorders, affecting up to 20% of children and 10% of adults in developed countries worldwide[1]. It generally begins in childhood and may persist in adulthood depending upon the severity of the disease, suggesting the likelihood of a lifelong illness[2]. In Korea, the rate of doctor-diagnosed AD in adults increased from 2.9% to 4.3% from 2009 to 2019 as per the Korean National Health Statistics[3]. Moreover, in 2009, the prevalence of AD, as assessed by dermatologists, was 2.6% among adults in South Korea visiting health service centers for annual health check-ups[4]. Recurrent eczematous lesions and intense itch predominate clinical manifestations of AD and have a profound negative impact on the psychological and social well-being of the affected individual[5], making it essential to identify the grade of disease severity to optimize treatment and care. Eczema Area and Severity Index (EASI) and the scoring atopic dermatitis (SCORAD) measures are extensively validated tools for objective measurement of the clinical severity of AD[6]. However, the Harmonising Outcome Measures for Eczema (HOME) initiative recommends the use of EASI to measure clinical signs of AD in clinical trials[6]. In 2010, Kim et al.[4] observed that the prevalence of mild, moderate, and severe AD, as assessed by the EASI tool, was reported in 70.6%, 25.5%, and 3.9% of adults with AD in South Korea, respectively. A retrospective data analysis of 5,000 patients with AD observed that the EASI score increased with age and disease severity and that severe AD was more prevalent in adults (>18 years old) than in younger patients (≤18 years old)[7].

Patients with AD, apart from cutaneous lesions, have substantial subjective symptoms, such as pruritus and sleep disturbances[8]. Furthermore, the effect of AD on mental health, emotional well-being, and social functioning is more than that on the physical level in adults with AD, resulting in a significant impact on the quality of life (QoL)[9]. Stress, depression, and suicidal ideation have significant association with the presence of AD[10]. Thus, adults with AD have significantly lower QoL than those without AD[9,10]. The presence of eczema lesions on exposed body parts such as hands, head, neck, and face may lead to social problems, such as, social stigma or isolation[11,12]. As EASI assessment focuses on the cutaneous signs of AD, it may not adequately reflect the overall severity of AD, including impairment of QoL, mental health, and emotional well-being. QoL should be assessed using a comprehensive tool to holistically determine the disease severity in an individual and to select optimal treatment for AD control[13]. The Dermatology Life Quality Index (DLQI) is a widely used tool for assessing the QoL in patients with AD as well as the severity of AD. Moreover, Korean Atopic Dermatitis Association (KADA) consensus guidelines recommended the use of DLQI[13].

The mainstay of treatment in AD includes topical corticosteroids (TCS) with basic and optimal skin care regimens involving the use of moisturizers. Considering the adverse effects of TCS, topical calcineurin inhibitors such as tacrolimus and pimecrolimus are the recommended second-line of therapy for long-term as well as short-term treatment[14]. Individuals with severe AD who fail to respond to topical therapy require systemic immunosuppressants and phototherapy[14]. A survey of consultant physicians from South Korea indicated that dermatologists preferred the use of cyclosporin, phototherapy, and systemic corticosteroids as the first-line treatment regimens in moderate-to-severe AD[15]. Despite receiving conventional systemic treatments, individuals with AD may remain symptomatic and develop recurrent flares impairing QoL[16]. This unmet therapeutic need calls for a deeper understanding of current treatment patterns in the management of AD. This study aims to provide updated information about disease severity, QoL, and systemic treatment experience in adults with AD utilizing specialist dermatology services in South Korea. These data also evaluate the significance of assessing AD severity using a multi-dimensional approach that is not limited to EASI but is inclusive of patient reported outcomes.

MATERIALS AND METHODS

Study design

This national, multicenter, non-interventional (observational) study was conducted at 24 university or tertiary hospitals in South Korea between October 2018 and June 2019. The participating investigators screened each consecutive patient with AD who visited the study site for routine consultation and assessed their eligibility for enrollment in the study. This study, comprising a cross-sectional survey and a medical record review of a retrospective 12-month period, was completed within a period of 8 weeks.

Study population

Patients aged ≥19 years who visited the principal investigator's site for a routine AD-related consultation and/or sought treatment for AD and who were able to read and write in Korean were included in the study. Patients were excluded if they had participated in non-marketed investigational drug clinical trial(s) (excluding moisturizer-based trials) for the treatment of AD within 12 months from the study enrollment date or patients whose AD diagnosis was uncertain to the investigator.

Adults fulfilling all the eligibility criteria were invited to participate in the study. Those who agreed to complete the survey questionnaire and provided a written informed consent were enrolled into the study. Eligible patients were recruited in the study over a period of 8 weeks.

The investigator performed clinical assessment of the eligible patients including assessment of the disease severity of AD using EASI tool. Thereafter, patients were given a set of paper questionnaires (including DLQI) that they had to self-complete. These paper surveys intended to collect patient's responses related to QoL and other functional questions related to AD. In addition, data about AD- or treatment-related complication of special interest (pertaining to visual function and psychological function) were collected using a patient questionnaire. This questionnaire included a question enquiring whether the patients had been diagnosed with depression or anxiety at any time since the diagnosis of AD. Further information on depression or anxiety was collected as a part of the 5-level EuroQoL 5 Dimensions Assessment (EQ-5D-5L). Data abstraction from the patient's medical record was performed by the investigators or his/her investigating team member.

Study endpoints

The study objective was to document the severity of AD disease and the associated effect of AD on QoL, along with examination of patients' characteristics and AD treatment patterns. The primary endpoints included AD disease severity (mild, moderate, and severe), patient reported QoL measures (general and disease-specific), and patient's experience of systemic treatment use (yes/no). The secondary endpoints included patient's socio-demographic, clinical characteristics, and AD treatments.

On the basis of EASI scores, the patients were classified into the following subgroups: mild (EASI between 1.1 and 7.0), moderate (EASI between 7.1 and 21.0) and severe (EASI between 21.1 and 50.0)[17]. The QoL measured using DLQI was scored as follows: 0~1, no effect at all on patient's life; 2~5, a small effect on patient's life; 6~10, a moderate effect on patient's life; 11~20, a very large effect on patient's life; and 21~30, an extremely large effect on patient's life[18]. The use of systemic treatment was examined via data abstraction of medical records at the investigators' discretion. It was measured as any use of systemic treatment for AD in the past 12 months from the date of study enrollment. Use of systemic corticosteroids, dupilumab, cyclosporine, azathioprine, mycophenolate mofetil, and methotrexate were considered as a part of systemic treatment evaluation in this study.

Statistical analysis

For continuous variables, descriptive statistics (means, standard deviations, median) were reported. For categorical variables, frequencies and percentages were used. For bivariate analyses, all variables were presented per severity subgroups and the differences in subgroups by level of severity were examined at a 5% threshold.

For continuous variables, the distribution was examined before the statistical analysis. If the distribution was approximately normal, t-test was used; otherwise, Wilcoxon rank test was employed to test the statistical difference. For categorical variables, chi-square test was used to test the statistical difference. Fisher's exact test was used instead in case the expected value of one category of a variable was sparse. For all the tests performed, *p*-values were reported. All steps of data processing and statistical analyses were performed using the R Statistical programming language software (10) version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria). Differences in subgroups by level of severity were examined at a 5% threshold.

Ethics

The study was approved by the ethical review board at each participating site (Supplementary Table 1). The study was conducted in accordance with the principles of Declaration of Helsinki and good clinical practice and local applicable regulatory guidelines.

RESULTS

Patient disposition

Overall, 1,195 patients with AD from South Korea were screened for eligibility, of which 32 patients (2.7%) were not eligible for study inclusion (Fig. 1). A total of 1,163 patients, who were enrolled over a period of 8 weeks, completed the study.

Patient demographics and clinical characteristics

Overall, the mean±standard deviation age of the eligible patients was 31.6±12.1 years and 59.8% (695/1,163) of the patients were males. The body weight (kg) was higher in patients with severe AD. Nearly 7.0% (76/1,088) of patients reported that they were single, separated, or divorced because of AD; this proportion was significantly more in subgroups with moderate AD (7.2%; 33/460) and severe AD (13.4%; 16/119) compared with the subgroup having mild AD (p<0.05; Table 1). Three-fourth of the patients (76.7%; 892/1,163) had at least one visible or functionally important body area affected by AD. The most commonly AD-affected area was the perioral area (39.7%; 462/1,163), followed by eyelids (39.4%; 458/1,163), genital area (23.1%; 269/1,163), palms (20.7%; 241/1,163), and soles (10.6%; 123/1,163) (Table 2).

Primary endpoints

1) Extent of AD disease severity and the impact of AD on quality of life

The severity of AD as measured by EASI, was noted to be mild, moderate, and severe in 47.1% (548/1,163), 42.0% (488/1,163), and 10.9% (127/1,163) of the patients, respectively. Approximately, 52.9% (615/1,163) were considered having moderate-to-severe disease (EASI >7) at the time of assessment.

As per the DLQI measure, AD had a moderate-to-severe impact on QoL (6~30) in 72.3% (840/1,163) of patients and a no-to-small impact on QoL (0~5) in 27.7% (322/1,163) of patients. DLQI severity was significantly associated with EASI severity (p<0.0001), indicating that the decline in QoL corresponded with an increase in disease severity (Fig. 2, Supplementary Fig. 1).

2) Overall AD treatment pattern

The treatments were evaluated as systemic or topical. Overall, 51.9% (603/1,163) patients used systemic immunosuppressant treatments at least once within the 12 months before study enrollment (Table 3). The most commonly used systemic immunosuppressant was cyclosporin (45.7%; 531/1,163) followed by systemic corticosteroid (40.5%; 471/1,163) (Supplementary Fig. 2). The use of systemic immunosuppressants increased with increasing disease severity (p<0.05). Systemic antihistamines were used by 87.5% (1,018/1,163) of patients; their use was significantly higher in the subgroup with moderate AD compared with the subgroup with mild AD (p<0.05). TCS were used by 74.2% (863/1,163) patients prior to the study assessment, with the highest use reported in the subgroup with severe AD (80.3%; 102/127). Nearly 50% of the patients (579/1,163) used TCS in the past one month. Methylprednisolone (48.5%; 281/579) was the most frequently used TCS (Table 3).

Secondary endpoints

Overall, 35.2% (409/1,163) of the patients reported at least one of the atopic comorbidities. Diabetes was the most commonly reported non-atopic comorbidity (2.5%, 27/1,102). The frequency of AD flare in the past 12 months was significantly higher in the severe AD (1.3±2.0) and the moderate AD subgroups (0.9±1.7) than in the mild AD subgroup (0.6±1.1; p<0.05). Overall, 10.8% (126/1,163) patients had

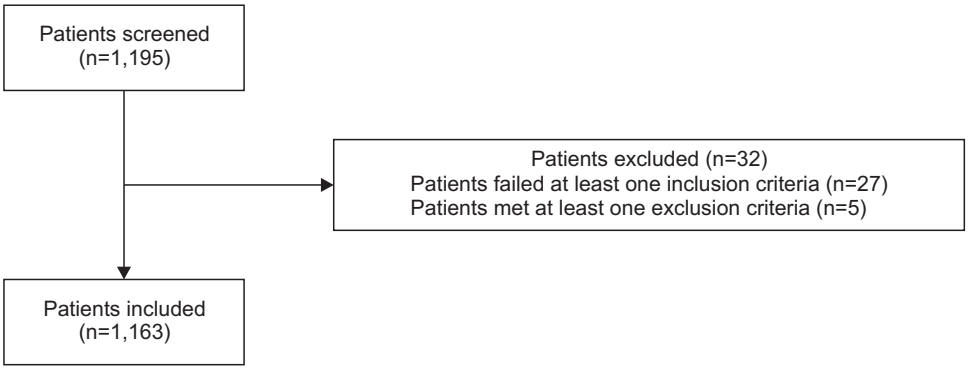

Fig. 1. Patient disposition.

Table 1. Demographics and baseline characteristics of patients with AD, overall and across disease severity subgroups

Characteristic	All patients (n=1,163)‡	Disease severity by EASI			
		Mild (n=548)§	Moderate (n=488)§	Severe (n=127)§	Moderate-to-severe (n=615)§
Age at enrolment (yr)	31.6±12.1	32.0±12.2	31.0±12.2	32.1±11.4	31.2±12.0
Age at diagnosis (yr)	23.5±15.8	26.0±15.5	22.0±15.8*	18.0±15.1*†	21.2±15.7*
Sex					
Male	695 (59.8)	280 (51.1)	318 (65.2)	97 (76.4)	415 (67.5)
Female	468 (40.3)	268 (48.9)	170 (34.8)	30 (23.6)	200 (32.5)
Anthropometry measures					
Weight (kg)	66.5±13.9	65.0±13.4	67.6±13.9*	68.7±15.1*	67.8±14.2*
BMI (kg/m^2)	23.3±3.8	23.1±3.7	23.5±3.7	23.8±4.3	23.5±3.8*
Current employment status	1,161	547	487	127	614
Working full-time	363 (31.3)	172 (31.4)	149 (30.6)	42 (33.1)	191 (31.1)
Working part-time	88 (7.6)	38 (6.9)	39 (8.0)	11 (8.7)	50 (8.1)
Homemaker disable	80 (6.9)	37 (6.8)	40 (8.2)	3 (2.4)	43 (7.0)
Unemployed and seeking work	139 (12.0)	63 (11.5)	57 (11.7)	19 (15.0)	76 (12.4)
Retired	15 (1.3)	8 (1.5)	6 (1.2)	1 (0.8)	7 (1.1)
Student	337 (29.0)	163 (29.8)	142 (29.2)	32 (25.2)	174 (28.3)
Other	139 (12.0)	66 (12.1)	54 (11.1)	19 (15.0)	73 (11.9)
AD related: single, separated or divorced	1,088	509	460	119	579
Yes	76 (7.0)	27 (5.3)	33 (7.2)*	16 (13.4)*	49 (8.5)*
No	562 (51.7)	285 (56.0)	225 (48.9)	52 (43.7)	277 (47.8)
Unsure	141 (13.0)	44 (8.6)	75 (16.3)	22 (18.5)	97 (16.8)
Not applicable	309 (28.4)	153 (30.1)	127 (27.6)	29 (24.4)	156 (26.9)
Highest level of education	1,161	547	488	126	614
No certificate, diploma or degree	10 (0.9)	8 (1.5)	2 (0.4)	0 (0.0)	2 (0.3)
High school certificate or equivalent	483 (41.6)	226 (41.3)	212 (43.4)	45 (35.7)	257 (41.9)
Undergraduate	505 (43.5)	237 (43.3)	209 (42.8)	59 (46.8)	268 (43.6)
Graduate	123 (10.6)	61 (11.2)	47 (9.6)	15 (11.9)	62 (10.1)
Other	40 (3.4)	15 (2.7)	18 (3.7)	7 (5.6)	25 (4.1)
Level of monthly income (KRW)	1,042	484	446	112	558
<1,000,000	456 (43.8)	211 (43.6)	200 (44.8)	45 (40.2)	245 (43.9)
1,000,000~2,000,000	157 (15.1)	71 (14.7)	73 (16.4)	13 (11.6)	86 (15.4)
2,001,000~3,000,000	156 (15.0)	74 (15.3)	67 (15.0)	15 (13.4)	82 (14.7)
3,001,000~4,000,000	126 (12.1)	59 (12.2)	47 (10.5)	20 (17.9)	67 (12.0)
4,001,000~5,000,000	55 (5.3)	26 (5.4)	19 (4.3)	10 (8.9)	29 (5.2)
5,001,000~6,000,000	42 (4.0)	24 (5.0)	17 (3.8)	1 (0.9)	18 (3.2)
>6,000,000	50 (4.8)	19 (3.9)	23 (5.2)	8 (7.1)	31 (5.6)

Values are presented as mean±standard deviation, number (%), or number only. AD: atopic dermatitis, EASI: Eczema Area and Severity Index, BMI: body mass index, KRW: South Korean won. *p<0.05 compared to mild EASI severity, †p<0.05 compared to moderate EASI severity. ‡Number of patients analyzed. §Number of patients with non-missing results at the visit.

consulted or received treatment for eye-related problems, and this proportion was significantly more in the subgroups with moderate-to-severe AD or severe AD versus those with mild AD (p<0.0001). Among patients seeking consultation or treatment for AD-related eye problems, 40% (50/126) of patients reported poor or very poor eyesight or completely blind status.

Occurrence of depression or anxiety after the diagnosis of AD was reported in overall 16.7% of patients (192/1,152). Depression was noted to be significantly higher in the subgroups with moderate-to-severe AD and severe AD compared to those with mild AD (p<0.05). Moreover, about one-third of patients (35.5%, 410/1,155) reported suicidal ideation or suicidal attempt (Table 4, Supplementary Fig. 3).

DISCUSSION

This nationwide survey from South Korea describes the characteristics of AD including disease severity, underlying comorbidities, impact on QoL, and treatment patterns in the real-world settings. More than half of the adults with AD (52.9%) had moderate-to-severe disease (EASI >7), and at least one visible or functionally important body area was affected in about 77% of the patients. Nearly three-fourths of the patients (72.3%) endured a moderate-to-severe impact on their QoL (DLQI score: 6~30). Occurrences of suicidal ideation or attempt (35.5%) and diagnosis of depression or anxiety after diagnosis of AD (16.7%) recorded in the study were numerically higher in those with severe AD disease. TCS (74.2%) and conventional systemic immunosuppressants (51.9%) were the most commonly employed treatments for AD in South Korea.

In the present study, 10.9% of the patients were assessed having severe disease (EASI ≥21). An earlier survey conducted among physicians' specialties in Korea (allergists and dermatologists) assessed the pattern of AD management in clinical practice. The proportion of patients with moderate-to-severe AD attended by dermatologists in their clinical practice was 10%~50% and >51%, as reported by allergists[15]. Although EASI is a widely used tool for evaluating AD severity[19], this tool may be inadequate to assess AD severity in some specific areas, for example, a genital area or exposed areas such as palms and soles. Presence of lesions in these areas cause social and functional impairment, leading to a low QoL; this represents the true extent of disease severity prevailing in a patient with AD. A previous study on psoriasis indicated that involvement of visible body area(s) by skin disease is an important factor that can impact the patients' overall QoL[20]. Thus EASI may not fully delineate disease severity when such areas are involved. Highly visible body areas or those important to function should be considered additionally when assessing the overall disease severity[21]. In this study, nearly three-fourths of the patients had at least one visible or functionally important body area (such as the perioral area, eyelids, genital area, palms, and soles) affected by AD. As per the Italian guidelines, features such as lesions over the face, genitalia or experience of intense

Table 2. Extent of functionally important or visible area involvement among study patients

Body area involved	Patients (n=1,163)*
Any functionally important or visible area involved	892 (76.7)
Perioral area	462 (39.7)
Eyelids	458 (39.4)
Genital area	269 (23.1)
Palms	241 (20.7)
Soles	123 (10.6)

Values are presented as number (%). *Number of patients analyzed.

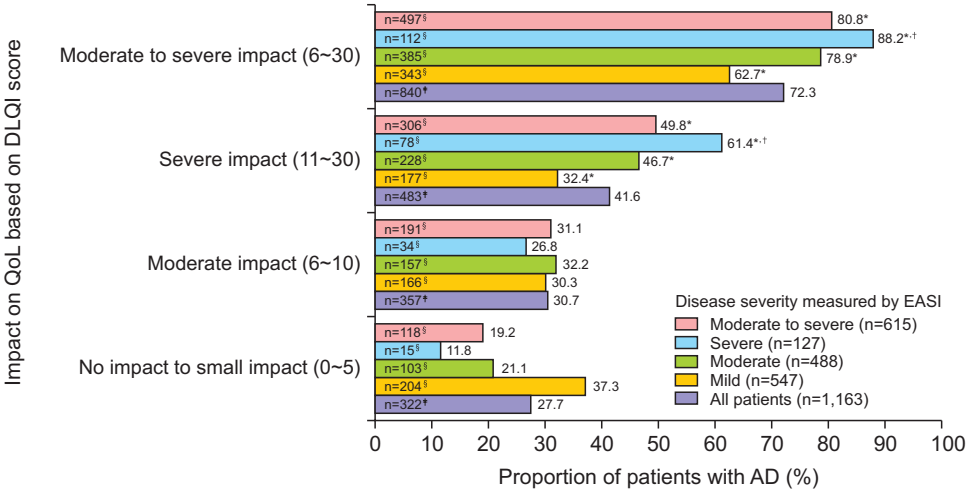

Fig. 2. Impact on QoL of patients with AD, overall and across disease severity subgroups. Values are presented as number (%). QoL: quality of life, DLQI: Dermatology Life Quality Index, AD: atopic dermatitis, EASI: Eczema Area and Severity Index, *p<0.05 compared to mild EASI severity; †p<0.05 compared to moderate EASI severity. ‡Number of patients analyzed. §Number of patients with non-missing results at the visit.

Table 3. AD-related treatments received in the past 12 months, overall and across subgroups by disease severity

AD Treatment	All patients (n=1,163)‡	Disease severity by EASI			
		Mild (n=548)§	Moderate (n=488)§	Severe (n=127)§	Moderate-to-severe (n=615)§
Medical					
Systemic					
Any of systemic immunosuppressant (cyclosporin, azathioprine, mycophenolate, methotrexate, and other ST)	603 (51.9)	233 (42.5)	283 (58.0)*	87 (68.5)*†	370 (60.2)*
Cyclosporin	531 (45.7)	197 (35.9)	255 (52.3)*	79 (62.2)*†	334 (54.3)*
Systemic corticosteroid	471 (40.5)	195 (35.6)	216 (44.3)*	60 (47.2)*	276 (44.9)*
Dupilumab	51 (4.4)	8 (1.5)	26 (5.3)*	17 (13.4)*†	43 (7.0)*
Methotrexate	30 (2.6)	12 (2.2)	13 (2.7)	5 (3.9)	18 (2.9)
Azathioprine	3 (0.3)	0 (0.0)	1 (0.2)	2 (1.6)*	3 (0.5)
Mycophenolate	3 (0.3)	1 (0.2)	2 (0.4)	0 (0.0)	2 (0.3)
Other ST	114 (9.8)	57 (10.4)	45 (9.2)	12 (9.5)	57 (9.3)
Antibiotic	187 (16.1)	82 (15.0)	77 (15.8)	28 (22.1)	105 (17.1)
Antihistamine	1,018 (87.5)	468 (85.4)	438 (89.8)*	112 (88.2)	550 (89.4)*
Topical					
TCS	863 (74.2)	402 (73.4)	359 (73.6)	102 (80.3)	461 (75.0)
TCI	569 (48.9)	230 (42.0)	269 (55.1)*	70 (55.1)*	339 (55.1)*
PDE-4 inhibitors	2 (0.2)	0 (0.0)	1 (0.2)	1 (0.8)	2 (0.3)
Other topical (e.g. antibiotic, antihistamine)	124 (10.7)	52 (9.5)	60 (12.3)	12 (9.5)	72 (11.7)
Adjuvant					
Immunotherapy	70 (6.0)	24 (4.4)	36 (7.4)*	10 (7.9)	46 (7.5)*
Phototherapy (UV treatment)	42 (3.6)	12 (2.2)	21 (4.3)	9 (7.1)*	30 (4.9)*
Non-medical					
Comprehensive					
Emollients	259 (22.3)	112 (20.4)	118 (24.2)	29 (22.8)	147 (23.9)
Soap/cleanser for AD	84 (7.2)	45 (8.2)	31 (6.4)	8 (6.3)	39 (6.3)
Used TCS in the past 1 month	579 (49.8)	255 (46.5)	255 (52.3)	69 (54.3)	324 (52.7)
Top 5 TCS used	579	255	255	69	324
Methylprednisolone	281 (48.5)	115 (45.1)	129 (50.6)	37 (53.6)	166 (51.2)
Desonide	105 (18.1)	40 (15.7)	49 (19.2)	16 (23.2)	65 (20.1)
Prednicarbate	58 (10.0)	26 (10.2)	26 (10.2)	6 (8.7)	32 (9.9)
Mometasone	56 (9.7)	30 (11.8)	18 (7.1)	8 (11.6)	26 (8.0)
Hydrocortisone	53 (9.2)	21 (8.2)	28 (11.0)	4 (5.8)	32 (9.9)

Values are presented as number (%). AD: atopic dermatitis, EASI: Eczema Area and Severity Index, ST: systemic treatment, TCS: topical corticosteroids, TCI: topical calcineurin inhibitors, PDE-4: phosphodiesterase-4, UV: ultraviolet. *$p<0.05$ compared to mild EASI severity, †$p<0.05$ compared to moderate EASI severity. ‡Number of patients analyzed. §Number of patients with non-missing results at the visit.

itching or sleep disturbances are indicative of moderate-to-severe disease despite an EASI score below 16[22]. Therefore, the severity of AD should be determined taking into account additional important factors such as severe itching, presence of visible/functional lesions, and/or poor QoL.

DLQI is one of the core instruments used for assessment of patient reported outcomes that subjectively evaluates disease severity and provides reliable results for dermatological diseases in adults[23]. Employing DLQI in this study revealed that the lives of 72.3% of patients were affected moderately-to-severely in the

Table 4. Clinical characteristics of patients with AD, overall and across disease severity subgroups

Comorbidities	All patients (n=1,163)†	Disease severity by EASI			
		Mild (n=548)‡	Moderate (n=488)‡	Severe (n=127)‡	Moderate-to-severe (n=615)‡
Atopic comorbidities					
Asthma	81 (7.0)	34 (6.2)	34 (7.0)	13 (10.2)	47 (7.6)
Allergic rhinitis	200 (17.2)	83 (15.1)	95 (19.5)	22 (17.3)	117 (19.0)
Allergic conjunctivitis	31 (2.7)	11 (2.0)	13 (2.7)	7 (5.5)	20 (3.3)
Seasonal allergies	11 (0.9)	4 (0.7)	5 (1.0)	2 (1.6)	7 (1.1)
Food allergies	30 (2.6)	9 (1.6)	17 (3.5)	4 (3.1)	21 (3.4)
Allergic urticaria	72 (6.2)	34 (6.2)	29 (5.9)	9 (7.1)	38 (6.2)
Other atopic comorbidities	151 (13.0)	70 (12.8)	65 (13.3)	16 (12.6)	81 (13.2)
Any atopic comorbidities	409 (35.2)	177 (32.3)	187 (38.3)	45 (35.4)	232 (37.7)
Non-atopic comorbidities	1,102	515	466	121	587
Diabetes mellitus	27 (2.5)	13 (2.5)	12 (2.6)	2 (1.7)	14 (2.4)
Connective tissue disease	10 (0.9)	7 (1.4)	3 (0.6)	0 (0.0)	3 (0.5)
Liver disease	9 (0.8)	5 (1.0)	4 (0.9)	0 (0.0)	4 (0.7)
Malignancy	7 (0.6)	4 (0.8)	1 (0.2)	2 (1.7)	3 (0.5)
CVA or TIA	6 (0.5)	4 (0.8)	2 (0.4)	0 (0.0)	2 (0.3)
COPD	3 (0.3)	0 (0.0)	3 (0.6)	0 (0.0)	3 (0.5)
Peripheral vascular disease	2 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)
Peptic ulcer disease	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
Hemiplegia	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
Myocardial infarction	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
CHF	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
AIDS	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
Other comorbidities	94 (8.5)	34 (6.6)	44 (9.4)	16 (13.2)	60 (10.2)
Frequency of AD flares experienced in the past 12 months	0.8±1.5	0.6±1.1	0.9±1.7*	1.3±2.0*	1.0±1.8*
Estimated duration of the last flare in days (n=434)	24.1±46.0	32.6±64.1	18.3±27.2	22.1±39.2	19.1±30.1
Treatment or consultation needed because of AD related eye or vision problems					
Yes	126 (10.8)	36 (6.6)	65 (13.3)*	25 (19.7)*	90 (14.6)*
No	897 (77.1)	446 (81.4)	364 (74.6)	87 (68.5)	451 (73.3)
Not sure	140 (12.0)	66 (12.0)	59 (12.1)	15 (11.8)	74 (12.0)
Eyesight using both eyes	125	35	65	25	90
Excellent or good	25 (20.0)	9 (25.7)	13 (20.0)	3 (12.0)*	16 (17.8)
Fair	50 (40.0)	14 (40.0)	28 (43.1)	8 (32.0)	36 (40.0)
Poor, very poor or completely blind	50 (40.0)	12 (34.3)	24 (36.9)	14 (56.0)	38 (42.2)
AD–related mental health	1,152	542	483	127	610
Diagnosed with depression or anxiety after the diagnosis of AD	192 (16.7)	81 (14.9)	83 (17.2)	28 (22.0)	111 (18.2)
Depression after the diagnosis of AD	166 (14.3)	66 (12.1)	75 (15.4)	25 (19.7)*	100 (16.3)*
Anxiety after the diagnosis of AD	144 (12.6)	61 (11.3)	63 (13.1)	20 (15.7)	83 (13.7)

Table 4. Continued

Comorbidities	All patients (n=1,163)†	Disease severity by EASI			
		Mild (n=548)‡	Moderate (n=488)‡	Severe (n=127)‡	Moderate-to-severe (n=615)‡
Thought about or attempted to suicide	1,155	544	485	126	611
Never	745 (64.5)	388 (71.3)	292 (60.2)*	65 (51.6)	357 (58.4)
Suicidal ideation or attempt	410 (35.5)	156 (28.7)	193 (39.8)	61 (48.4)	254 (41.6)

Values are presented as number (%), number only, or mean±standard deviation. AD: atopic dermatitis, EASI: Eczema Area and Severity Index, CVA: Cerebrovascular accident, TIA: transient ischemic attack, COPD: chronic obstructive pulmonary disease, CHF: congestive heart failure, AIDS: acquired immunodeficiency syndrome. *$p<0.05$ compared to mild EASI severity. †Number of patients analyzed. ‡Number of patients with non-missing results at the visit.

week before the study participation. QoL showed strong correlation with disease severity. A positive association ($p<0.0001$) between DLQI and EASI scores noted in this study substantiates the fact that QoL correlates with disease severity[24]. As factors other than objective disease severity significantly impact QoL, and increasing disease severity results in significant deterioration in QoL, the 2019 Consensus Korean Diagnostic Guidelines to Define Severity Classification and Treatment Refractoriness for AD defines moderate AD as AD with an EASI score <16 with DLQI >10 and severe AD as AD with an EASI score ≥16 but <23 with DLQI >10[13].

AD is also accompanied with various non-atopic complications, including psychological problems. In this study, AD related suicidal ideation or attempt, depression or anxiety, and eye-problems were observed in a considerable proportion of patients. A systematic review and meta-analysis demonstrated that the likelihood of suicidal ideation and suicide attempts was, respectively, 44% and 36% higher in patients with AD than in those without AD[25]. A study by Simpson et al.[26] observed that moderate-to-severe AD was associated with severe itching, pain, adverse effects on sleep, high prevalence of anxiety and depression, and health-related QoL impairment. Hence, identifying critical non-atopic complication is essential in people with AD, and presence of ocular, mood or suicidal issues need to be considered as severe AD. These complications represent important aspects of AD care; healthcare managers/policy makers should consider them carefully when making decisions.

In this study, more than half of the study patients had received at least one systemic immunosuppressant during the 12 months period before the study participation. The most commonly used systemic immunosuppressant among the study patients was cyclosporin (45.7%) and systemic corticosteroid (40.5%). Although systemic immunosuppressants were widely used over the past year in the present study, the outcome was sub-optimal and the frequency of occurrence of AD flare-up among the patients was positively correlated with disease severity. The treatment pattern of systemic immunosuppressants observed in this study was largely similar to that observed in a previous physician survey study wherein most of the South Korean dermatologists preferred to use cyclosporin initially, along with phototherapy and systemic corticosteroids[19].

This study has achieved a relatively large sample size, thus adding to the study strengths and its credibility. This study used several well-known and widely validated instruments to capture the key variables, especially in terms of disease severity and health-related QoL of the patients. This study has also captured other variables, such as the usage pattern of systemic treatment and clinical and socioeconomic characteristics of the patients. This study has also provided an insight into previously unavailable clinical challenges of AD, such as AD-related eye problems and eyesight and mental conditions. Our findings suggest to further explore this area of the impact of AD.

There are a few limitations in this study. Firstly, the study was limited to the adult population. Second, the study collected data from a retrospective chart review, which may have led to unavailability of some patient or clinician specific characteristics. Moreover, the cross-sectional nature of the survey could have resulted in a recall bias during the collection of responses. The "missing data" is a central challenge occurring in any real-world and retrospective study, which may have led to variance in the data of this study. Nevertheless, multiple imputation techniques in the regression analyses were employed to minimize the potential bias. There is a possibility that the

data on severity and QoL might have been slightly skewed upwards as the seasonal flare of AD had occurred at the time of the investigation.

In this study, a high burden of moderate-to-severe AD prevailed among patients with AD in South Korea. In addition, a large proportion of patients with chronic AD were poorly controlled despite the use of considerable systemic or topical therapies and had a low QoL. The severity of AD was accompanied by the involvement of functionally important or visible body areas, negative impact on QoL, and presence of co-morbidities such as ocular problems and mental health including suicidal ideation. The study findings highlight the need for an integrated approach in evaluating the severity of AD and also stresses that the management of AD should consider all aspects of the disease to reduce the true disease burden.

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SUPPLEMENTARY MATERIALS

Supplementary data can be found via http://anndermatol.org/src/sm/ad-21-239-s001.pdf.

CONFLICTS OF INTEREST

Dr. TY Han was involved in honorarium from Sanofi-Genzyme. Dr. EH Choi was involved in Sanofi advisory board meeting and post marketing surveillance. Dr. HC Ko was involved in presentations and participation in advisory board for Sanofi. Dr. JY Roh was involved in advisory meeting and provision of study material, received clinical trial contract, expert consult fee, honorarium for lecture. Dr. S Lee is an employee of Sanofi. Rest of the authors have nothing to disclose.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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