

QUALITY OF LIFE

Childhood Allergies Affect Health-Related Quality of Life

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Objective. The majority of studies investigating the effects of allergy on the children's health-related quality of life (HRQoL) address one particular allergic disease, using a disease-specific HRQoL instrument. This work aims to assess the comparative impact on HRQoL of several allergic conditions of childhood (asthma, rhinitis, eczema, and food hypersensitivity) in a large, population-based sample of Swedish 8-year-olds. **Methods.** Data were obtained from a Swedish birth cohort (BAMSE). At the 8-year follow-up, parents of 3236 children completed the standardized generic HRQoL instrument EQ-5D and reported on the children's symptoms of asthma, rhinitis, eczema, and food hypersensitivity. Information on allergic sensitization and lung function was available for a sub-sample of the children ($n = 2370$ and 2425 , respectively). **Results.** Children in the study population had a median EQ visual analog scale (VAS) of 98 (Inter Quartile Range, IQR, 90–100). The median EQ VAS was significantly lower in children with allergic diseases. Children with asthma had the lowest median EQ VAS (90, IQR 85–98) and reported the highest prevalence of problems of "pain or discomfort" (18.2%, compared to 5.5% in children without asthma). Frequent wheezing and effort-induced wheezing were associated with high prevalence of problems of "anxiety or depression" (23.3% and 15.4%, respectively). **Conclusions.** Swedish 8-year-olds enjoy a good HRQoL, which though is significantly impacted by allergic diseases and particularly by asthma. Asthma symptoms are important determinants of HRQoL and symptom control should be a major goal in asthma management.

Keywords asthma, BAMSE, eczema, EQ-5D, food hypersensitivity, rhinitis, wheezing

INTRODUCTION

Allergic diseases such as asthma, rhinoconjunctivitis, eczema, and food hypersensitivity are common in children (1) and may impact their health-related quality of life (HRQoL). HRQoL encompasses physical, psychological, and social domains of health (2) and may be influenced by age, gender, personality, ethnicity, family structure, and socioeconomic status (3). Since improving the patients' HRQoL is now recognized as a major therapeutic goal in chronic illnesses, evaluation of quality of life and other patient-reported outcomes is increasingly used in clinical trials (4).

A multitude of validated instruments, both disease-specific and generic, are available for assessing HRQoL. Disease-specific questionnaires investigate areas of HRQoL considered to be most relevant for one particular disease or condition. They are sensitive to changes in disease severity (3) and tend to have high response rates, since directly disease-related questions are highly meaningful to the sufferers (5). Generic instruments, on the other hand, have the advantage of being applicable across a wide range of populations and interventions (6), in both healthy and chronically ill subjects. They can be used for measuring effects of comorbidity and for comparison

between groups of patients with different diseases (7). Previous research has shown that allergic rhinitis (8, 9), asthma (10), atopic eczema (11), and food hypersensitivity (12) affect HRQoL in both children and adults. However, many of the previous studies in this field were done in clinical settings and using disease-specific instruments. The use of a generic instrument has allowed us to investigate the comparative impact of different allergic diseases on the HRQoL of children from a large, population-based cohort in Stockholm, Sweden.

METHODS

This study includes children who participated in the 8-year follow-up of the BAMSE (Children, Allergy, Milieu, Stockholm, Epidemiological Survey) birth cohort, a prospective study assessing the impact of environmental factors on childhood allergy. Between 1994 and 1996, 4089 new-born children from Stockholm, Sweden, were included in a prospective study (13). Parents of the participating children completed an exposure questionnaire when the child was 3 months old, as well as detailed symptoms questionnaires at the child's age of 1, 2, 4, and 8 years. The response rates were 96%, 94%, 91%, and 84%, respectively. At the 8-year follow-up, the responding families were invited to a clinical investigation, including

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blood sampling for allergy screening as well as lung function measurement. Sera were analyzed for the presence of IgE antibodies to common inhalant allergens (birch and grass pollens, house-dust mite, mold and cat, dog and horse dander) as well as to food allergens (soy, wheat, fish, egg, milk, peanut) by using the ImmunoCAP System (Phadia AB, Uppsala, Sweden). Values exceeding 0.35 kU/L (the standard cut-off value for antigen-specific IgE used by the laboratory at Karolinska University Hospital) were regarded as positive. Lung function was assessed by measuring peak expiratory flow (PEF) and maximum expiratory flow volume, using a methodology consistent with the European Respiratory Society's guidelines (14). The PEF value marking the 25th percentile in the distribution of PEF readings was chosen as a cut-off point between "poor" and "good" PEF. All parts of the BAMSE study have been approved by the ethics committee of Karolinska Institutet, Stockholm, Sweden.

Assessment of HRQoL

At the 8-year follow-up, the parents also reported on the child's HRQoL by completing the standard generic instrument EQ-5D. While any of the existing generic instruments could have been used for the purpose of this work, EQ-5D was chosen for its being relatively short and user-friendly. Since a validated youth version of EQ-5D was not available in Swedish at that time, data on the children's HRQoL could only be collected via proxies (in this case the parents). They were asked to complete the standard EQ-5D bearing in mind that it was their children's quality of life that was assessed, not their own. EQ-5D was developed by the EuroQol Group and a detailed description as well as the user guide are available at www.euroqol.org. EQ-5D captures the respondent's health status at the time of completion and consists of a descriptive system and a standard, 20-cm-long EQ visual analog scale (EQ VAS), with end points marked 0 for "worst imaginable health state" and 100 for "best imaginable health state". The descriptive system investigates five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, with three levels of impairment per dimension: "no problems," "some problems" and "extreme problems". At the BAMSE 8-year follow-up, the responding parent answered the 5 domain questionnaire and rated the child's health status by drawing a line from a box marked "your child's health state today" to whichever point on the scale indicating how good or bad the child's health state was.

Definition of Health Outcomes

Children were considered as having asthma if they had at least 4 episodes of wheeze in the last 12 months, or at least 1 episode of wheeze in the last 12 months in combination with prescribed inhaled steroids, occasionally or regularly. (15).

Eczema was defined as dry skin in combination with an itchy rash with typical localization, occurring in the last 12 months and lasting at least 2 weeks, and/or a doctor's diagnosis of eczema from the age of 7 (16).

The children were considered to have allergic rhinitis if they had symptoms of prolonged sneezing, or a runny or blocked nose without a common cold during the last 12 months (16).

The definition of food hypersensitivity was fulfilled if at least one specific food item had either caused symptoms (itchy eyes and/or runny nose, wheeze, facial edema, vomiting/diarrhea, eczema, urticaria) during the last 12 months or was excluded from the child's diet due to symptoms earlier (17).

"Any allergic disease" was defined as fulfilling the definition criteria for at least one disease, i.e., asthma and/or eczema and/or allergic rhinitis and/or food hypersensitivity.

Statistical Analyses

All statistical analyses were performed with Stata Statistical Software (release 11.0, College Station, TX, USA). Differences between groups with regard to median EQ VAS were tested with two-sample Wilcoxon–Mann–Whitney's test and considered significant at a p -value of $<.05$. Potential confounders were controlled for using a linear quantile regression model. A continuous variable with the values 0 (no allergic disease), 1 (one isolated allergic disease) and 2 (≥ 2 allergic diseases) was analyzed in a quantile regression model to test whether allergic comorbidity affected the median EQ VAS. Differences between groups regarding the percentage of reported problems in the descriptive system of EQ-5D were tested with the two-sample test of proportion. The PEF value corresponding to the 25th percentile (260 L/min) was chosen as cut-off point between "poor" ($\text{PEF} \leq 260$ L/min) and "good" ($\text{PEF} > 260$ L/min) lung function. A valid EQ VAS was the criterion used to define the study population ($n = 3236$). Data on allergic sensitization were available for 2370 children and valid PEF values were registered for 2425 children.

RESULTS

The distribution of background factors in the study population ($n = 3236$) was similar to that of the baseline cohort (4089 children, data not shown). The EQ VAS scores ranged from 39 (one child) to 100 (1359 children) with a median of 98 (IQR 90–100). Having heredity for allergy, being a male, being a first born and having a young mother were associated with statistically significant ($p < .05$) lower median EQ VAS, whereas socioeconomic status, having an immigrant parent and having been exposed to environmental tobacco smoke did not affect the median EQ VAS (Table 1).

Prevalence of Allergic Diseases in the Study Population

Eczema was present in 508 children (16.1%) and had the highest prevalence as allergy manifestation, followed by allergic rhinitis (425, 13.2%), food hypersensitivity (417, 12.9%) and asthma (199, 6.2%). About 32.2% of the children had at least one allergic disease and 34.5% were

TABLE 1.—Distribution of selected exposure characteristics at birth in relation to EQ VAS at age 8 years in the BAMSE birth cohort, Sweden ($n = 3236$).

	<i>n</i>	%	Mean EQ VAS (SD)	Median EQ VAS (IQR 25–75%)	<i>p</i> -value
All children	3236	100	94.9 (7.4)	98 (90–100)	–
Heredity for allergy					
No	2243	69.9	95.1 (7.35)	98 (91–100)	<.01
Yes	966	30.1	94.3 (7.5)	97 (90–100)	
Missing	27	0.008	94.1 (7.2)	97 (90–100)	
Male					
No	1607	49.7	95.2 (7.3)	98 (92–100)	.02
Yes	1629	50.3	94.6 (7.5)	98 (90–100)	
Only child at birth					
No	1373	42.5	95.4 (6.9)	99 (92–100)	<.01
Yes	1863	57.5	94.5 (7.7)	98 (90–100)	
Young mother					
No	3005	92.9	94.9 (7.4)	98 (90–100)	.03
Yes	230	7.1	93.8 (7.9)	96 (90–100)	
Parent born outside of Sweden					
No	2569	79.6	94.9 (7.5)	98 (90–100)	.84
Yes	659	20.4	94.9 (7.0)	98 (91–100)	
Missing	8	0.00	92.3 (4.8)	90 (90–95)	
Exposed for ETS at time for enrolment					
No	2556	87.2	94.9 (7.4)	98 (90–100)	.65
Yes	662	12.8	94.8 (7.4)	98 (90–100)	
Missing	18	0.00	92.8 (6.3)	91 (90–99)	
White collar worker ^a					
No	493	16.3	94.8 (7.9)	99 (90–100)	.63
Yes	2702	83.7	94.9 (7.3)	98 (90–100)	
Missing	41	0.01	94.9 (8.7)	100 (92–100)	

Heredity: mother and/or father with doctor's diagnosis of asthma and asthma medication and/or doctor's diagnosis of hay fever in combination with furred pets and/or pollen allergy.
Young mother: < 25 years old.

^aSocioeconomic status for the household according to dominance order in three classes ("Socioeconomic division; Reports on Statistical Coordination 1982:4").

proven sensitized. The prevalence of sensitization was 25.9% for inhalant allergens and 19.7% for food allergens. Allergic comorbidity was common and 73.4% of the children with asthma also had rhinitis, eczema, or food hypersensitivity.

Impact of Allergic Diseases on the Children's Quality of Life

The associations between different allergy manifestations and the children's EQ VAS scores are shown in Table 2. Children with allergic diseases had significantly lower median EQ VAS ($p < .01$) and this held true also after

Table 2.—EQ VAS^a at age 8 years in relation to allergic diseases in the BAMSE birth cohort, Sweden ($n = 3236$).

Allergic disease	<i>n</i>	%	Mean EQ VAS (SD)	Median EQ VAS (IQR 25–75%)	<i>p</i> -value for difference in EQ VAS ^b
Asthma					
No	3021		95.2 (7.1)	98 (91–100)	<.01
Yes	199	6.2	89.9 (10.0)	90 (85–98)	
Missing	16		92.4 (5.5)	92 (90–97)	
Rhinitis					
No	2789		95.2 (7.1)	99 (92–100)	<.01
Yes	425	13.2	92.3 (8.6)	95 (90–100)	
Missing	22		96.6 (4.8)	99.5 (95–100)	
Eczema					
No	2648	16.1	95.4 (6.9)	99 (92–100)	<.01
Yes	508		92.2 (9.1)	95 (90–100)	
Missing	80		93.1 (8.9)	96.5 (90–100)	
Food hypersensitivity					
No	2801	12.9	95.3 (7.1)	99 (92–100)	<.01
Yes	417		92.2 (8.7)	95 (90–100)	
Missing	18		91.8 (6.6)	90 (90–98)	
Any allergic disease ^c					
No	2134	32.2	95.9 (6.5)	99 (95–100)	<.01
Yes	1013		92.6 (8.6)	95 (90–100)	
Missing	89		95.1 (7.2)	98 (92–100)	

^aScores registered on EQ-5D's visual analog scale.

^bTested with the two-sample Wilcoxon–Mann–Whitney's test.

^cChildren fulfilling the diagnostic criteria for any of the allergic diseases in the study.

adjustment for potential confounders (heredity for allergy, male gender, being a first born child and having a young mother). Children with asthma had the lowest median EQ VAS (90, IQR 85–98), whereas a median EQ VAS of 95 (IQR 90–100) was obtained in each of the other allergic diseases. Allergic comorbidity was associated in the quantile regression model with a significant linear decrease in median EQ VAS, with a 2-unit decrease of the predicted median VAS for every 1-unit increase in number of allergies (95% CI –3.3 to –0.7).

Sensitization did not seem to influence the HRQoL of the children with allergic diseases. In the asthma group, for example, the EQ VAS was comparable between sensitized (median 95, IQR 85–98) and non-sensitized children (median 95, IQR 80–95). Similar results were obtained for rhinitis and eczema, with median EQ VAS = 95 for both sensitized and non-sensitized children, whereas for food hypersensitivity the median EQ VAS was 94 in non-sensitized children, compared with 95 in sensitized.

In the descriptive EQ-5D system (Table 3), we found a statistically significant increase ($p < .01$) in the prevalence of problems of “pain or discomfort” in all allergic diseases, regardless of the actual disease diagnosis. Eczema was further associated with statistically significant increase in reported problems in the domains “anxiety or depression” ($p < .01$) and “usual activities” ($p < .01$). Children with asthma reported the highest prevalence of problems of “pain and discomfort” (18.2%) as well as significantly more problems (compared with children not having asthma) in the domains “mobility” ($p = .02$) and “usual activities” ($p < .01$).

Correlates of HRQoL in Children with Asthma

Since children with asthma had lower median EQ VAS than children with other allergic diseases, we assessed the HRQoL

in this particular group, focusing on factors commonly associated with increased asthma severity or poor asthma control. The results (Table 4) showed high prevalence of poor night sleep (72.4%) as well as prevalence rates exceeding 50% for effort-induced wheezing and impaired daily activities. Frequent wheezing (more than 12 episodes of wheezing in the past 12 months) had a prevalence of 15.1% and was associated with the lowest median EQ VAS (85) and with a high prevalence of problems of “pain or discomfort” (26.7%) and “anxiety or depression” (23.3%). Significantly more problems of “anxiety or depression” were reported by children with asthma experiencing frequent wheezing ($p < .01$) or effort-induced wheezing ($p < .001$) compared to children with asthma not having these symptoms. Poor night sleep due to cough or dyspnea was not associated with significant increase of reported problems in any of the EQ-5D domains. A PEF value in the lowest quartile of the study population (≤ 260 L/min) was recorded in 53 of the children having asthma (31%), but it was not associated with significant impact on either EQ VAS or the EQ-5D domains.

DISCUSSION

In our cohort of 3236 Swedish 8-year-olds, the children were reported by their parents to have a good HRQoL, as indicated by generally high EQ VAS scores. However, children with asthma, rhinitis, and eczema had a statistically significant decreased median EQ VAS and a significantly higher prevalence of reported problems of “pain and discomfort”. This shows the detrimental influence of symptoms on HRQoL in childhood allergies. Asthma seemed to exert the strongest influence on the children's HRQoL, being associated with the lowest median EQ VAS and with the highest prevalence of problems of “pain or discomfort” in the EQ-

Table 3.—Prevalence of reported problems in the five dimensions of EQ-5D in 8-year-olds with allergic diseases from the BAMSE birth cohort, Sweden ($n = 3236$).

Allergic disease	<i>n</i>	% of children reporting some/a lot of problems in the EQ-5D domains									
		Mobility	<i>p</i>	Self-care	<i>p</i>	Usual activities	<i>p</i>	Pain/ discomfort	<i>p</i>	Anxiety or depression	<i>p</i>
All children	3236	0.2		2.4		1.8		6.4		6.7	
Asthma:											
No	3021	0.2		2.4		1.6		5.5		6.5	.11
Yes	199	1.0	.02	2.5	.90	4.5	<.01	18.2	<.01	9.5	
Rhinitis:											
No	2789*	0.3		2.5		1.7		5.7		6.7	
Yes	425	0.2	.95	1.9	.43	2.35	.36	11.1	<.01	6.8	.99
Eczema:											
No	2648*	0.1		2.2		1.4		4.5		5.8	
Yes	508	0.6	.06	3.3	.14	3.1	<.01	16.0	<.01	11.0	<.01
Food hypersensitivity:											
No	2801*	0.2		2.6		1.8		5.2		6.5	
Yes	417	0.2	.96	1.0	.04	1.4	.58	13.7	<.01	8.0	.32
Any allergic disease:											
No	2134*	0.05		2.4		1.4		3.5		5.8	
Yes	1013	0.6	<.01	2.4	.91	2.4	.04	12.1	<.01	8.7	<.01
One allergic disease	635	0.8		2.7		1.9		10.25		8.7	
≥2 allergic diseases	378	0.3		2.1		3.4		16.45		8.75	

*numbers not adding up to the total of 3236 due to missing data (non-respondents on disease questions, see also table 2).

P-values obtained with two-sample test of proportion.

Table 4.—Determinants of health-related quality of life in asthma: EQ VAS and percentage of reported problems in EQ-5D in 8-year-olds with asthma in the BAMSE birth cohort, Sweden ($n = 199$).

Symptoms and signs during the previous 12 months	N	%	EQ VAS (median and IQR)	% of children reporting some/a lot of problems in the EQ-5D domains				
				Mobility	Self-care	Usual activities	Pain or discomfort	Anxiety or depression
Frequent wheezing^a:								
No	169		95 (89–98)	1.2	3	4.1	16.7	7.1
Yes	30	15.1	85 (68–95)	0	0	6.7	26.7	23.3 ^b
Poor night sleep due to cough or dyspnea:								
No	55		95 (90–99)	0	3.6	3.6	10.9	7.3
Yes	144	72.4	90 (80–98)	1.4	2.1	4.9	21.0	10.4
Impaired daily activities:								
No	86		95 (90–100)	0	3.5	3.5	15.1	5.8
Yes	113	56.8	90 (80–95)	1.8	1.8	5.3	20.5	12.4
Effort-induced wheezing:								
No	81		95 (88–100)	1.2	3.7	3.7	12.5	1.2
Yes	117	59.1	90 (84–97)	0.85	1.7	5.1	22.2	15.4 ^b
Having sought healthcare professional for asthma:								
No	76		92.5 (90–98)	1.3	5.3	3.95	14.5	5.3
Yes	120	61.2	90 (82.5–98)	0.8	0.8	5.0	21.0	12.5
School absenteeism due to asthma or allergy:								
No	116		92.5 (89–98.5)	0.9	3.45	4.3	16.4	7.8
Yes	83	41.7	90 (80–97)	1.2	1.2	4.8	20.7	12.0
PEF $\leq$ 260 L/min								
No	118		92 (85–98)	0	2.5	4.2	16.95	11.9
Yes	53	31	90 (85–95)	0	0	0	21.15	7.55

^a>12 episodes of wheeze in the 12 months prior to questionnaire completion.

^b $p < .01$, two-sample test of proportion.

5D. Frequent wheezing and effort-induced wheezing were associated with high prevalence of problems of “anxiety or depression”.

A major strength of this work relies in the fact that it is population based and has a relatively large study population. In contrast to many previous studies, we had information on multiple allergy manifestations in the same children and were able to study allergic comorbidity. The use of a generic HRQoL instrument allowed us to compare the impact of different allergic diseases on the children’s quality of life. Although we cannot exclude the possibility of parents of children having more severe disease or poorer quality of life being more prone to remain in the study and report on HRQoL, the prevalence of allergic diseases in our study population is similar to that reported in other population-based studies in Scandinavian children (18, 19). Moreover, the EQ VAS in our population was somewhat higher than that of a random sample of 260 8-year-olds in Stockholm County (mean EQ VAS 93) (20), speaking against any major selection of children with more impaired HRQoL into our study. We used a validated HRQoL instrument, but the fact that information about the children’s HRQoL was provided by the parents is a limitation, since previous research on pediatric HRQoL has indicated variable degree of parent–child agreement (21). In their review of 19 studies on HRQoL in children, Upton et al. (21) found differences between parent proxy report and child self-report in 17 (90%) of the studies. However, only two of the reviewed studies reported statistically significant

differences in mean HRQoL scores, and these were in opposite directions. Although parent rating of the child’s HRQoL may not always be a good substitute for the child’s own perception, it is not likely to explain the differences in HRQoL observed in our study.

All the allergic diseases in the study were associated with a significant decrease of the median EQ VAS, showing the detrimental influence of allergies on the children’s general well-being. Allergic rhinitis and food hypersensitivity affected significantly only the “pain or discomfort” item of the EQ-5D, while both eczema and asthma were associated with significant changes in three of the instrument’s five dimensions. Children with eczema reported significantly more problems with “usual activities” and “anxiety/depression”. The psychological impact of eczema is well documented (22) and a recent population-based study showed that German children and adolescents with eczema also experience impairment in physical functioning (23). In asthma, we found significant impact on EQ-5D items related to physical functioning (“mobility” and “usual activities”) which is consistent with previous research (23, 24). Using the generic HRQoL instrument KINDL-R, Matterne et al. reported impaired physical functioning but no impact of newly diagnosed asthma on the children’s total HRQoL. In our study, asthma was associated with the lowest median EQ VAS. A linear decrease in children’s well-being with increasing number of concurrent health problems has previously been reported (25). Our data, as well as the findings of the Matterne et al. (23), support this observation, showing a

linear decrement in HRQoL with increasing number of allergic conditions.

In line with previous reports (26), allergic sensitization was not associated with additional impact on the well-being of asthmatic children in our study. Instead, we found that factors commonly associated with more severe or poorly controlled asthma, such as frequent wheezing, decrease the HRQoL of asthmatic children. Other studies have also reported that increased asthma severity (27) and/or poor asthma control (28) predict impaired HRQoL.

In this study, frequent wheezing and effort-induced wheezing impacted significantly only the emotional domain of EQ-5D, whereas a Finnish study reported that wheezing during the past 12 months affected most areas of HRQoL in asthmatic school children (29).

Nocturnal asthma symptoms were shown to be an independent determinant of HRQoL in a previous study (30). Although highly prevalent in asthmatic children in our study, poor night sleep due to cough or dyspnea had no major impact on any of the EQ-5D items. Moreover, we did not find low PEF to be associated with decreased HRQoL, which is consistent with previous reports on respiratory symptoms exerting a stronger influence on asthmatics' HRQoL than lung function (30).

CONCLUSIONS

The HRQoL of young school-children is impaired by allergic diseases, with asthma exerting the strongest impact on general well-being. The frequency and intensity of asthma symptoms are major determinants of HRQoL in children with asthma, whereas diminished lung function and allergic sensitization are not. This emphasizes the importance of achieving good therapeutic control of symptoms when treating asthma. Clinicians should also be aware of the strong detrimental influence of allergic comorbidities on the HRQoL of children.

DECLARATION OF INTEREST

The authors deny having any financial, consulting, or personal relationship with other people or organizations that could influence the present work.

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