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Health-related Quality of Life in Children with Moderate to Severe Atopic Dermatitis

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ABSTRACT Atopic dermatitis (AD) is a common, chronic skin disease in children that may affect their quality of life (QoL). The aim of this study was to assess QoL in children in Montenegro with moderate to severe AD. A cross-sectional study was conducted at the Clinic of Dermatology and Venereology, Clinical Center of Montenegro, Podgorica, between January and December 2014. The study group included 200 children (97 boys and 103 girls) with the diagnosis of AD. The Infants' Dermatitis Quality of Life Index (IDQOL) and the Children's Dermatology Life Quality Index (CDLQI) were used to determine QoL for 90 infants (<4 years old) and 110 children (4-16 years old), respectively. Severity of disease was measured by the three-item severity (TIS) score. The mean scores were 14.38±5.57 for IDQOL and 18.43±4.88 for CDLQI. A positive correlation was observed between AD clinical severity (TIS) and all the items of IDQOL with Spearman's correlation coefficient (ρ) ranging from 0.31 to 0.74, and between AD clinical severity and all domains of CDLQI (ρ=0.31-0.69). The impact of AD on health-related quality of life (HRQoL) was more severe for younger girls, but only in some domains (IDQOL), and for older boys (CDLQI). The linguistically validated Serbian versions of both IDQOL and CDLQI questionnaires showed good internal consistency with Cronbach's alpha values of 0.88 and 0.73, respectively. In conclusion, our results demonstrate that AD has a great impact on QoL. A positive correlation between clinical severity and quality of life was seen.

KEY WORDS: atopic dermatitis; quality of life; CDLQI; IDQOL; children

INTRODUCTION

Atopic dermatitis (AD) or "eczema" is the most common chronic inflammatory skin disease in children, with a prevalence of over 20% in most developed countries (1,2). Over the recent decade, AD prevalence in developed countries did not significantly increase or even decreased, whereas it continued to rise in most developing countries, especially in young children and in low income countries such as Africa and eastern Asia (3).

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The chronic nature of AD taken together with its high prevalence makes it a major public health problem worldwide, with great social and financial implications for individuals, health care systems, and whole societies (4-7).

There is evidence to suggest that childhood AD poses a significant burden on health-related quality of life (HRQoL) and quality of life (QoL) of the family unit (7-13). The impairment of QoL caused by AD has been shown to be greater than or equal to other chronic diseases of childhood, such as asthma and diabetes (14).

The aim of this study was to assess HRQoL in children with AD aged ≤16 years from Montenegro, Europe, and to explore the relation between HRQOL and gender and disease severity.

PATIENTS AND METHODS

Patients and study design

A cross-sectional study was conducted at the Clinic of Dermatology and Venereology, Clinical Center of Montenegro (CCM), Podgorica, between January and December 2014. The study group included 200 children with AD (97 boys and 103 girls) ranging from 0 to 16 years. The Hanifin and Rajka diagnostic criteria for AD were used (15).

The study was approved by the Ethics Committee of the CCM. Written informed consent was obtained from all patients.

Instruments

Patients' characteristics such as age, sex, age at onset of disease, comorbidities, and family history of atopic diseases were recorded by using a short questionnaire.

HRQoL was assessed by completing the Serbian versions of the Infant's Dermatitis Quality of Life Index (IDQOL) (16) and the Children's Dermatology Life Quality Index (CDLQI) questionnaires, respectively (17).

The Infant's Dermatitis Quality of Life Index questionnaire

This questionnaire is designed for use in infants with AD below the age of 4 years (18). It is self-explanatory and should be completed by the child's parent or guardian. IDQOL is calculated by summing the score of each question (0-3) resulting in a maximum of 30 and a minimum of 0. The higher the score, the more QoL is impaired. The severity of eczema as assessed by the parents is scored separately and can be correlated with the main questionnaire.

The Children's Dermatology Life Quality Index questionnaire

This questionnaire is designed for use in children, i.e. patients from age 4 to age 16. It is self explanatory and can be simply given to the patient who is asked to fill it in with the help of the child's parent or guardian (19). The total score of CDLQI is calculated by summing the score of the 10 questions (0-3), resulting in a maximum of 30 and a minimum of 0. The higher the score, the more the QoL is impaired.

Three-item severity (TIS) score

Severity of disease was measured with the three-item severity (TIS) score (20). It is a simple scoring system using three of the intensity items of the SCORAD (SCORing AD) index: erythema (redness) 0-3, edema 0-3, and excoriations (scratches) 0-3 in one or several different representative areas, and it can be regarded as a global scoring system (21). The maximum score is 9. Based on the TIS score, the severity of AD can be classified into mild (<3), moderate (3-5), and severe (≥6). The mean time to assess the TIS is less than one minute.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed through frequency and percentage. To assess differences between variables, Student's t-test and chi-squared test were used where appropriate. To verify how IDQOL and CDQOL items correlated with disease severity we used Spearman's rho (ρ) correlation coefficient. Nine multiple linear regression models were used to determine whether IDQOL and CDLQI scores were related to independent variables, such as age, sex, age at onset of disease, disease severity, other atopic diseases, and family history of atopic diseases. A two-tailed probability value of 0.05 or less was considered significant. All statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS), version 20.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

Demographic and clinical characteristics of 200 children (97 boys and 103 girls, mean age 5.23±4.35) with moderate to severe AD are shown on Table 1.

Girls were older, had later onset and longer duration of the disease. However, there were no significant differences between boys and girls with regard to disease severity, presence of other atopic diseases (such as asthma, allergic rhinitis or allergic conjunctivitis), and family history of atopic diseases.

Table 1. Characteristics of the studied children

Characteristic	Total sample (N=200)	Boys (N=97)	Girls (N=103)	*P*
Age, years (mean ± SD)	5.23±4.35	4.40±3.92	6.00±4.60	**0.009**[*]
Age, years at onset (mean ± SD)	2.07±2.41	1.77±2.27	2.35±2.51	**0.090**[*]
Disease duration (mean ± SD)	3.14±2.85	2.59±2.37	3.65±3.17	**0.008**[*]
Disease severity, n (%)				
Moderate (TIS=3-5)	168 (84.0)	78 (80.4)	90 (87.4)	0.179[†]
Severe (TIS ≥6)	32(16.0)	19 (19.6)	13 (12.6)	
TIS (mean ± SD)	5.40±1.42	5.40±1.62	5.39±1.22	0.946[*]
Other atopic disease[‡], n (%)	86 (43.0)	37 (43.0)	49 (57.0)	0.178[†]
Family history of atopic disease[‡], n (%)	146 (73)	69 (47.3)	77 (52.7)	0.564[†]

[*]t-test; [†]χ^2 test
[‡]Asthma, allergic rhinitis, and/or allergic conjunctivitis
SD: Standard deviation; TIS: Three-Item Severity score

The 10 items scores of IDQOL and 6 domains scores of CDLQI, differentiated according to sex are presented in Table 2.

The highest scoring items/domains in children with AD in our study were those related to the "child's mood" (1.93±0.82), "itching and scratching" (1.91±0.71), and "problems caused by the treatment" (1.76±0.86) – items of the IDQOL; and "leisure time" (5.09±1.88), "symptoms (such as itching and soreness) and feelings" (4.28±1.35), and "personal relationship" (2.63±1.59) – domains of the CDLQI. The items of IDQOL, "itching and scratching", "disturbed family activities", and "problems at bath time" were more prevalent in girls than in boys, while the opposite was true for all CDLQI domains, except for "leisure" where such differences did not reach statistical significance.

A positive correlation was observed between clinical severity (TIS) and all the items of IDQOL, with Spearman's correlation coefficient ranging from 0.31 to 0.74, and between total IDQOL score and its items (ρ=0.60-0.78). Clinical disease severity (TIS score) and severity assessed by parents also strongly correlated

Table 2. The Infants' Dermatitis Quality of Life Index (IDQOL) and Children's Dermatology Life Quality Index (CDLQI) domains and total scores according to sex

IDQOL (n = 90 infants)	Total	Boys	Girls	*P*[*]
	Mean ± SD			
Itching and scratching	1.91±0.71	1.75±0.76	2.13±0.58	**0.011**
Child's mood	1.93±0.82	1.94±0.80	1.92±0.85	0.904
Time to get to sleep	1.08±0.75	1.02±0.78	1.16±0.72	0.391
Sleep disturbances	1.27±0.75	1.23±0.78	1.32±0.70	0.596
Disturbed playing	1.34±071	1.25±0.68	1.47±0.72	0.138
Disturbed family activities	1.34±0.72	1.19±0.71	1.55±0.69	**0.018**
Problems during meal times	1.22±0.82	1.17±0.76	1.29±0.90	0.508
Problems from treatment	1.76±0.86	1.67±0.88	1.87±0.84	0.293
Dressing problems	1.19±0.85	1.10±0.82	1.32±0.87	0.226
Problems at bath time	1.33±0.98	1.15±0.96	1.58±0.98	**0.042**
Total score	14.38±5.57	13.48±5.30	15.60±5.77	0.074
CDLQI (n=110 children)				
Symptoms and feelings	4.28±1.35	4.62±1.34	4.05±1.32	**0.027**
Leisure	5.09±1.88	5.44±1.67	4.85±1.99	0.101
School or holidays	2.27±0.66	2.51±0.51	2.11±0.71	**0.001**
Personal relationships	2.63±1.59	3.09±1.66	2.32±1.47	**0.012**
Sleep	1.86±0.72	2.11±0.83	1.69±0.58	**0.002**
Treatment	2.28±0.62	2.47±0.50	2.15±0.67	**0.009**
Total score	18.43±4.88	20.24±4.88	17.17±4.49	**0.001**

[*]t-test; SD: Standard deviation

Table 3. Correlation matrix of atopic dermatitis severity and Infants' Dermatitis Quality of Life Index (IDQOL)

	IDQOL											TIS
	IDQOL1	IDQOL2	IDQOL3	IDQOL4	IDQOL5	IDQOL6	IDQOL7	IDQOL8	IDQOL9	IDQOL10	Total score	
TIS	0.60**	0.53**	0.65**	0.31**	0.60**	0.61**	0.50**	0.40**	0.54**	0.60**	0.74**	
Severity†	0.50**	0.62**	0.67**	0.39**	0.57**	0.51**	0.44**	0.42**	0.34**	0.50**	0.70**	0.71**
IDQOL												
Total score	0.67**	0.68**	0.77**	0.68**	0.70**	0.66**	0.68**	0.60**	0.66**	0.78**		
IDQOL10	0.38**	0.36**	0.50**	0.50**	0.44**	0.48**	0.48**	0.42**	0.73**			
IDQOL9	0.32**	0.24*	0.43**	0.33**	0.35**	0.38**	0.41**	0.40**				
IDQOL8	0.41**	0.40**	0.28**	0.45**	0.45**	0.11	0.26*					
IDQOL7	0.40**	0.36**	0.56**	0.45**	0.39**	0.54**						
IDQOL6	0.36**	0.50**	0.56**	0.37**	0.41**							
IDQOL5	0.44**	0.52**	0.57**	0.50**								
IDQOL4	0.41**	0.40**	0.43**									
IDQOL3	0.55**	0.58**										
IDQOL2	0.55**											

*P< 0.05; **P< 0.01; †Assessed by parents; IDQOL1: Itching and scratching; IDQOL2: Child's mood; IDQOL3: Time to get to sleep; IDQOL4: Sleep disturbances; IDQOL5: Disturbed playing; IDQOL6: Disturbed family activities; IDQOL7: Problems during meal times; IDQOL8: Problems from treatment; IDQOL9: Dressing problems; IDQOL10: Problems at bath time; TIS: Three-Item Severity score

between themselves (ρ=0.71) (Table 3).

As shown in Table 4, a positive correlation was found between clinical severity and all domains of CDLQI (ρ=0.31-0.69), as well as between total CDLQI scores and all its domains (ρ=0.43-0.83) (Table 4).

The results of multiple linear regression analyses are shown in Table 5.

The effect of severity (TIS score) was highly significant for all observed domains of IDQOL and CDLQI. The highest values of standardized regression coefficients related to severity were seen for total IDQOL and total CDLQI scores, following by those for "symptoms and feelings" and "leisure" – domains of CDLQI. The presence of atopic diseases other than AD was significantly related to "problems with treatment" and total IDQOL score, whereas other variables (sex, age, age at onset, and family history of atopic diseases) were not significantly related to any of the IDQOL score. A weak association was seen between "symptoms and feelings" and "leisure" (domains of CDLQI) and the presence of atopic diseases in study subjects and their families. The effects of sex, age, and age at disease onset were also weak for total CDLQI score, and "symptoms and feelings" of CDLQI (Table 5).

All scales of both IDQOL and CDLQI questionnaires showed good internal consistency with mean Cronbach's alpha coefficients of 0.88 and 0.73, respectively.

DISCUSSION

To our knowledge, this is the first published study to investigate HRQoL in a Montenegrin sample of

Table 4. Correlation matrix of atopic dermatitis severity and Children's Dermatology Life Quality Index (CDLQI)

	CDLQI						
	Symptoms and feelings	Leisure	School or holidays	Personal relationships	Sleep	Treatment	Total score
TIS	0.60**	0.53**	0.31**	0.58**	0.34**	0.37**	0.69**
CDLQI							
Total score	0.79**	0.83**	0.43**	0.67**	0.65**	0.61**	
Treatment	0.57**	0.49**	0.12	0.16	0.46**		
Sleep	0.43**	0.45**	0.17	0.29**			
Personal relationships	0.37**	0.41**	0.42**				
School or holidays	0.14	0.25**					
Leisure	0.61**						

**P<0.01
TIS: Three-Item Severity score

Table 5. Standardized regression coefficients in multiple regression models of the most affected domains and total scores on the Infants' Dermatitis Quality of Life Index (IDQOL) and Children's Dermatology Life Quality Index (CDLQI)

Variable	IDQOL				CDLQI				
	Itching and scratching	Mood	Treatment	Total score	Symptoms and feelings	Leisure	Personal Relationships	Treatment	Total score
Sex	ns	ns	ns	ns	ns	ns	ns	ns	-0.18**
Age, years	ns	ns	ns	ns	0.20**	ns	ns	ns	ns
Age at onset	ns	ns	ns	ns	-0.19*	ns	ns	ns	ns
TIS	0.53**	0.54**	0.32**	0.76**	0.77**	0.69**	049**	0.43**	0.79**
Atopic disease†	ns	ns	0.32**	0.18*	0.25**	0.18*	ns	ns	ns
Family history of atopic disease†	ns	ns	ns	ns	0.27**	0.23**	ns	ns	0.20**

*P<0.05; **P<0.01; †Asthma, allergic rhinitis, and/or allergic conjunctivitis

ns: non-significant; TIS: Three-Item Severity score

children with AD. Two questionnaires were used to assess QoL: the IDQOL index for infants of less than 4 years of age and the CDLQI index for children aged 4-16 years. Our study showed the negative effect of AD on HRQL. The total IDQOL and CDLQI scores were found to be 14.38 and 18.43, respectively, much higher than in all previous studies (9-13,18,22-24). These high scores can be explained by the fact that the most severe forms of AD are treated at the CCM as a tertiary care hospital and center of excellence for dermatology in Montenegro. It seems reasonable that patients referred to a specialist would be likely to have more severe disease than patients treated at a general practice. All patients analyzed in the present study suffered from a moderate to severe form of the disease.

As in almost all studies that have the used IDQOL index, we found "child's mood" and "itching and scratching" to have the highest negative impacts on HRQoL in children affected by AD (10,13,18,22-26). Chronic itch in pruritic diseases such as AD is quite frustrating and very damaging to HRQOL. It induces scratching and thus worsens the condition of the skin, resulting in a vicious itching-scratching cycle (27) with consequences on the child's mood.

AD is a chronic remittent skin disease which requires long-term treatment. Despite the positive impact of topical anti-inflammatory therapy on patient quality of life (28), "problems caused by treatment" have been frequently reported (7,22), which is in accordance with our results.

We used the TIS score to assess AD severity, which corresponds well with the more detailed SCORAD. The simplicity of TIS makes it a suitable tool for research studies or daily clinical practice (20,21,29).

Our results showed a strong correlation between HRQoL and clinical disease severity (ρ=0.74 for IDQOL; ρ=0.69 for CDLQI), that is in agreement with previous studies (23-25,30,31). Correlation of IDQOL with clinical severity as assessed by parents were insignificantly lower (ρ=0.70 for overall IDQOL score), but higher than in a study by Lewis-Jones *et al*. (ρ=0.58) (18). The comparison between clinical disease severity and parent-assessed severity in the present study indicated a strong correlation (ρ=0.71). In opposition to our findings, Brazilian authors reported a discrepancy between clinical and parent assessment of the children's disease severity (22).

Our study showed a significant gender difference in overall CDLQI score – the impact of AD on QoL was more severe in boys. We also found that IDQOL items "itching and scratching", "disturbed family activities", and "problems at bath time" had higher scores in girls, but we failed to find a significant difference in overall IDQoL score. According to Chernyshov, the impact of AD on QoL measured by IDQOL was more severe in girls (10). In contrast, several other studies did not detect any significant gender difference in QoL in their patients (13,23,24,26).

AD is characterized by eczematous changes in the epidermis, and most patients have an atopic background with past and familial histories of bronchial asthma, allergic rhinitis, and/or allergic conjunctivitis (32). In the present study, a weak significant association between the presence of other atopic disorders and QoL was seen only for the total score and "treatment problems" (IDQOL), and "symptoms and feelings" and "leisure" (CDLQI). Ganemo *et al*. reported that AD with other concomitant atopic diseases impaired QoL more than AD did alone (13). In contrast, in two other studies no significant differences were observed concerning the association of QoL and other atopic disorders (23,24).

The Serbian validated and culturally adapted

versions of both IDQOL and CDLQI questionnaires showed good internal consistency with a Cronbach's alpha values of 0.88 and 0.73, respectively. In addition, they are easy to use and can usually be completed within few minutes.

However, the study has some limitations. First of all, only subjects with moderate to severe forms of AD were enrolled in the study. Because of that it is not possible to generalize the results of our study to other subjects in the population of Montenegro affected by AD. Furthermore, we had no control group so it was not possible to compare QoL of children affected by AD and other dermatological diseases.

CONCLUSION

Our study found a strong negative impact of AD on patient HRQOL. Greater severity of disease was associated with greater impairment in HRQOL. The impact of AD on HRQoL was more severe for younger girls, but only in some domains, and for older boys. Establishing of the degree of QOL impairment associated with AD might help doctors improve their relationship with patients and facilitate the management of treatment.

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