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Utility of Pediatric Allergic Disease Quality of Life Questionnaire for childhood eczema

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Abstract:

Aim: It is important to objectively evaluate quality of life (QoL) impairment in atopic diseases in children.

This study aims to investigate the utility of a Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ) in children with eczema.

Methods: PADQLQ, Patient-Oriented Eczema Measure (POEM, a short-term subjective-symptom score), Nottingham Eczema Severity Score (NESS, a long-term subjective-symptom score), Children Dermatology Life Quality Index (CDLQI, a short-term subjective-symptom score) were compared and correlations evaluated.

Results: PADQLQ, POEM, NESS, CDLQI correlated well with each other (n=132 sets; spearman's correlations $\rho = 0.48-0.70$, $p < 0.001$). Bland Altman Plot showed a reasonably good agreement between CDLQI and PADQLQ. PADQLQ showed symptoms of asthma, allergic conjunctivitis and allergic rhinitis were present in 20-30%, 45-71%, and 58-67%, respectively. Nevertheless, there was no association of eczema symptomatology by POEM or NESS with the severity of other allergic diseases.

Conclusion: PADQLQ correlates well with AD-specific severity and QoL scores and reflects all allergic symptoms that holistically influence QoL in children with AD. PADQLQ is hence a composite severity score in terms of clinical symptomatology and QoL impairment for AD.

Key words: Atopic dermatitis; quality of life; PADQLQ; POEM; NESS; CDLQI

Introduction

Childhood atopic dermatitis (AD) or eczema is a chronic inflammatory disease associated with pruritus and sleep loss.¹ In clinical research, it is crucial to “measure” and quantify AD in terms of disease severity. Nowadays, there are a number of scoring systems for measuring AD severity.^{2;3} Some of the more frequently used severity scores are SCORAD (SCORing Atopic Dermatitis), POEM (The Patient Oriented Eczema Measure) and NESS (Nottingham Eczema Severity Score).^{2;3} Like many chronic diseases, AD also significantly impairs quality of life (QoL).^{4,5} Measuring the severity of disease and QoL impairment form an integral part of its management as QoL reflects the overall well-being of the patient. QoL tools measure patients' subjective experience on physical, emotional and social domains affected by their disease. Health-related QoL questionnaires are being increasingly available for clinical

and research use, most of them are either generic or disease-specific. For example, the Children's Dermatology Life Quality Index (CDLQI) is a health-related QoL questionnaire designated for dermatology. It is a well-validated questionnaire with 10 questions, focusing on the impact of the dermatological illness on the affected children over the past one week.⁵ Questions within CDLQI covered broad domains, including symptoms, emotional aspects like embarrassment, and practical aspects including friendships, clothes, playing, sports, school, bullying, sleep and the impact of treatment, and has been widely used to assess QoL among AD patients especially in AD clinical trials.⁴ Nonetheless, patients attending dermatology clinics for AD often suffer from co-existing atopic diseases. According to the "Atopic March" hypothesis, AD is part of a complex atopic diathesis with coexisting allergic disease of asthma, allergic rhinitis and conjunctivitis. AD is often the first step in the atopic march that results in asthma, allergic conjunctivo-rhinitis. All these conditions in the allergic complex act together and impair QoL of affected AD children and their families. Therefore, it is very likely that dermatological-specific QoL scores like CDLQI may not adequately reflect severity and extent of QoL impairment of AD patient in their multiple-atopic state.

In 2003, the Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ) was developed by a UK team⁶. PADQLQ is a 26-items questionnaire which assesses QoL for children and teenagers with multisystem allergic disease. The approximate time for a child to complete PADQLQ is less than 10 minutes. In addition to standard questions like those in CDLQI, the questionnaire incorporates symptoms that are often not objectively measured by physicians caring for children with AD and airway allergies. It is a tool (with questions for respiratory, ocular, nasal and skin symptoms) which assesses the various aspects of allergic diseases in the domains of practical details, emotion and symptomatology

[Practical aspect: PADQLQ Q1-7, 26; Emotional aspect: PADQLQ Q23-25; Symptom aspect: PADQLQ Q8-22).^{6;7} Each item was graded with a 7-point Likert scale (from not troubled (0), hardly troubled at all (1), somewhat troubled (2), moderately troubled (3), troubled quite a bit (4), very troubled (5), to extremely troubled (6)).

For CDLQI: Practical aspect: CDLQI Q4-7, 9-10; Emotional aspect: CDLQI Q2-3, 8; Symptom aspect: CDLQI Q1]

Recently, a Chinese version of PADQLQ has been translated and validated ⁷. Our study aims to investigate the utility of PADQLQ in children with AD.

Methods

AD patients within the age range of 6 to 16 years-old attending the paediatric dermatology clinic of a university teaching hospital during the period of August 2017 to December 2017 were consecutively recruited. AD was diagnosed according to criteria proposed by Hanifin and Rajka.⁸ Patients without AD, children of age beyond our designated age range and non-ethnic Chinese were excluded. Severity of AD symptoms was evaluated with a translated Chinese version of POEM.⁹ Longer term AD severity (in the previous 12-months) based on symptoms and signs were measured with NESS.^{10;11} QoL was measured with CDLQI.^{4;5}, whereas PADQLQ holistically measures QoL of allergic diseases.⁷

Skin hydration (SH) and trans-epidermal water loss (TEWL) were recorded by MoistureMeterSC (Delfin Technologies Ltd, Kuopio, Finland) in arbitrary units and Vapometer (Delfin Technologies Ltd, Kuopio, Finland) in g/m²/h respectively; and skin erythema by SkinColorCatch (Delfin Technologies Ltd, Kuopio, Finland) in arbitrary units.³ These three measurements were done on the right forearm (2 cm below the antecubital flexure). Our group documented that a site 2 cm distal to the right antecubital flexure was optimal for standardization of measurement in our previous publication.^{3,12} Data were summarized as proportion or mean with standard deviation (SD) unless otherwise specified. Mann-Whitney U test was used to analyze numerical variables. The correlations between different components of the scores were analyzed by Spearman's partial correlation coefficients. Bland-Altman plot was constructed in order to determine the level of agreement between the two QoL questionnaires. All comparisons were made two-tailed, and *p*-values less than 0.05 were considered to be statistically significant.¹² Clinical Research Ethics Committee of the University approved this survey of clinical scores.

Results

200 set of scores were distributed out as hard copies. 34 questionnaires did not reach any respondents due to unattended visits. Other than that, only those age-eligible subjects with all four questionnaires (i.e. POEM, NESS, CDLQI, PADQLQ) completed entered the study. This result in a final of 132 sets clinical scores from eczema patients (mean age: 11.2 ±3.1 years; 50.8% male) being reviewed. Patients were separated into two groups, namely "mild-moderate" and "severe", based on the clinical severity scores by POEM (short-term) and NESS (long-term). AD patients in the "mild-moderate" group were significantly different from those from "severe" group in their QoL, as reflected by both PADQLQ and CDLQI. Severe AD patients suffered over 2 folds more than mild-moderate AD patients in the "practical", "emotional" and "symptoms" domains of PADQLQ. In particular, severe AD patients expressed more

intensely affected “practical and emotional domain” than mild to moderate AD patients. Nevertheless, age, gender and other objective parameters (including the non-invasive measurement of SH, TEWL and erythema) showed no significant differences among the two groups (Table 1), and age and gender were not correlated with PADQLQ score by Spearman’s Correlation.

Significant correlations were found between the QoL and severity scores. CDLQI correlated with POEM and NESS with a $\rho=0.70$ and 0.68 respectively; while PADQLQ showed a significant correlation of $\rho=0.48$ with POEM and $\rho=0.51$ NESS respectively. Such correlation analyses showed that CDLQI correlated slightly better than PADQLQ with AD disease severity by POEM and NESS. Most questions about other allergic symptoms (e.g. involving allergic rhinitis and asthma) in PADQLQ had insignificant correlations with POEM and NESS (Table 3).

The two QoL questionnaires were further divided into practical, emotional and symptom domains and Spearman's correlations for each domain of the same category were performed. The practical domain of CDLQI (Q4-7) and PADQLQ (Q1-7) correlated the best with a significant correlation coefficient of 0.73 . Their emotional domains (CDLQI Q2-3, 8; PADQLQ Q23-25) correlated with a coefficient of 0.64 while symptom domains (CDLQI Q1; PADQLQ Q8-22) correlated the least with a coefficient of 0.52 (all with p -value <0.05). Bland-Altman plot of agreement between the questions concerning AD among the two QoL questionnaires shows the mean difference between CDLQI and PADQLQ was only 0.81 , very close to 0 (Figure 1). Besides, the dots within the plot were largely within the 95% limit of agreement of -9.54 to 11.2 , with constant variance of measures across the entire range of measures. These all demonstrated a reasonably good agreement between CDLQI and PADQLQ. To a large extent, this support that items within the 26-question PADQLQ could already cover the 10-question CDLQI with the additional advantage of covering other atopic symptoms.

Furthermore, on grouping PADQLQ questions among the symptom domain to their corresponding atopic diseases, symptoms of asthma, allergic conjunctivitis and allergic rhinitis were present in 20-30%, 45-71%, and 58-67% of patients, respectively (Table 3). Although there was no or weak association of eczema severity by POEM or NESS with the severity of the other allergic diseases, the percentage of patients reporting allergic symptoms of respective atopic diseases is reasonably consistent. For example, 20-30% of our patients reported concerns for PADQLQ questions 6-10 which were all on symptoms of asthma; and around 60-70% of patients reported concerns for PADQLQ questions 13-16 which were on symptoms of allergic rhinitis. Though PADQLQ is a questionnaire that focuses on the occurrence of allergic symptoms without specifying the disease, our data demonstrate that AD patients have a high prevalence of symptoms of diseases of “atopic march”.

Discussion

PADQLQ, POEM, NESS, CDLQI correlated very well with each other, reflecting that severity in terms of clinical symptomatology or QoL impairment is an inter-correlated domain. Although our study has a limitation, namely, PADQLQ and CDLQI are not designed for young children or young person approaching adulthood, one important strength is that the all the 4 questionnaires are available in validated Chinese translations.

AD is one manifestation of a complex atopic diathesis. Measuring severity of disease and QoL impairment forms an integral part of its management. QoL reflects the overall well-being of the patient. Previous studies demonstrate that psychosocial, immune and treatment factors other than disease

severity also affect QoL. QoL does not necessarily demonstrate a strong correlation with disease severity and therefore should be individually assessed.¹³

The percentage of patients reporting allergic symptoms of respective atopic diseases is reasonably consistent. For example, 20-30% of our patients reported concerns for PADQLQ questions 6-10 which are all on symptoms of asthma; and 60-70% of patients reported concerns for PADQLQ questions 13-16 which are on symptoms of allergic rhinitis. Though PADQLQ is a questionnaire that focuses on the occurrence of allergic symptoms without specifying the disease, our data demonstrate that AD patients have a high prevalence of symptoms of diseases of “atopic march”. PADQLQ is not designed to replace all the AD-specific scores but would certainly enhance and complement of objective evaluation of AD. In a patient with AD alone, AD-specific CDLQI may suffice; whereas the allergic disease-specific PADQLQ may better represent the QoL or general well-being of the patient with multiple atopic diseases.

Quality of life in children with eczema using CDLQI has been extensively studied. Selected publications from Brazil, Hong Kong, Italy, Korea, Montenegro and Singapore are tabulated (table 4). These studies demonstrate that quality of life correlated with disease severity. However, none of them used PADQLQ and took other atopic diseases into consideration in their study designs. Our group believe that will be useful to investigate if PADQLQ may show similar utility in these populations.

“We proposed that PADQLQ is an appropriate measure in patients who primarily have atopic dermatitis because from our observation in our dermatology clinic, many patients with AD suffer from co-existing atopic disease as well, mainly allergic rhinitis, followed by asthma. It is a pity that the

PADQLQ did not specifically use patients with AD during the validation phase. We believe that they didn't choose AD patients because they would like to obtain a big enough significant changes in QOL during a specific short period of time. Therefore, patients who are affected by pollen seasons most would be their target group. Eczema is included as an allergic disease in an Ohio study with PADQLQ (J Pediatr 2007). In a subsequent local publication to validate the questionnaire, all allergic diseases including eczema are included. Importantly, we found significantly good correlations among PADQLQ and all the other eczema-specific scores."

To conclude, the 26-question PADQLQ is an all-rounded score for health-related QoL, covering practical, emotional and symptoms aspects of allergic diseases.⁷ As a single score, PADQLQ has the capability to assess co-existing atopic symptoms of conjunctivitis, rhinitis, and asthma, and QoL in childhood AD. It correlates well with AD-specific clinical and QoL severity scores. In particular, it has a good correlation and agreement with CDLQI. CDLQI may be more appropriate to be used to access AD patients' QoL in AD-specific interventional studies. Nonetheless, unlike POEM, NESS, or CDLQI, PADQLQ has the advantage of reflecting all allergic symptoms that holistically influence QoL in children with AD. It is important to balance between "specific" and "generic" measures. Looking into the overall quality of life, using a generic measure would be too non-specific for AD patients with co-existing allergic symptoms. With the support from the "atopic march hypothesis", we believe that using a semi-specific quality of life measure (i.e. PADQLQ) would be a suitable choice. PADQLQ questions indicate that around 60% of our reviewed AD children have allergic rhinitis, over 40% of them have conjunctivitis, and over 20% have asthma symptomatology. These symptoms may contribute to the overall impairment of QoL. In patients with AD alone, AD-specific CDLQI may suffice; whereas the allergic disease-specific PADQLQ would

better reflect the QoL or general well-being of the patient with multiple atopic diseases. PADQLQ is hence a composite severity score in terms of clinical symptomatology and QoL impairment for AD.

Table 1. Demographics, clinical and quality of life scores, and objective skin parameter measurements of AD patients grouped according to disease severity defined by NESS and POEM scoring systems

	Total (N=132)	By NESS [^]			By POEM [#]		
		Mild- moderate (N=68)	Severe (N=64)	P-value	Mild- moderate (N=77)	Severe (N=55)	P-value
Male (N (%))	67 (50.8)	37 (54.4)	30 (46.9)	0.496	36 (46.8)	31 (56.4)	0.198
Age at visit	11.2 ±3.1	11.8 ±3.0	10.7 ±3.2	0.692	11.1 ±3.1	11.5 ±3.2	0.419
NESS	10.8 ±2.8	8.8 ±2.1	13.2 ±1.2	<0.001	9.5 ±2.6	12.6 ±1.9	<0.001
POEM	14.3 ±7.1	11.1 ±5.8	17.7 ±6.8	<0.001	9.2 ±4.1	21.4 ±3.4	<0.001
CDLQI	8.2 ±5.4	5.2 ±3.3	11.5 ±5.4	<0.001	5.5 ±3.3	12.1 ±5.5	<0.001
PADQLQ[@]	29.1 ±21.0	19.2 ±15.0	39.6 ±21.3	<0.001	21.7 ±17.0	39.4 ±21.7	<0.001
-Practical	8.4 ±7.1	4.3 ±4.0	12.8 ±7.1	<0.001	5.8 ±6.1	12.1 ±6.9	<0.001
-Emotional	4.2 ±3.9	2.3 ±2.5	6.2 ±4.0	<0.001	2.7 ±2.7	6.3 ±4.3	<0.001
-Symptom	17.0 ±12.8	12.8 ±10.4	21.4 ±13.6	<0.001	13.2 ±11.4	22.3 ±12.8	<0.001
SH	20.3 ±14.9	22.4 ±16.1	18.0 ±13.2	0.093	24.0 ±16.2	19.1 ±14.5	0.001
TEWL	9.7 ±5.5	8.3 ±4.1	11.2 ±6.4	0.003	8.5 ±4.6	11.5 ±5.2	0.004
Erythema	411 ±49.9	410.8 ±69.3	412.8 ±11.7	0.822	407.2 ±59.9	418.2 ±30.7	0.180

[^] - Mild-moderate AD defined by NESS score 3-11; severe AD defined by NESS score 12-18

[#] - Mild-moderate AD defined by POEM score 3-16; severe AD defined by POEM score 17-28

[@] - Practical aspect: PADQLQ Q1-7, 26; Emotional aspect: PADQLQ Q23-25; Symptom aspect: PADQLQ

Q8-22

Table 2. Spearman's correlation between AD severity (POEM & NESS) and quality of life (CDLQI & PADQLQ) questionnaires

	CDLQI	PADQLQ (total)	PADQLQ (practical)	PADQLQ (emotional)	PADQLQ (symptom)
POEM	0.696**	0.483**	0.558**	0.471**	0.420**
NESS	0.682**	0.509**	0.645**	0.583**	0.355**

**p<0.001

Table 3. Percentage of AD patients who reported allergic symptoms in PADQLQ

Symptom of:	PADQLQ question	AD patients reported having symptom	Spearman's correlation of such symptom severity with AD severity	
			(POEM)	(NESS)
Asthma	Q6 - Coughing or wheezing while running or playing	29.5 %	0.115	0.144
	Q8 - Coughing at night	25.0 %	0.102	0.121
	Q9 - Coughing or wheezing	24.2 %	0.153	0.161
	Q10 - Feeling out of breath or tightness in chest	20.5 %	0.116	0.103
Allergic conjunctivitis	Q11 - Needing to rub your eyes	71.2%	0.058	0.138
	Q12 - Swollen or puffy eyes	45.5 %	0.296**	0.305**
Allergic rhinitis	Q13 - Itchy nose	58.3 %	0.126	0.007
	Q14 - Blocked or stuffy nose	66.7 %	0.222*	0.108
	Q15 - Needing to rub your nose	61.4 %	0.121	0.065
	Q16 - Needing to blow your nose	62.1 %	0.199*	0.115
Atopic dermatitis	Q17 - Rashes on your skin	69.7 %	0.344**	0.386**
	Q18 - How your skin looks	73.5 %	0.474**	0.486**

*p-value = 0.05

**p-value<0.001

Table 4. Selected CDLQI studies for eczema

	Population and tools	Results	Conclusions	References
Korea	415 children Infants' Dermatitis Quality of Life Index (IDQOL), CDLQI and the Dermatology Life Quality Index (DLQI) was used to determine the QOL for infants (n=71), 197 children (n=197) and adults (n=147) Rajka & Langeland scoring system and the SCORAD	Mean scores: 7.7 ± 5.5 for IDQOL, 6.6 ± 6.3 for CDLQI, and 10.7 ± 7.9 for DLQI.	QOL scores are correlated with AD severity scores as estimated by the Rajka & Langeland severity score and the SCORAD. Outcome of the QOL instruments demonstrates that atopic dermatitis of both children and adults affects their QOL.	Kim 2012 ¹⁴
Montenegro	200 children (90 infants +110 children) Infants' Dermatitis Quality of Life Index (IDQOL) CDLQI Three-item severity (TIS)	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 (p) ranging from 0.31 to 0.74, and between AD clinical severity and all domains of CDLQI (p=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).	AD has a great impact on QoL. Positive correlation between clinical severity and quality of life	Ražnatović Djurović 2015 ¹⁵
Brasil	Age 5-16 years 51 patients and their guardians CDLQI Dermatitis Family Impact (DFI). SCORAD	The average score was 5.4±5.1 for CDLQI, 6.6±4.5 for DFI, and 28.3±19.8 for SCORAD. Significant correlation among the scores CDLQI, DFI, and SCORAD (p<0,001).	Atopic dermatitis affects the quality of life of both children and their guardian	Campos 2017 ¹⁶
Italy	Forty children Disease severity assessed by the physician and the patients (or their parents) using the SCORAD and the patient-oriented SCORAD (PO-SCORAD)	SCORAD e PO-SCORAD were moderately but significantly correlated (p Spearman=0.55, P<0.01). After adjustment for age and sex, children with SCORAD>40 had significantly higher QoL scores (more impaired QoL) than those with SCORAD≤40 (median QoL of 5 and 4, respectively, P=0.048). Even higher differences emerged when AD severity was self-assessed (median QoL of 6 and 3.5 for children with PO-SCORAD>40 and PO-SCORAD≤40, respectively, P=0.01). AD children with concomitant food allergy had a significantly more impaired QoL than those with AD only (P=0.040). No significant difference in QoL was observed according to sex or age.	Increasing disease severity was associated with greater impairment in QoL. SCORAD and PO-SCORAD were fairly correlated and the association of QoL was somewhat stronger with the PO-SCORAD than the SCORAD Index. This supports the usefulness of PO-SCORAD for the self-assessment of AD in children	Boccardi 2017 ¹⁷
Singapore	Adolescents aged 11-16 years with eczema (n=50) Eczema area and severity index (EASI)	Patients with mild and moderate eczema had lower CDLQI scores. Adolescents were most affected by the disruption	Chronic sufferers of severe eczema experience poorer QOL than those with mild or moderate eczema. They also experience significant psychosocial impact as	Ng 2018 ¹⁸

	CDLQI	that their symptoms had on their leisure and physical activities and sleep as a result of itch and scratching	a consequence of their condition.	
Hong Kong	126 sets of clinical scores from eczema patients (mean age: 11.4 ± 5.6 years) POEM SCORAD NESS CDLQI	The modified-POEM, objective SCORAD, NESS and CDLQI correlated well with each other. Best correlations were obtained with POEM: Objective SCORAD ($\rho = 0.7$, $p < 0.001$), NESS ($\rho = 0.69$, $p < 0.001$), CDLQI ($\rho = 0.77$, $p < 0.001$) Linear stepwise-backward regression demonstrated that POEM was independently associated with CDLQI parameters of pruritus (B: 2.16; $p = 0.018$), activities (B: 1.80; $p = 0.009$), sleep disturbance (B: 2.78; $p < 0.001$) and NESS parameter of sleep disturbance (B: 1.02; $p = 0.003$).	Clinical scores for acute, chronic, subjective symptoms and objective signs correlated well with each other. CDLQI correlated with disease severity	Hon 2018 ¹⁹

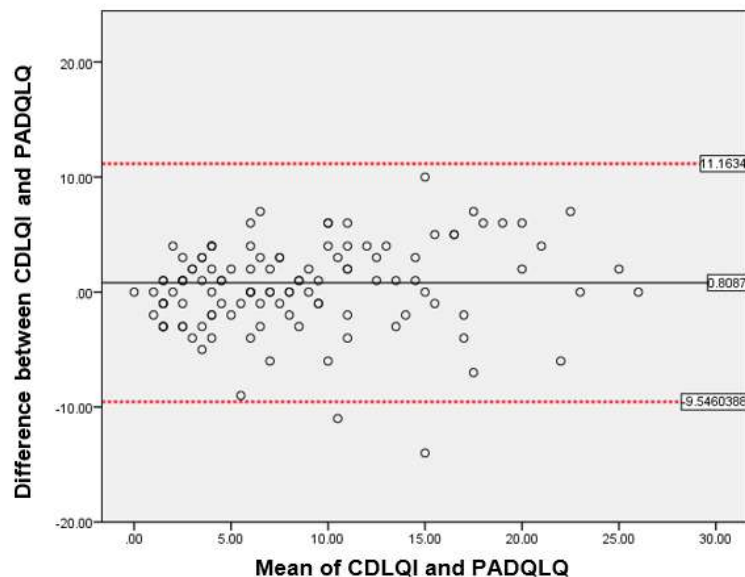
NESS: Nottingham Eczema Severity Score

POEM: Patient-Oriented Eczema Measure

Figure 1. Bland Altman Plot shows a good agreement between CDLQI and PADQLQ.

Bland-Altman plot is a commonly used graphic to demonstrate agreement. The mean of the two measurements (i.e. CDLQI & PADQLQ) contributed by each “questionnaire set responder” is the x-axis value, while the difference between the two values from the two questionnaires is the y-axis value.

The Bland-Altman plot is used to provide a visual impression of the agreement in each subject. Two basic assumptions must be fulfilled to analyze the Bland-Altman plots correctly: the difference between the methods must be constant, i.e. zero slope, and constant variance of measures across the entire range of measures, i.e. homoscedasticity.



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